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1. Cell sources (autologous & allogeneic)

1.1. Regenerative and modelling approaches in the cardiovascular field

Cardiovascular diseases (CVD) remain the first cause of death worldwide and are the focus of several research lines. Cardiovascular investigation aims to unravel the pathophysiological mechanisms behind CVD onset, progression and recovery. Thus, cardiac tissue engineering (CTE) is indispensable in order to produce cardiac substitutes that could regenerate the myocardium, as well as cardiac models for specific CVD. CTE is in continuous development and comprises several aspects which will be explained and exemplified during the symposium, such as:

- cell populations with cardiac regenerative purposes
- cardiac differentiation protocols for induced pluripotent stem cells derived cardiomyocytes
- non-cardiac cell populations to take into consideration for disease modelling and CTE
- potential matrices or scaffolds to contain the cells
- biocompatible hydrogels to embed the cells

1.2. Translating perinatal derivatives into effective therapeutics for immune-based diseases

Stem cells hold great promise in the evolving field of regenerative medicine. Over the past two decades, different perinatal tissues have been shown to harbor a vast array of stem cells with therapeutic potential. Perinatal tissues include the amniotic fluid and placenta-derived tissues and fetal annexes, such as the umbilical cord, the amniotic membrane, the chorion, and the maternal decidua. The cells isolated from perinatal tissues and the factors released from these cells are collectively referred to as perinatal derivatives (PnD).

The multidisciplinary knowledge obtained by the main actors of the scientific, clinical, and industrial research has afforded greater clarity about the therapeutic properties of PnD. PnD promote the regeneration of damaged tissues via cell replacement or via paracrine factors able to foster endogenous tissue regeneration. Bioactive mediators secreted by perinatal cells have been shown to modulate the immune response, thus a mechanism, in which cells could tame the magnitude of pro-inflammatory signals and support anti-inflammatory and pro-resolution immune components, thus creating a favorable environment for regenerative signals to stimulate resident cells for tissue regeneration.

To date, clinical trials use PnD to treat a variety of diseases, which includes critical limb-ischemia and hip fracture, with the aim to stimulate angiogenesis to bring oxygenated blood to ischemic tissue, heal damaged muscle, and dampen inflammation, thus supporting tissue regeneration.

This session is aimed at understanding the therapeutic potential of PnD and is based upon work from COST Action SPRINT, supported by COST (European Cooperation in Science and Technology). COST (European Cooperation in Science and Technology; www.cost.eu) is a funding agency for research and innovation networks supported by the Horizon 2020 EU Framework Programme. COST Actions help connect research initiatives across Europe and enable scientists to grow their ideas and boost their research, career and innovation.

1.3. iPSC-based bioengineering for tissue regeneration during aging and disease

Induced pluripotent stem cells (iPSCs) are produced from mature cells by reprogramming to pluripotency. It has been recognized that the process of reprogramming offers an opportunity to remove the marks of cellular aging, to confer a youthful regenerative potential to iPSC progeny, potentially presenting an advantage over adult cell therapies for elderly individuals.

This symposium will focus on the use of human iPSCs in tissue engineering and regenerative medicine (TERM), as they represent a highly promising therapeutic cell source in tissue and organ formation, due to their unlimited self-renewal and ability for differentiation into all lineages. Not only are the human iPSCs increasingly studied as models of human development and for in vitro drug testing, they also represent a valuable source of “rejuvenated” tissue progenitors and tissue components. The symposium will address the scientific advances in

iPSC biology, the potential for resetting the epigenetic clock by reprogramming, and the challenges associated with using iPSCs in TERM, including reproducible and efficient expansion without genomic alteration, differentiation and engineering of stable, mature organoids/tissue structures from iPSCs, as well as safety, costs and scale-up considerations on the path of clinical translation. How can we learn from developmental biology when directing iPSCs towards a specific tissue?

Various applications in TERM are invited for the presentation and discussion, including bioprinting with iPSCs for tissue formation or disease modelling and drug discovery, and the use of iPSCs with novel scaffolds and cultivation systems. Examples from cellular reprogramming, iPSC-derived secretome and tissue components, and the discovery that mature cells can be reprogrammed to pluripotency for 3D bioprinting tissues and organs will be discussed, to elucidate the current state and future directions in this exciting field.

1.4. Cell-based regenerative therapy for joint repair

Osteoarthritis is the most common joint disorder in the world, involving inflammation and joint-wide structural changes that lead to chronic pain and disability. It affects people across a wide age spectrum, from young athletes with injured joints (50% develop osteoarthritis within 5–15 years of injury) to elderly individuals (over 50% have osteoarthritis above 55–80 years of age). There is no cure for osteoarthritis, as all of the currently available treatments only try to reduce symptoms (e.g. relieve pain), but have no effects on slowing disease progression. Stem cell therapies have recently brought new hope for treating osteoarthritis, particularly mesenchymal stem cells due to their ability to secrete beneficial factors that reduce inflammation and induce endogenous tissue repair. A wide range of studies have explored the use of stem cells from different sources (e.g. bone marrow, adipose tissue, synovium), at different dosing concentrations and frequencies, applied to different stages of disease (e.g. directly after joint injury to try and prevent osteoarthritis development, or in established disease to try and stop osteoarthritis progression), and in different types of studies (e.g. preclinical and clinical). Recent exciting developments include pre-conditioning the stem cells (e.g. hypoxia, cytokines, biomaterials) to direct them towards specific functions prior to injection, using the derivatives of stem cells (e.g. their secretome) as therapeutics, and exploring new sources of stem cells (e.g. derived from induced pluripotent stem cells, identifying new chondrocyte progenitor populations). This symposium welcomes all of these topics to give a timely update on the status of this exciting field.

1.5. RNA Therapeutics for Bone Regeneration

Due to life style changes and ageing of our industrialized nations, bone traumatic injuries and osteoporosis induced fragile fracture are an enormous medical and socio-economic challenge. State-of-the-art therapies have failed until now in keeping their promises of reliable bone regenerative solutions.

The development of coding mRNA for the local expression of therapeutic proteins has most recently created encouraging results toward regenerative solutions. mRNA delivery offers many opportunities in regenerative medicine due to their ability to trigger transient and safe production of proteins, which can provoke robust regenerative response. The cmRNAbone H2020 project aims to create a novel bone regenerative therapeutic approach based on combination of chemically modified RNAs (cmRNAs)-vectors embedded in a 3D-printed guiding biomaterial ink tailored to patients need.

1.6. Cell-assembled tissue engineering therapies for tendon repair and regeneration

Tendon injuries are highly prevalent and constitute a major healthcare burden in the orthopaedic sector worldwide. Cell-based therapies for tendon regeneration have emerged utilising nature's engineer to rebuild of the injured / diseased tissues. Of paramount importance though for functional tendon repair and regeneration is to effectively either maintain tendon-derived cells native phenotype or induce tenogenic phenotype to stem cells. Various technologies are at the forefront of scientific research and technological innovation to provide functional therapeutic interventions, including direct stem cell delivery, cell-sheet engineering, magnetotherapy, genetic manipulation, multifunctional biomaterials. This symposium proposes a forum for the discussion of state-of-the-art advancements on scaffolds and scaffold-free strategies applied to tendon tissue engineering and

regenerative medicine, as well as to discuss potential obstacles regarding translation to clinic of such technologies.

1.7. Exogenous vs endogenous cell therapy for IVD regeneration

Low back pain is a particularly common affliction in the 21st century, with 80% of the world population experiencing it at some point in their life. It is now well established that 40% of the chronic LBP cases are related to degeneration of the intervertebral disc (IVD). This complex and multifactorial degenerative process manifests as cell death, , extracellular matrix (ECM) changes and dehydration, inflammation and culminates in failure of the IVD biomechanical properties. Conventional treatments are focused on pain or inflammatory relief, with pharmacological approaches as the first intention, followed by invasive and costly surgical procedures as the last option for treatment of severe cases. To date, there is no disease-modifying treatment available for IVD degeneration and it is believed that biologically inspired regenerative medicine approaches may offer relevant alternatives to surgery.

In this symposium, we aim to explore future advanced therapeutic strategies that could results in radical new treatments of IVD degeneration. Since IVD cell depletion is critical in the degenerative process, the supplementation of IVD with reparative cells has been considered. A variety of potential sources have been explored in the past two decades, and a consensus regarding the ideal cell population for IVD regeneration has not been reached yet. Recently, the discovery of endogenous reparative stem/progenitor cells in the IVD, which could constitute an alternative to the injection of exogenous cells, has led to increased interest in the potential of endogenous repair strategies. These reparative cells could be attracted from the peripheral niches, engraft in the degenerated IVD and restore the tissue homeostasis.

1.8. Immune cells: alternative approach for cell-based tissue regeneration

Cell-based bone regeneration merely relies on the use of autologous (adult) stem cells, either or not following in vitro expansion and osteogenic priming. This cumbersome approach is prone to time-consuming laboratory culture procedures, safety issues, and huge regulatory paths toward clinical translation. Further, a vast amount of recent evidence indicates that cell engraftment is low with no active participation of the cells in bone formation.

From a physiological perspective, the inflammatory response initiated directly upon surgical intervention appears to be pivotal for the final regenerative result. As such, the use of inflammatory and immune cells for tissue regeneration has emerged over the last few years. Interestingly, striking effects of inflammatory/immune cells on (stem) cell responses and tissue regeneration have been reported. Further, such approaches harnessing inflammatory/immune cells for tissue regeneration in many cases can be directly implemented with the standard of care using (synthetic) biomaterials as cell carriers/scaffolds. This would enable intra-operative preparation of cell-based constructs and would limit patient discomfort by reducing the number of hospital visits and reduce regulatory issues owing to construct preparation within the surgical theatre.

This symposium will highlight efforts toward the application of inflammatory/immune cells as alternative cell sources to stem cells to boost tissue regeneration.

1.9. Recent advances in Cell Transplantation and Angiogenesis

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the developed world. Restoring blood supply to ischemic tissues is an essential goal for successful treatment of CVD.

After successful completion of symposium on Cell Therapy and Angiogenesis in TERMIS 2018 global conference, and TERMIS-AP 2019. we would like to have a symposium on “Novel Innovations in Cell Transplantation and Angiogenesis” for TERMIS 2021. The symposium is to ameliorate the knowledge, awareness, and education on cell therapy/transplantation and angiogenesis leading to the discovery therapies which aid to alleviate the human

disease as it is the most significant emerging technology in the eyes of Medical, Biotechnology, Pharmaceuticals and Academia.

1.10. Tissue Regeneration, Senescence and Aging

The regenerative potential of human tissues and organs declines with aging. In view to endogenous stem and progenitor cells, a decrease in cell intrinsic repair capacity as well as regeneration inhibiting extrinsic factors including the systemic and tissue environment have been identified as contributors to this decline.

A phenomenon contributing to both, cell intrinsic and extrinsic regeneration is cellular senescence, which has evolved from a mere in vitro model system to study biological aging to a multifaceted phenomenon of in vivo importance. This is due to findings that senescent cell elimination delays the onset of a variety of age-associated diseases and also improves tissue regeneration.

Recently, senolytic drugs have been developed that specifically eliminate senescent cells or senomorphic/senostatic drugs, which are considered to block the pro-inflammatory and extracellular matrix remodelling activity of the senescence associated secretory phenotype (SASP), which is considered to be a specific culprit of reducing the regenerative capacity of organs and tissues. Recently, not only proteins, but also extracellular vesicles and their cargo of lipids and miRNA have been identified as members of the SASP.

In this symposium we will highlight latest developments in the context of tissue engineering, aging and senescence, and how senescent cells might be targeted in therapeutic strategies or how their secretome can be used as a diagnostic or prognostic tool to identify individuals who would benefit from senolytic drugs.

1.11. Engineering red blood cell membranes for drug delivery

Red blood cells (RBCs) have been extensively studied as a potential therapeutic delivery system for several decades. This research has been prompted by these cells' remarkable properties. RBCs are incredibly tenacious and robust, possessing the high mechanical flexibility needed to flow through the human vasculature for 120 days. Their unusual biconcave shape gives them a high surface-area-to-volume ratio, and the expression of a variety of immunomodulatory markers on the RBC membrane allows for excellent biocompatibility and low immunogenicity. Coupling therapeutics to RBCs has the potential to improve a drug's pharmacokinetics, pharmacodynamics, and immunogenicity. There are two primary approaches to therapeutic loading, either by encapsulation through an osmotic swelling process or conjugation to the RBC membrane with this session being focused on the latter. Several innovative and creative methods have already been developed to decorate RBC membranes with therapeutics in vivo and ex vivo. For example, one approach is to genetically engineer erythroid precursors so that the mature RBC will express the biotherapeutic protein itself. An alternative method is to conjugate the therapeutic to antibodies or polypeptides capable of binding the RBC surface in vivo. Therapeutics have also been chemically engineered to the RBC membrane through the use of synthetic polymers. While significant developments in the field have been achieved, RBC-based drug delivery systems have primarily been confined to the academic lab and are only just beginning to branch into industrial drug development.

2. Biomaterial design & development

2.1. Biomaterials and Immunomodulation

Physiochemical properties of biomaterials determine their fate and ultimate bioavailability. Establishing correlations between biomaterials properties and their physiological response is important for biomedical implants, tissue engineering and nanomedicines. When an artificial biomaterial is exposed to blood or in vivo environment, it may induce inflammation and exacerbate adaptive immune responses. Recent research in the vaccine and immunotherapy fields has revealed that biomaterials have the ability to activate immune pathways, even in the absence of other immune-stimulating signals. These responses are influenced by the physicochemical properties of the material. Meanwhile, studies in anti-inflammation area suggest that some biomaterials will attenuate inflammation by adhere/scavenge pro-inframammary molecular patters, which created a new application for biomaterials and established a different interface between the biomaterial and the physiological environment. To date, the correlations between the fundamental properties of biomaterials and their in vivo inflammation and immune response remains poorly understood. The lack of detailed understanding of biomaterial-immune system interactions, resulting in significant pathological changes in the microenvironment, is a major barrier to developing effective biomaterial-based therapies.

2.2. Biomaterials for Stem Cell Culture and Differentiation for Stem Cell Therapy

There is a shortage of tissues and organs for patients who suffer damage or loss of their tissues and organs. Stem cells hold promise for drug discovery and regenerative medicine. We would like to propose the symposium of "Biomaterials for Stem Cell Culture and Differentiation for Stem Cell Therapy". The development of a fully defined microenvironment for culturing and differentiating human stem cells will have a great effect on the use of stem cells in cell therapy and tissue engineering. In this symposium, we will discuss the design and strategy of biomaterials for stem cell culture and differentiation. Especially, we will discuss biomaterial design and preparation that can not only maintain the pluripotency and stemness of human stem cells, but also guide differentiation of stem cells (adult stem cells, fetal stem cells, human embryonic stem cells and human induced pluripotent stem cells) into specific lineages of cells (osteoblasts, chondrocytes, adipocytes, mesenchymal stem cells (from human pluripotent stem cells), hematopoietic stem cells (from human pluripotent stem cells), retinal pigment epithelium (from human pluripotent stem cells) and cardiomyocytes). We will further focus on the effects of physical cues (elasticity, micropatterning, electrical field and mechanical force), together with the biomaterials used in clinical application using stem cells and the translational development of stem cell therapies in various catastrophic illnesses including COVID-19 infection treated by hematopoietic stem cells.

2.3. Korea-EU combined symposium : Updates on tissue engineering approaches to treat osteoarthritis and degenerative disc disease

Korean Tissue Engineering and Regenerative Medicine Society (KTERMS) have held combined symposium with European partners during TERMIS meetings that were hosted in Europe since 2011. KTERMS is planning to organize a Korea-EU combined symposium also in TERMIS World Congress that will take place in Maastricht in 2021. The broad topic will be on tissue engineering approaches to treat osteoarthritis and degenerative disc disease.

Osteoarthritis (OA) is the most common form of arthritis, affecting millions of people worldwide. Still, regenerative treatment for OA and related articular cartilage disorders still remain challenging. Hyung Joon Cha will talk on new tissue engineering-based strategy to treat OA under the title of "Stem cell-loaded directly injectable adhesive protein-based immiscible condensed liquid for functional therapeutic treatment of osteoarthritis". Degenerative disc disease in spine also affects numerous people after middle age in the same way as OA in joints. Jerome Guicheux will deliver his newest concept on "Stem Cells and biomaterials for the regenerative medicine of intervertebral disc: A paradigm shift in spine surgery".

2.4. Gene Delivery and Therapy in Tissue Engineering

All human diseases have a disease-causing gene, by delivering functional genetic materials to repair the errant genes, the diseases can be treated. The success of gene therapy is largely dependent on the development of gene delivery vector. An optimal gene vector should mediate high gene transfection efficiency while inducing minimal cytotoxicity and immune response. Over 30 years, gene delivery, especially via the nonviral route, has become a powerful and popular research tool for elucidating gene structure and function. The ability to safely and efficiently transfer foreign DNA/RNA into cells is a fundamental goal in biotechnology. For this purpose, polymers are prepared by a combination of numerous functionalities and defined molecular structure. However, current synthetic DNA/RNA delivery systems are versatile and safe, but substantially less efficient than viruses. Indeed, most current systems address only one of the obstacles to DNA or RNA delivery by enhancing DNA/RNA uptake. In fact, the effectiveness of gene expression is also dependent on several additional factors, including the release of intracellular DNA/RNA, stability of DNA/RNA in the cytoplasm, release of the DNA/RNA–vector complex, and the targeting of DNA/RNA to the nucleus. The key issue of this symposium will be a critical discussion concerning the cutting-edge technology on polymer's design and synthesis, functionalization and structural improvements for DNA/RNA delivery in vitro and in vivo. Furthermore, this symposium will also discuss the establishment of efficient and safe gene delivery in vitro/vivo by a number of new techniques and concepts in targeted or controlled delivery of genes.

2.5. Functionalised living materials in cell and tissue engineering

A new generation of materials has been developed over the last few years with highly dynamic properties that recreate the adequate environmental signals found in native extracellular matrix (ECM). These materials are not only highly dynamic but also very responsive to external stimuli to modulate their biophysical properties and biological functionalities, including sustained delivery of proteins upon external stimuli, mechanical properties that change as a function of time and self-healing capacity. These living materials are based either on advanced chemical functionalities (e.g. self-assembling peptides) or, alternatively, through the radical approach of using living cells that have been genetically modified and incorporated as living parts of the material. Particularly exciting are advances in using genetically modified microorganisms to achieve high functionalities, such as light-triggerable expression of adhesive peptides secretion of growth factors.

The symposium will discuss next generation of materials able to provide (stem) cells with dynamic stimuli and so recapitulating these aspects of the ECM. It will allow critical discussions of different approaches to this field, contrasting advantages and pitfalls of different technologies from a broad perspective, including scientific capabilities, applications and regulatory challenges.

2.6. Engineering extracellular matrices: Fabrication methods and applications in Regenerative Therapies

The use of extracellular matrices (ECM) in regenerative therapies approaches has increased in the (past 5 years). The ECMs are the scaffolds that better resemble tissues and organs in terms of structure, composition and biophysical properties. Decellularized ECM (DECM) from organs and tissues are obtained after chemical and/or physical treatments that can affect the mechanical properties and composition. New protocols have been developed to maintain the features of the tissue while removing completely the residing cells. Novel fabrication technologies, such as 3D bioprinting, have also contributed to produce tissue like systems that can be used for physiological and drug screening studies.

Another interesting approach is using cell derived ECM (CDM), as they can be modified in order to mimic specific tissues conditions or diseases to understand better the processes and better help to precision medicine strategies. The use of biomaterials as cell inducing support can help to adjust the molecules produced by each cell type. Thus, different scaffolds with a variety of structures (particles, fibers, scaffolds) together with diverse cell type co-cultures and factors will lead to defined microtissues. CDMs can be used to provide tridimensional features for in vitro assays to evaluate the effect of factors, drugs or physical stimuli. Another application of these ECMs is to produce patient-specific disease models.

This symposium seeks to update the new research in the field of ECM fabrication to be used in regenerative medicine applications, like skin wound healing, cardiac patches or vessel grafts. In addition, its application in the development of disease and physiological models to better understand patient conditions and personalized treatments will be of main interest.

2.7. [Glycoscience in tissue engineering: from glycobiomaterials to glycosignature in regeneration](#)

The expression of glycans in pathological and physiological conditions has a terrific significance and impact for therapeutic and diagnostic purposes. The diversity of glycans in tissues and organs is linked to several parameters that range from the age of individuals to diet and development of pathological conditions. Today the full comprehension of glycan's functional role in tissue homeostasis and development has a dark side not yet deciphered.

There are several examples in which glycans are employed as tissue-specific signatures for diagnostic purposes (cell surface O- and N-glycosylations). Other approaches involve the employment of glycopolymers as scaffold hydrogels or printable polymers with regenerative purposes (ECM proteoglycans and glycosaminoglycan). Today, the role of glycosignature of ECM and the use of glycobiomaterials represent a new frontier to study new regenerative pathways and to induce cell fates and tissue functionality. The topic will show the state of the art on the role of glycans in cell fates and pathologies and the different glycan-based applications for tissue engineering purposes, opening the way to further research data and lines.

2.8. [Instructive materials for biomedical applications](#)

With the aim to develop effective and affordable regenerative therapies for damaged and diseased organs and tissues, an increasing demand exists for materials that are able to actively interact with the biological system to trigger and facilitate regenerative processes in the body. Such instructive biomaterials are designed in such a way that they, in a controlled and adaptive manner, can fulfill tasks of targeted delivery of (bio)molecules and interaction with cells and extracellular matrices. In the past decade, different strategies have been pursued to develop instructive biomaterials. These range from the molecular design of polymers, combinatorial chemistry approaches to develop hybrid materials, micro- and nanoscale surface-structuring methods and a variety of scaffolding techniques.

This symposium will deliver an overview of the state of the art in designing and fabricating instructive biomaterials. The invited speaker will discuss the synthesis and macromolecular architectures with a high degree of structural precision, synergistic properties through multifunctionalization, controlled bridging of length scales from the nanoscale to the macroscopic range and adaptive features that react to their respective nano- or micro-environments. These developments will be discussed in the context of regenerative therapies, with emphasis on neuroregeneration. The keynote lecture will be complemented by lectures selected from the submitted abstracts that deal with development of instructive biomaterials.

2.9. [Injectable Biomaterials for Translational Medicine](#)

The evolution of traditional clinical practice to a minimally invasive and regenerative regime makes injectable biomaterials one of the most promising classes of biomaterials developed to date. Compared to pre-formed biomaterials, injectable ones allow for more precise implantation to deep enclosed anatomical locations and adaption to irregularly shaped lesions, demonstrating great translational potential. Continuously advances in materials science and regenerative medicine engineer injectable biomaterials from structural filler to multifunctional platform with enhanced therapeutic efficiency. Yet integrating disparate functions to design injectable biomaterials satisfying multiple treatment needs in the human body remains a considerable challenge, as does the selection of the appropriate design criteria and fabrication strategy for specific applications. This symposium will discuss recent efforts in injectable biomaterials R&D, including but not limited to design and fabrication considerations in the context of clinical translation, innovative and smart engineering strategies of

injectable biomaterials to meet the demands in regenerative medicine, and reports of emerging products for certain clinical applications.

2.10. [Bioengineering of dynamic-instructive cell microenvironments for enhanced tissue engineering applications](#)

The development of a new generation of materials and systems for Tissue Engineering and Regenerative Medicine (TERM) should include spatio-temporal control of signals (e.g. mechanical, biochemical, topographic/geometrical, or physicochemical stimuli) that will be recognized by cells at different time points to accomplish specific therapeutic functions. Novel materials and systems are being developed to recapitulate the dynamic properties of the extracellular matrix (ECM) that should result in the engineering of microenvironments that are bioinspired to trigger regeneration processes. Micro/nano-technologies, combined with chemical strategies could be used to assemble proteins, cells, soluble factors and supporting biomaterials into multi-scale structures with potential to have clinical impact in tissue repair. This symposium will embrace the bioengineering of 3D microenvironments, and their integration into larger structures using bottom-up methodologies. The state-of-the-art research and discussion in regulation impact of enabling scaffolds on cellular behaviors are encouraged, including, but not limit to: new design and fabrication techniques of scaffolds to induce epithelial and mesenchymal transition for tissue engineering strategies; smart drug release strategies in scaffold design leading controllable exogenous signals release in a responsive and sustainable manner; immunomodulated scaffolds with controlled inflammatory response; smart hydrogel design and application with mechanisms to response to external cellular environment; controlling of degradation profile in scaffolds for tissue turnover.

2.11. [Novel Biomaterials for the Repair of the Intervertebral Disc](#)

The seminar will primarily focus on recent advancements in the development of biomaterials, such as naturally derived or synthetic polymers for intervertebral disc repair; utilising hydrogel-like materials for the repair of the nucleus pulposus or fibre-like materials for the repair of the annulus fibrosus. Future discussions will consider whether composite materials that mimic both biomechanical and biological environments should be considered or whether for clinical approval it is more feasible to engineer single material systems. Finally, the symposium will consider whether tissue engineering or regenerative medicine is more appropriate for disc repair strategies and specifically explore the rationale, benefits and limitations of cell seeding and tissue engineering approaches compared to fabricating self-instructive biomaterial environments whereby in vivo resident cell populations are encouraged to migrate into implanted materials and deposit de novo matrix?

2.12. [Multifunctional surfaces and biomaterial risk assessment in tissue engineering](#)

Incomplete implant-tissue integration and bacterial infection are recognized as major causes of biomaterials failure in clinical settings. To overcome these issues, the development of multifunctional surfaces that simultaneously tune host eukaryotic cell functions while inhibiting bacterial colonization stands out as a promising strategy. However, the interplay and dynamic interactions between eukaryotic cells and bacteria to reach and colonize the biomaterial surface, the so-called “race for the surface”, remain to be well understood.

In addition, another aspect of paramount importance for the application of biomaterials in tissue engineering is risk assessment. Such assessment is particularly complicated as the need for biodegradability and remodelability translates into dynamic systems that can result in the emergence of biological and mechanical risks during the lifetime of the device.

Thus, the aim of this symposium is to bring together leading researchers working in the development of cell instructive and antibacterial surfaces, as well as on their risk assessment. The symposium will cover multifunctional surfaces, with particular attention on innovative approaches using chemical coatings and topographical modifications, and biosensing methods to monitor cell-material interactions. Furthermore, the symposium will also cover macroscale in vitro models, in silico systems, disease models and on-chip organ models for the new biomaterial assessment and personalized medicine.

2.13. Endogenous tissue regeneration: bioactive materials and novel technologies

Ex-situ tissue engineering is handicapped by the need to develop the tissue in a bioreactor where the conditions may not be optimum for cell growth and function maintenance. In addition, the use of allogeneic or xenogeneic cells as well as stem and progenitor cells have their own associated complications such as demanding cell manipulation and immunologic responses.

These limitations make the traditional tissue engineering approach expensive, time consuming and laborious. Moreover, its commercialization is considered limited due to strong regulatory issues as well as complexities of transportation, storage, and scaling-up capability. Altogether makes the traditional tissue engineering approach less accessible and less clinically viable.

The challenges and limitations of traditional tissue engineering have given rise to a new concept known as in situ tissue engineering or endogenous tissue engineering. This new approach provides ready-to-use biodegradable, cell-free constructs that are designed to induce regeneration upon implantation, directly in the functional site. Biomaterials for in endogenous tissue engineering include natural biomaterials, synthetic polymers, bioceramics, and ECM-based materials and are expected to fully occupy the anatomy of the defect site. They need to provide an instructive microenvironment that allows for colonization and remodelling of host cells to achieve an autologous tissue over time. The properties of the scaffold for endogenous tissue engineering may vary depending on the target damaged tissue, but generally they should possess features including physical properties, chemical composition, and biological functions to modulate cell behaviours.

2.14. In situ tissue regeneration: endogenous cell recruitment, bioactive signals, and biomaterial design

The principle of “in situ tissue regeneration” is to take advantage of the body’s own regenerating capacity by using the host’s ability to mobilize endogenous stem cells to the site of injury. For a simple example, when a smart biomaterial scaffold, combining with both biochemical and physical cues, is implanted, these stimulations unlock the body’s own regenerating capacity. In turn, this induces the recruitment of tissue-specific stem/progenitor cells, drives differentiation of these cells into the targeted cell types, and regenerates functional tissues. This session will provide the recent development of strategies for in situ tissue regeneration in terms of mechanism of host cell recruitment, cell sourcing, cellular and molecular roles in cell differentiation, navigational cues, and niche signals, and a tissue-specific smart biomaterial system from the perspective of regenerative medicine and tissue engineering.

This special session will report state-of-the-art research and development of using novel physical, chemical, biological, and/or engineering process; 1) fundamentals of in situ tissue regeneration, 2) endogenous cells sources, 3) biochemical and physical cues, 4) smart biomaterials developments, and 5) tissue-specific applications.

2.15. Electroactive bioinks for biofabrication and tissue regeneration

This symposium plans to discuss the latest contributions to the design, synthesis and optimisation of bioinks for bioprinting, and bioprinted structures. With emphasis on pre-clinical validation for central and peripheral nervous systems and cardiac tissue regeneration. Up to now bioprinting has tended to focus on the technology itself rather than on materials development and therefore there are many technical opportunities to move these printed materials/inks to higher performance levels. Current deposition and fabrication technologies allow researchers to design and build structures with increasingly intricate architectures. However, in achieving this, many concessions are being made regarding the biological aspects of printed materials. Therefore, there is a pressing need for novel engineering approaches to obtain biomimetic inks for electroactive tissue stimulation. The symposium will be dedicated to several significant contributions concerning the development naturally derived bioinks including enzymatic-, ionic-, and photo-crosslinking, reinforcement strategies and conductivity. Aspects of materials selection, design and printing parameters will be discussed in terms of

structure/property/printing relationships in order to produce mimetic bioprinted structures with higher spatial resolution. In addition, we provide future perspectives on in vivo bioprinting, patient-specificity and storage requirements, as well as a vision for clinical scale-up will be also presented and discussed in terms of utilising imaging techniques (e.g. MRI) etc. The symposium proposers are committed to the development of early career researchers (ECRs) and therefore two slots will be dedicated to ECRs whilst ensuring gender balance.

2.16. [Advances in natural and bioinspired hydrogels for regenerative medicine](#)

It is today increasingly accepted that biomimetics is a leading concept towards the development of advanced materials and technologies in the field of regenerative medicine. In fact, there is increasing evidence that the use of biomedical devices showing substantial mimicry of the composition and multi-scale structure of target native tissues have enhanced regenerative ability. In this respect, the adoption of nature-inspired processes and structures is an emerging fabrication concept, uniquely able to provide biomaterials with superior biological performance. Therefore, bioinspired and biomimetic approaches, in combination with nanotechnology, are emerging as a new strategy capable of overcoming disadvantages of molecular therapeutics and amplifying their biological activities. More recently, advances in the development of naturally derived and bioinspired hydrogels, coupled with technological progress in additive manufacturing techniques, including laser-based stereolithography (SLA), digital light projection-based stereolithography (DLP) and two-photon polymerization (2PP), has led to new utility of hydrogels for regenerative medicine applications.

This symposium will aim to provide an overview on recent progress in biomaterials science alongside advances in processing techniques (from cryogelation and porogen leaching to bioprinting and additive manufacturing) to develop biologically derived and bio-inspired materials that have led to technology-driven (clinical) applications.

2.17. [Supramolecular biomaterials](#)

The cell, and its environment, is made up of complex systems of dynamic and responsive macromolecules and materials. Many of the functions of around a cell are a direct result of transient non-covalent supramolecular interactions. As biomaterials science progresses, we now are able to effectively harness and recreate functional, responsive, and sometimes life-like materials using these same supramolecular strategies.

This symposium will feature the recent progress of using supramolecular materials to effect strategies for regenerative medicine. Led by keynote speaker Prof. Patricia Dankers, an expert in the translation of supramolecular materials into functional systems for regenerative medicine, this symposium will feature groundbreaking submissions in this growing research area. This symposium will cover areas from fundamental materials function, to concrete applications of supramolecular materials in vivo. Focus and preference will be given to the more innovative solutions and strategies generated in the past few years.

This symposium will focus mostly on the creation of designed supramolecular systems to address needs in regenerative medicine. At least one highly fundamental talk, and one highly translation focused talk is desired. This symposium will incorporate all career stages and maintain gender balance in its selected speakers.

2.18. [Smart-materials for tissue engineering under external stimulus](#)

Tissue engineering requires the development of physiologically relevant cell microenvironments to drive cell lineage commitment and functional tissue formation. Scientific research has traditionally been focused on the exploitation of biochemical signals such as growth factors, media supplements, etc., or on physical cues such as topography, material mechanical properties, etc., in the case of scaffold-based cell therapies, to promote cell commitment to specific phenotypes. However, these are generally not sufficient to fully mimic or provide cells with an optimal microenvironment where they can differentiate towards specific and well-defined phenotypes. To this end, scientist have recently started to investigate the potential of other stimuli such as electrical, acoustic, mechanical (external dynamic loading) or vibrational, that can be applied externally and enhance cell differentiation and tissue formation. This symposium will discuss the state-of-the-art and future directions of key external cell stimulation strategies (vibrational, electrical, acoustic, mechanical, etc.), biomaterials and devices

developed to this end, and the impact of these onto cell differentiation and tissue formation. The symposium will also discuss the potential clinical translation and commercialization of these novel strategies.

2.19. Targeted delivery using medical devices in regenerative medicine

An important factor in clinical translation of regenerative medicine is an effective localized delivery system for both cell based therapies and direct drug delivery. Poor retention of stem cells or small molecules is a major issue with systemic administration. Multi-modal drug delivery systems comprised of different biomaterials like hydrogels and polymer-based scaffolds may represent a solution to this problem. Studies have shown better retention rates of stem cells when encapsulated and delivered using such systems, for example, localized stem cell delivery to infarcted heart. However, minimally invasive delivery of biomaterials require specialized biocompatible catheters and medical devices. Furthermore, multiple dosing is sometimes required which warrant multiple surgical/catheterization procedures. This clinical need led to the development of in-situ devices to replenish the therapeutic agents. Tissue-engineered biomaterials coupled with a minimally invasive delivery system could contribute in structural improvement and function of repaired organs and hence may provide revolutionary therapeutic opportunities.

2.20. What about the bacteria?

Within tissue engineering, the development of implantable biomaterials and scaffolds has mainly focused on promoting cell homing, attachment and integration into the host tissues. Nevertheless, if it was possible to directly translate these biomaterials into the clinics, their implantation would not be in completely sterile conditions since a surprisingly high number of bacteria are present in the standard operating theaters. Furthermore, the material properties that favor cell attachment also tend to provide an excellent environment for bacterial adhesion and biofilm formation, the main culprits of bacterial-induced infections. Currently, there is a relatively constant infection rate for different biomaterials and medical devices (5-15% get infections that require treatment). The typical strategy to suppress and eradicate the pathogenic bacteria is the combination of debridement strategies (if possible due to the complex surface geometry) and adjunctive systemic administration of antibiotics, despite to the alarming rise in antibiotic resistance and the lack of strong supporting scientific evidence for its efficacy.

In the context of TERM researchers there is an undeniable and urgent need to create awareness and improve the understanding of biomaterial-associated infections since the outcomes of regenerative therapies can be jeopardised by recurrent bacterial infection. Furthermore, the role of immune response and inflammation, which are both key players in the regenerative pathways, are directly related to these.

In this symposium, an overview of biomaterial-associated infections will be provided by the Keynote speaker Prof. Rikke L. Meyer (Denmark). We will welcome presentations from the following topics (not limited to): 1) innovative cell-friendly and anti-infective biomaterials, 2) tissue (engineered) models to test biomaterial-associated infections, and 3) inflammation and immune response related to biomaterial-associated infections.

2.21. 20 years in silk technologies from production, clinical translation, to commercialization

Please note that this is a merged symposium and the final description will be available soon.

2.22. Bio-inspired technologies for Peripheral Nerve Repair

Repair and regeneration of injured peripheral nerves is critical and challenging. Around the world, more than one million patients suffer peripheral nerve injuries annually, most of whom are affected with life-long disabilities due to the lack of effective therapeutic measures. Thus, there is a great need for developing new and innovative therapies mirroring the bio-inspired features in order to improve the quality of patient's life. This symposium will cover the innovative technologies for peripheral nerve repair, combining the current knowledge and past achievements. A variety of the nerve guidance conduits typically used in the field will be presented – from natural

and synthetic biomaterials to decellularised matrices – including their use as platforms for cell, drug and gene delivery. A particular emphasis will be placed on the translation of promising therapies into the clinical setting.

3. Biofabrication

3.1. Disruptive biofabrication techniques, materials and strategies for application in TE&RM

As the field of biofabrication progresses, it is essential to develop innovative ways to enhance our capacity of recreating the complexity and functionality of native tissues. Nature-inspired 3D printing offers an opportunity to engineer these biological structures with increasing precision. However, innovative approaches that either improve current or develop novel biofabrication techniques are required to make the necessary step-change that would truly make biofabrication a revolutionary strategy with broad impact in tissue engineering and regenerative medicine. This symposium will be dedicated to innovative approaches that are pushing the boundaries of biofabrication to create more complex and functional structures. Key areas of development in biofabrication such as bioinks, fabrication processes, fabrication techniques, and resulting functional structures will be covered by a world-leading panel of experts in the field.

3.2. Melt Electrowriting

This symposium will focus on an emerging additive manufacturing technology, melt electrowriting (MEW) which permits the design of advanced complex biomedical materials with micro-scale features. The use of electrohydrodynamic phenomenon provides a new class of manufacturing scaffolds for tissue engineering or biofabrication. This electrohydrodynamic phenomenon allows MEW to alter the diameter on demand and provides another set of design variables, as well as multiple options for biomechanically designing scaffolds and implants. MEW is a technology that builds on many decades of melt processing for medical devices from the regulatory perspective. The benefit for the biomaterials and TERM community is a robust, reproducible and low-cost manufacturing technology that we predict will become a major additive manufacturing technology by 2025.

3.3. Smart biomaterials and dynamic biofabrication processes powered by light

In the quest to capture the complex environment of living tissues within lab-made systems, light emerged as a uniquely powerful stimulus for enabling dynamic and spatio-temporal control over cell and biomaterial properties. Merging knowledge from photochemical biological processes, recent advances in light-sensitive proteins, optogenetics, and photopolymers, innovative approaches to design biomaterials and 3D constructs are opening new avenues in regenerative medicine and tissue engineering.

Light-responsive moieties permit to non-invasively trigger mechanical actuation and shape-changes in cell-laden constructs, to modulate stiffening or softening of the extracellular milieu, as well as to provide spatio-temporal control over drug and growth factor release. Moreover, photocrosslinkable and light-sensitive hydrogels are becoming more relevant for tissue culture and as bioinks for bioprinting. Cell-laden building blocks can be sculpted with unprecedented degrees of geometrical freedom into high resolution architectures, via stereolithography, volumetric tomographic bioprinting and multiphoton bioprinting. This symposium offers a forum to discuss i) novel photoresponsive systems (molecules and initiators) and biomaterials, ii) the impact of light stimuli on cell response (including tissue functions beyond viability), as well as iii) the integration of such discoveries in light-based biofabrication and 3D printing technologies, to obtain highly biomimetic constructs. The symposium will encourage discussion on smart regenerative grafts that can be modulated in situ, and advanced in vitro models that can be remotely stimulated to capture more closely their native counterparts, with potential applications in drug discovery.

To cover the multidisciplinary impact of this field within the TERM community, the symposium will start with two invited talks, focusing on novel light-responsive biomaterials with spatio-temporal tunable properties (Dr. Cole DeForest, USA), and on light as tool for high-resolution bioprinting of tissues, in which chemico-spatial features can be modulated post-printing (Prof. Aleks Ovsianikov, Austria). The program will be completed by podium presentations selected from abstracts submitted to the conference.

3.4. [Microfluidic Biofabrication: a hybrid platform for the printing of functional hierarchical tissues](#)

Biofabrication is advancing apace, now capable of building hierarchical and complex physiological tissue substitutes for the clinically relevant repair of damaged or disease tissues. The ability to deposit multiple materials and cells in a single printing process is now becoming paramount for the fabrication of functional constructs for tissue engineering and regenerative medicine (TERM) purposes. Accordingly, most of the biofabrication systems available on the market have evolved and now enable the fabrication of heterogeneous constructs through the combined use of multiple printheads. Despite being effective, these systems suffer from major issues such as longer printing time and relatively low resolution.

Recently, a new biofabrication strategy based on the use of microfluidic printing heads has come to the fore enabling the single-step manufacturing of heterogeneous multi-materials and/or multi-cellular constructs able to closely mimic specific tissue functionality. To date, the use of custom microfluidic printheads has allowed the spatial patterning of growth factors, materials and cell components, which have greatly contributed to the manufacturing of clinically relevant implants. This is an emerging field with unbounded potential for advanced hierarchical construct design and this symposium entitled "Microfluidic Biofabrication: a hybrid platform for the printing of functional hierarchical tissues" will report the current advancements highlighting new opportunities for TERM applications.

3.5. [Scaffold-free strategy for tissue engineering](#)

Cell-based tissue engineering has been widely investigated to treat patients as an alternative strategy over conventional chemical or biological drugs. A common approach involves implantation of in vitro cultured cells on or in biodegradable materials, including porous sponges, hydrogels and other 3D structured scaffolds. However, these materials can potentially induce inflammatory responses and may not provide appropriate instructive signals for cell survival. In contrast, cell aggregates, in which cells are assembled as spheroids or sheet under in vitro culture environment, have attracted a great deal of attention as they do not suffer from the aforementioned scaffold-based issues. In particular, cell aggregates exhibit improved regenerative potentials and survival upon their transplantation to tissue defects, representing functional and therapeutic modules for scaffold-free tissue regeneration. In this symposium, the latest exciting research in scaffold-free tissue engineering will be discussed by bringing together leading experts in the field.

3.6. [Clinical applications of the Kenzan method](#)

In this symposium, we will introduce our original biofabrication system called ""Kenzan method"" including the first clinical results of blood vessel regeneration done in Saga university hospital, and other pipelines which are getting closer to clinical application.

3.7. [Bioprinting and bioassembly as means for automated realization of 3D tissue constructs](#)

This symposium is dedicated to the latest innovations in the field of biofabrication and addresses its clinical aspects with regard to tissue engineering and regenerative medicine. We would like to propose to hold a double-symposium in order to cover the wide variety of the relevant topics in this popular field of research. We envision two sessions in the same day, one in the morning and one in the afternoon. For each session, we envision two invited speakers, always including one clinician reporting on their most recent works. From our experience with previous TERMIS conferences, only a double-symposium will allow us to accommodate an increasing number of submitted abstracts matching this theme. The first part of the symposium is dedicated to bioprinting and bioassembly as means for automated realization of 3D tissue constructs. It includes a keynote talk by Prof. James Yoo from (WFIRM, USA) and Dr Yan Yan Shery Huang (University of Cambridge, UK). The second part of this double-symposium is dedicated vascularization and the recent breakthroughs enabled by biofabrication. It features a keynote talk by Prof. Koichi Nakayama (Saga University, Japan) and Prof. John Slater (University of Delaware, USA). We aim then to select the most innovative approaches from the submitted abstracts targeting various tissue applications, for which this exciting strategy shows a viable route for functional regeneration.

Since the TERMIS World online system only allows to submit regular format symposia, the two parts are submitted separately. For the same reason the second speaker in each session is only mentioned in the description.

The proposed symposium is endorsed by the International Society for Biofabrication (ISBF) and is in accordance with the TERMIS Thematic Group Biofabrication.

3.8. Biofabrication of (multiscale) vasculature and vascularized organs and tissues

To date, engineering a functional vascular network remains the bottleneck in engineering tissues and organs, as it controls proper tissue engraftment and survival after implantation in vivo, and facilitates the physiological response when the tissue is used for in vitro screening purposes. Vascular networks are multiscale complex entities and include multiple components, such as endothelial cells, pericytes, smooth muscle cells, and extracellular matrix. They also present a high level of organization, such as venules, capillaries, and arterioles. Reproducing this complexity within engineered tissues is important to facilitate proper vascular function, and requires cutting-edge biofabrication technologies. Biofabrication is a field of research that has experienced rapid growth in the tissue engineering sector within the past years, leading to several breakthroughs in the field of tissue engineering and regenerative medicine applications. Compared to previous traditional fabrication methods, 3D biofabrication offers unprecedented ability to bioprint constructs with precise control over their composition and spatial distribution, producing biomimetic tissue architecture and properties. Major advances in this area include the development of high-throughput and high-resolution bioprinting technologies that can print an engineered vasculature as part of a thick tissue engineered construct, as well as novel bioinks that can induce neovascularization in surrounding tissues and encourage integration with the host vasculature. This symposium intertwines with multiple tracks and application areas for neovascularization of tissues and organs, including: i) Biofabrication (e.g. bioinks, bioprinting, bioassembly), ii) Biomaterial design & development (e.g. hydrogels, natural polymers, responsive biomaterials), iii) Process engineering (e.g. automation, manufacturing, robotics), iv) Preclinical models (e.g. tissue models, animal models). This symposium is endorsed by the International Society for Biofabrication.

3.9. Osteochondral defects: engineering the cell-matrix interface with additive manufacturing. The AO Collaborative Research Program.

Osteochondral defects are still a major clinical challenge. They represent a large societal burden as they limit employment and impede daily life activities of millions of people. These injuries often lead to further degeneration of the joint, into disabling osteoarthritis. The defect bridges two types of tissue (cartilage and bone) with internal zonal structures and specific healing capacities. The challenge of healing osteochondral defects has been tackled with multilayered materials combined with cell-therapy; however, the effectiveness of such approaches is still lacking universal consensus and clinical validation, given the lack of systemic studies. Additionally, the cartilaginous surface must follow the patient specific contour of the surrounding tissue to avoid early failure and arthritic changes.

Within this consortium started in June 2017, the AO has brought together multidisciplinary expertise in materials, cell niche, bioprinting, bioreactors, biomechanics, immune response and preclinical models. Additive manufacturing was adopted as common platform to produce constructs with precisely controlled internal architecture, chemical and biological properties, with a patient-specific approach. Towards the understanding of cellular microenvironments, metabolic labeling techniques were developed to visualize newly secreted extracellular matrix components and to probe how this nascent matrix influences cell function, such as during chondrogenesis or when exploring questions related to cellular mechanosensing in 3D. In addition, engineered hydrogel platforms have been designed as in vitro models of tissue repair and for the assessment of 3D printed constructs on macrophage behavior.

Interdisciplinary and international collaborations are needed to bring diverse ideas and technologies to bear. In this Symposium, we will describe the outcome of multidisciplinary, multinational consortium with complementary expertise as a collaborative research project of the AO Foundation.

3.10. Image-based High-resolution Biofabrication

Most biological tissues such as bone and liver have a highly sophisticated internal architecture across several length scales. Recapitulating the structural and functional complexity in biological tissues requires the development of high-resolution biofabrication techniques that faithfully recreate tissue architecture down to the subcellular level. One promising approach is to combine computer models derived from biomedical imaging data such as computed tomography (CT) with light-based additive manufacturing (AM) techniques. Using light as the stimulus, photopolymer solutions can be locally deposited and solidified through extrusion-based bioprinting or stereolithographic patterning in accordance with CT data. Despite significant progress, AM techniques relying on a layer-by-layer process suffer from low printing velocity, lengthy fabrication process, and poor cell-compatibility.

In this symposium, we seek to highlight a few examples of enabling image-based high-resolution biofabrication techniques with a focus on 1) high-resolution tomographic volumetric AM and 2) image-based biomimetic 3D laser microprinting. In the Keynote, Professor Christophe Moser will introduce the fundamentals and principles of tomographic volumetric AM and highlight the potential of this technique for tissue engineering applications. Other talks will present recent efforts in developing image-based biomimetic CAD models down to subcellular level, the design of cell-compatible photopolymers and their applications in creating 3D microprinted in vitro models using nanoscale two-photon photolithography. Additional talks on “Image-based High-resolution Biofabrication” will be selected from the submitted conference abstracts with a focus on unpublished data and the significance of these contributions.

Altogether, the proposed symposium aims to highlight the most important progress and challenges in “Image-based High-resolution Biofabrication” and point out new directions for future developments towards creating complex functional tissues.

3.11. Biofabrication and Stem Cell Research in Space

Worldwide interest in space exploration is increasing which has led to a return to human spaceflight in the United States and other countries, along with numerous new expeditions for further exploration missions, including landing the first woman and next man on the Moon in this decade, construction of a Lunar Gateway by international partners, and future missions to Mars. In addition, access to space is becoming increasingly routine with launch vehicles provided by private companies. In addition to the benefits to life on Earth that research in microgravity can provide, better understanding of behavior of cells, stem cells and tissues under microgravity and space conditions is important for long-duration space missions. Biofabrication is believed to play an important role as it can be used to generate complex three-dimensional tissue models and organoids from cells and stem cells that can be used to study the effects of microgravity and space radiation better in comparison to conventional two-dimensional cell cultures. The keynote lectures will provide insights from teams who have conducted research on the ISS using three-dimensional human iPSC brain organoid models to study neurodevelopmental biology and the recently announced NASA public-private partnership initiative with the UC San Diego Health/Sanford Consortium for Regenerative Medicine team related to the development of an Integrated Space Stem Cell Orbital Research (ISSCOR) Laboratory along with recent experiments on magnetic levitation, using the Russian Organ.Aut bioassembler developed by 3D Bioprinting Solutions. The session will give an overview of state-of-the-art technology and discuss future opportunities for both biofabrication and stem cell research under microgravity conditions in space.

3.12. Embedded Approaches for Advanced Biofabrication

This symposium will focus on the growth of Freeform Reversible Embedding of Suspended Hydrogels (FRESH) 3D bioprinting and related embedded 3D bioprinting approaches as a platform for advanced tissue and organ

engineering. Embedded printing has emerged as a versatile approach that eliminates the effects of gravity by extruding hydrogels and cells within a yield-stress support bath, often composed of microparticles. This has greatly expanded the range of bioinks that can be used and the structural complexity of scaffolds that can be achieved. First published in 2015, the past 5 years has seen an exponential growth in the number of research labs that have successfully used FRESH and related embedded printing approaches in their research. Recent advances include rapid fabrication of vascularized tissue constructs, functional collagen heart valves and beating ventricles. A Keynote by Prof Brenda Ogle from the University of Minnesota on FRESH 3D bioprinted human ventricle-like constructs will highlight the latest advances in organ-scale engineering.

3.13. [Medical electrospinning: art of science?](#)

Electrospinning is a highly versatile and tuneable fabrication technique to produce fibrous scaffolds that mimic the extra-cellular matrix of biological tissues. There is an extensive range of natural and synthetic polymers (and combinations thereof) that can be used and allow to tune the scaffold to specific biological and medical needs. Controlling all the parameters, which create the base of this method's versatility, has proven to be a challenge, leading to a lot of inconsistencies and batch to batch variability. To produce reproducible scaffolds for medical applications, all environmental parameters need to be controlled by climate-controlled electrospinning devices. Even if precise and reproducible scaffolds can be manufactured, the question remains what mechanical, structural and biological properties a scaffold should have for a specific medical application. Biological tissues vary considerably, including mineralised bone, non-vascularised cartilage, elastic skin, highly organised functional structures like the liver, contractile smooth muscle organs in cardiovascular tissues and uterus, dense basal membranes, and mechanical tensile elements like ligaments and tendons. Each tissue type has its own repair kinetics which can be controlled by providing the right biomaterial with specific mechanical and architectural properties. On top of that, there is a variety of cell types, roughly divided into epithelial cells, nerve cells, muscle cells, connective tissue cells and stem cells. Each of these have subtypes with specific properties in terms of attachment, migration, proliferation, differentiation and matrix production.

The question addressed in this symposium is how to design a scaffold that will fulfil its prospective functionalities in clinical tissue engineering and regeneration. Is there science behind the design, or should we accept that medical electrospinning is an art that proceeds by trial and error?

3.14. [When biofabrication meets bioreactors: implementing construct maturation and functional tissue culture](#)

Advancements in manufacturing techniques allow the biofabrication of tissues to promote their applications as in vitro disease models or tissue surrogates. Biofabrication techniques allow increasing precision and control over the spatial positioning of both cells and embedding biomaterials, to better replicate the architecture of human tissues. The development of functional models with certain levels of tissue maturation however requires the design of culture protocols able to provide the optimal combination of biochemical and biophysical stimuli to the biofabricated constructs. Bioreactors and advanced cell culture devices are systems that can be adapted to the specific tissue requirements and offer the possibility to culture the biofabricated constructs in a strictly controlled environment promoting their proper maturation to achieve adequate tissue metabolic and structural functions.

This symposium promotes the integration of approaches for the survival and differentiation of fabricated constructs by addressing all those methodologies developed to achieve a proper transition from basic cell aggregates into mature functional tissues. The main purpose is to focus on the importance of optimizing and streamlining the maturation phase as a necessary step for the development of functional tissues. In consideration of the strong relationship between tissue fabrication and maturation, the aim will be highlighting the different solutions that can be implemented, either simultaneously or after the biofabrication step, to achieve integrated solutions for the whole tissue biofabrication process.

The symposium welcomes submissions from the broad biofabrication community (e.g. bioprinting, bioassembly, 3D printing, additive manufacturing) which involve the application of parallel and post- fabrication approaches for tissue culture, tissue physico-chemical stimulation or the design of multiscale culture devices. It also

encourages submissions from all those techniques that add to the pure fabrication step a maturation phase showing significant integration possibilities over traditional cultures.

3.15. [Sound patterns as a novel biofabrication platform](#)

Morphogenesis, a complex process, ubiquitous in developmental biology, regenerative medicine, and many pathologies, is based on self-patterning of cells. Spatial patterns of cells, organoids, or inorganic particles can be forced on-demand using acoustic field-based assembly processes.

In this symposium, we will present a novel class of emerging biofabrication technologies based on acoustic manipulation, enabling cell assembly and patterning, which aims at overcoming the main limitations of existing bioprinting approaches.

Acoustic patterning of cells in biomaterials is contactless. It allows tuning of parameters (such as sound frequency, amplitude, chamber shape) under fast and mild culture conditions, for morphologically relevant tissue generation.

The symposium welcomes submissions from the broad biofabrication community intending to develop the next generation of biofabrication process powered by acoustic patterning capable of creating functional tissues at a physiological relevant scale and in a time-effective manner. It also encourages submissions from all those interested in a) the hybridization of cutting-edge acoustic cell patterning with additive manufacturing technologies, b) rapid fabrication of large and functional tissues, c) the use of acoustic stimulation to trigger tissue maturation.

3.16. [Toward a model-based control of biohybrid implant maturation - MoReBioMed / DFG PAK 961 patterns as a novel biofabrication platform](#)

Known design approaches for the fabrication of biohybrid implants do not specifically consider the individual dynamics of the cellular component, so that only a few implant concepts have so far made their way into clinical use. As a prerequisite for individualized production, a deeper understanding of the biological maturation processes of the cell-based biohybrid implant is required, which can be understood as a complex adaptive system. It is therefore the aim of the project to create a maturation model of biohybrid implants using the heart valve as an example. Building on this, a model-based control system is to be developed that allows implant maturation in a bioreactor matched to the individual dynamics of the cellular components of biohybrid implants.

4. Mechanisms of action

4.1. Developmentally inspired therapies for joint diseases and large bone defects

Bone, cartilage and joint regeneration using biomaterials and stem cells are expected to have a significant impact in the treatment of injury and diseases. Hundreds of millions of people worldwide are suffering from cartilage pathologies, and 5-10% of all bone defect cases require intervention to heal. There is, therefore, an urgent need for new therapeutic solutions, leaving the TERM community with this challenging question: can we do any better than contemporary autografting, pain relief and prostheses?

This symposium will focus on state-of-the-art strategies for the treatment of joint diseases and bone defects, with a special emphasis on tissue development as a source of inspiration. Cartilage and bone are tissues that are closely linked to each other, both on the anatomical and developmental levels. Thus, naturally occurring processes that involve both tissue types, such as the endochondral bone formation, are of particular interest to better understand how to steer essential cellular decisions from an engineering perspective.

After revisiting developmental and embryological processes, this symposium will discuss progress in cellular engineering, biomaterial design and biologics delivery, for the treatment of joint diseases and large bone defects. Cutting-edge techniques, including decellularization, biofabrication and bioprinting will be discussed, as new tools to engineer endochondral bone and cartilage. Finally, the combined challenges of bone and cartilage regeneration, and their integration in joint regenerative medicine will be featured.

4.2. Immunomodulation to enhance bone healing

Treatment of large bone defects due to trauma, cancer, infection and developmental disorders remains a difficult clinical problem. Bone healing is a finely tuned sequence of processes, which result in fully regenerated and functional bone. There is a growing realization that the inflammatory cells, the cytokines they secrete, and the timing of inflammatory cascades are essential in initiating healing processes such as revascularization and matrix formation. Recently it was proven that both the innate and adaptive immunity are important for collagen deposition and thus the resulting bone quality. Furthermore, the interaction with the immune system in allogeneic cell based therapies is of increasing relevance. Biomaterials play a pivotal role in the treatment of large bone defects. However, most biomaterials only act as bone replacements, failing to induce bone regeneration, suggesting improvements should be made on the design and development of these materials. Biomaterials have been found to affect the local immune response, some of which trigger on-going inflammation inducing fibrous tissue formation. The cross talk between material and immune system—termed as “material biology”, should be considered as a vital component in material design. The aim of this symposium is to discuss the impact of immune cells on bone healing, encompassing the latest advances regarding the regulatory effects of biomaterials on the immune response, and this material-directed immunomodulation on bone regeneration. Understanding the immune cell interactions in the host with tissue engineered bone-forming constructs or biomaterials, may lead to the identification of novel therapeutic targets. This symposium aims to discuss the role of cells of both the innate and adaptive immune system as regulators of musculoskeletal tissue repair and regeneration. Knowledge of these processes will enable harnessing the immune system to influence bone-forming processes and ultimately to develop new therapeutic approaches using immunomodulation to enhance bone healing.

4.3. To Scaffold or not to Scaffold? Strategies for the realization of biomimetic neuronal microenvironments

The realization of biomimetic neuronal microenvironments assumes nowadays a crucial relevance for the development of tissue engineering and in-vitro drug screening strategies. This is particularly true for neurodegenerative disorders such as stroke, spinal cord injury, Alzheimer’s and Parkinson’s diseases. The creation of neuronal microenvironments involves a plethora of research fields ranging from cell biology to biochemistry, neurosciences, physics, nanotechnology, microfluidics, mechanobiology. In the last two decades, this multi-disciplinary activity led to the blooming of numerous approaches aiming at creating architectures able to mimic the topological, biochemical and mechanical properties of the extracellular matrix present in the central and peripheral nervous system. This symposium will be focused on the two main strategies which are explored nowadays: scaffold-based and scaffold-free.

Scaffold-based approaches rely on top-down or bottom-up fabrication of 3D/4D biomaterial architectures. Biomaterials from natural sources show a very good biological response but often lack reproducibility and it is difficult to define or have control over their components. In contrast, synthetic materials are well defined, allow to tune multiple parameters but often they are not as much biocompatible as natural ones. Both synthetic and native materials offered useful insights into how neural systems respond to different biomaterials.

Scaffold-free approaches on the other hand include a family of cellular self-assembly techniques that lead to the formation of spheroids/organoids (i.e. multicellular 3D tissue-like architectures). Neuro-spheroids have been shown to exhibit improved biological properties with regard to regenerative capacity, since they facilitate intense cell–cell interactions. In brain-organoids, stem cells self-organize through cell sorting and spatially defined differentiation to resemble organ cell types, structures and functions, and need a matrix for their generation and organization.

The symposium will be also open to hybrid approaches targeting an optimal synergy between the advantages of scaffold-free and scaffold-based techniques for the realization of truly biomimetic neuronal microenvironments.

4.4. [Harnessing the Extracellular Matrix for driving tissue repair](#)

This symposium will explore the role of the extracellular matrix (ECM) as a biochemical and biomechanical driver of tissue repair processes. The ECM is emerging as an important, if not the most important, element in the cellular microenvironment that determines the outcome of a cell. The composition of this highly complex and organized arrangement of structural fibrous proteins and globular, growth factor binding glycoproteins is intricately regulated. Disruption of this regulation leads to adverse events such as fibrosis or cancer. In thinking about repairing tissue it is imperative to consider the role of the ECM in regenerating the healthy microenvironment. Without the correct ECM composition, the native tissue structure and function cannot be achieved.

This multidisciplinary symposium will focus on the ECM as a central element in therapeutic strategies for advancing tissue engineering, and address questions like: How can the native tissue ECM be recapitulated, using decellularized ECM scaffolds and hydrogels as tools for enhancing vascularization and cellular functioning in therapeutic implants? How does the ECM enhance survival of stem / stromal cells and programs cells for appropriate differentiation in organ specific lineage? How is the use of native ECM hydrogels providing novel 3D model systems for better understanding disease processes?

4.5. [Harnessing the host response for materials-driven in situ tissue regeneration](#)

Materials-driven regeneration relies on the use of resorbable materials that are engineered to boost the body's natural regenerative capacity to regenerate damaged tissues directly in situ. By avoiding costly and lengthy in vitro procedures, this strategy is attractive for clinical translation. The immune system plays a commanding role in tissue regeneration. The fate and regenerative potential of an implanted material is predominantly dependent on the host's immunological response to the implant. Immune cells, such as macrophages and helper T cells, dictate both the deposition and remodelling of extracellular matrix in close cross-talk with tissue-forming cells (e.g. (myo)fibroblasts, mesenchymal stromal cells), and drive the degradation of biomaterials by secreting reactive oxygen species and enzymes. This recognition has led to the development of immunomodulatory biomaterials for a wide range of clinical applications. They are engineered to steer the host response to harness the evoked inflammatory response and promote the regeneration of functional tissue in situ. Immunomodulation is dependent on the local biochemical and biomechanical microenvironment imposed, on the one hand, by the biomaterial (e.g. microstructure, biofunctionalization), and on the other hand, by the body itself (e.g. mechanical loads, inflammatory environment). While proof-of-concept studies highlight the potential of such inflammation-centered materials-driven regeneration approaches, these strategies rely heavily on the intrinsic regenerative capacity and –related to that- the immunological condition of the patient. Patient-specific factors, such as age, sex and systemic comorbidities (e.g. diabetes and obesity) have a profound effect on the inflammatory response to an implanted biomaterial, and, therefore, the long-term outcome. This symposium

will discuss the potential of immunomodulatory materials for materials-driven in situ tissue regeneration, and will explore the potential need and opportunities for employing a personalized approach therein in the pursuit of developing robust clinical treatments.

What we wanted to propose was a number of speakers that we could invite as a second keynote speaker. We've chosen those as their research fits well with the one proposed topic of the symposium. By providing a list of potential speaker, we also hope that requirements regarding diversity (gender, geographical, seniority) can be fulfilled.

4.6. [Biomimetic elastin-generating approaches to restoring functional elastic tissues](#)

Soft tissues contain architecturally complex elastic matrix structures that provide tissue stretch and recoil properties. Besides providing such unique elasto-mechanics, the elastic matrix is also directly involved in tissue homeostasis and cellular signaling. This property is important for many tissues including the heart, blood vessels, the lung, the skin, connective tissues, etc. A growing body of research has elucidated the importance of "elastokines" as elastin fragments with cytokine-like signaling properties that are generated in degradative tissue disorders. Despite major advances in tissue engineering technologies, a continuing challenge to generating fully functional elastic tissue constructs, lies in difficulties in achieving robust generation of mature elastic matrix structures within. This has been primarily attributed to inherently poor synthesis of elastin precursors by most adult cell types, and their compromised ability to assemble these precursors into higher-order architectures. This also limits our ability to repair in situ, elastic-fiber rich tissues that are compromised by chronic proteolysis associated with disease conditions. The proposed session will feature keynote and abstract-based talks by leading researchers in the field that will cover important steps needed to develop tissue engineering and regenerative medicine strategies to improve elastic fiber generation. These range from developing a better understanding of the complex matrix biology to applying elastin-generating strategies and to translating these strategies into grafts tested in animal models. Additionally, the symposium will review current state of art in the engineering of advanced materials bioinspired by elastin, i.e. elastin-like biomaterials, which have been developed as excellent tools to cover the gap between the need of elastin in tissue equivalents and the inability to achieve cell-secreted elastin in vitro. The session will also include a) approaches to circumvent or overcome aberrations of complex processes of elastin and ECM regenerative repair and neoassembly, and b) biomimetic stem cell, scaffolding-based, and nanomedicine approaches used to form complex ECM architectures that recapitulate elastic-fiber assembly and fiber maturation.

4.7. [Advanced therapies for cardiac regeneration](#)

Cardiac diseases represent a leading cause of morbidity and mortality worldwide. Heart diseases, such as cardiomyopathy or myocardial infarction, cause the loss of functional cardiomyocytes together with inflammation, remodelling of cardiac extracellular matrix and myocardial fibrosis, that progressively leads to reduced cardiac functions and heart failure. Heart transplantation, being the only therapeutic solution, is limited by the poor availability of organ donors and the need for an immunosuppressive therapy. Hence, many research efforts are ongoing to develop new advanced approaches aimed at promoting cardiac regeneration. The generation of functional cardiomyocytes from the differentiation of stem cells, such as pluripotent stem cells and cardiac progenitor cells has paved the way to new cell therapies for heart regeneration. However, hurdles for clinical translation include poor cell transplant efficiency, risk of tumorigenicity and immune rejection. During the last years, engineered biomaterial patches that recapitulate the biochemical and biomechanical properties of cardiac extracellular matrix have been explored as mechanical supports to the injured heart and/or carriers for cell delivery. A new promising regenerative strategy is the generation of de novo cardiomyocytes via resident cardiac cell reprogramming: cardiac fibroblasts that populate fibrotic scar can be directly reprogrammed into induced cardiomyocytes by transfection with transcriptional factors and/or microRNAs. Through direct reprogramming, common problems of cell therapies can be avoided, including low cell engraftment, immune rejection and poor functional maturation of in vitro differentiated cardiomyocytes. Additionally, resident cardiomyocyte proliferation can be induced through other specific reprogramming methods. Such new regenerative strategies may benefit from nanomedicine and other bioengineering tools for targeted, more

effective and safer reprogramming procedures. Furthermore, high-throughput screening platforms may be exploited in synergy to evaluate the efficiency of such novel approaches in in vitro engineered systems mimicking human cardiac pathological microenvironment. Hence, the symposium will stimulate critical discussion and multidisciplinary cooperation.

4.8. [Towards effective vascularisation and angiogenesis of tissue engineered grafts](#)

Rapid vascularization with blood and lymphatic vessels is of vital importance for survival and function of tissue-engineered grafts of clinically relevant size. Oxygen and nutrient supply/waste removal, interstitial fluid drainage, as well as control of its composition and of oncotic pressure, are ensured by the formation of pervasive microcapillary networks derived from vascular endothelial cells that need to connect with the host vascular systems. Furthermore, functional vascularization needs to be established within days of in vivo implantation to allow survival of progenitors and effective tissue formation. Lastly, the crucial role of immune cells in regulating vascular formation and function, as well as tissue regeneration, is increasingly appreciated. Several strategies have been pursued to either produce an already vascularized tissue that will be implanted and connected to the host vascularization network or to fabricate a graft that once implanted will promote a fast and efficient angiogenic process from the host's own network. Thus, the recreation of instructive environments that can send the specific signals to cells to rapidly activate the processes are key for a fast and equilibrated vascularization.

4.9. [Engineering functional in vitro microenvironments to control cell fate](#)

Cell-based therapies require removal of cells from their optimal in vivo tissue context and expansion in vitro to acquire suitable cell number. However, bereft of their optimal tissue niche, cells lose their phenotype and with it, their therapeutic potential. Scientific research and technological innovation are directed towards reconstruction of more functional in vitro microenvironments. Numerous technologies, including spheroid cultures, co-culture systems, three-dimensional biomaterials, biophysical cues (e.g. topography, rigidity, localized density, mechanical loading), biochemical beacons (e.g. media supplements, oxygen tension) and biological signals (e.g. growth factor supplementation, gene delivery) are under intense investigation as a means to control permanently cell fate during ex vivo culture. This symposium will critically discuss advances and shortfalls of various in vitro microenvironment modulators and elucidate how the newly developed knowledge will allow effective control of cell function during in vitro culture and ultimately development of functional cell-based therapies.

4.10. [Lung and airway engineering](#)

Lung disease is the third leading cause of death worldwide. The most frequent respiratory diseases include respiratory infections, chronic obstructive pulmonary disease and airway/lung cancer. Currently, there is a limited number of therapeutic options for these life-threatening conditions. For the case of end-stage lung disease (ELD), lung transplantation represents the only currently available therapeutic treatment. However, donor shortage and organ rejection represent major limitations. Owing to this, there has been an increased interest in recent years for developing engineering solutions to combat lung disease. Such approaches include regenerative medicine, cell therapy, improved extracorporeal membrane oxygenators (ECMO) and biohybrid implants for restoring lung and airway function. However, these approaches are still in their infancy and there are only a few of such treatment strategies close to clinical translation. The aim of this symposium is to generate a hub and a platform for the academic, clinical and industrial communities that are engaged with research in the field, with a view to presenting the progress and stimulating discussion and collaboration towards the development of lung and airway engineering technologies. Such technologies have the potential to provide a step change in the treatment of lung disease by offering not only a more effective and longer term bridge to transplantation, but most importantly a destination therapy. The symposium will cover a number of topics, including biohybrid lung, protocol optimisation for organ-specific cell isolation, expansion, differentiation and seeding, development and evaluation of scaffolds for airway and lung regeneration, in-vitro airway and lung tissue conditioning, cell therapy and delivery strategies, in-vitro models for basic research and personalized therapeutic testing, and computational modelling.

4.11. Tissue Engineering innovations in Otology

The ear is an exciting target for regeneration and repair. In this organ, physiology is tightly linked to anatomy, therefore successful tissue replacements should take morphological and functional inspiration from their native counterparts. The minute size, variegated shape and histological nature of the tissue components, the diverse vibrating interfaces providing signal transmission and transduction, the frequent infections and the ototoxicity issues, ultimately challenge the long-term efficacy of biomaterials in the ear. This symposium aims to collect the advancements in ear Tissue Engineering, from auricle to eardrum and ossicles up to the cochlea, in order to enable a comprehensive and updated overview oriented towards clinical applications. Thus, the pathological scenario, including frequent infections and inflammation processes as well as traumatic and genetic issues underlying tissue and functional damages has to be specifically considered. A Tissue Engineering approach in ear reconstruction needs creative and diversified strategies, including technology integration, to go beyond complexity and provide solutions for deafness.

4.12. Mechanobiology for 3D soft materials

Three dimension soft materials such as hydrogel and nano-fibrous scaffold have been an attractive candidate for tissue engineering scaffolds or in vitro study models for various tissue engineering applications. Not only because of the wide variety of material selections from natural to synthetic polymers, and different forms and fabrication options from hydrogel, nano-fibrous scaffolds to 3D-printed scaffolds, 3D soft materials are valuable to tissue engineering because they also provide the tuneable and biomimicking mechanical microenvironment for reconstructing human tissues. Many studies in the past decade have demonstrate the physical and mechanical cues in the cell microenvironment can affect and regulate cell behaviors through cellular mechano-sensing. Understanding the mechanobiology of how cells are interacting with the materials will provide essential knowledge in engineering functional tissues.

In this symposium, we aim to focus on the discussion of the mechanobiology studies on cell-interaction with their microenvironments. Recent studies have shown that various parameters of the biomaterials could affect the mechanobiology of the cell-material interaction, including the rigidity, viscoelastic properties, 3D structures, biodegradability and even extracellular matrix composition. Knowledge of the mechanobiology of cell-materials interaction will be essential in the development and functional improving of using soft biomaterials for various tissue engineering applications such as cardiac, vascular, cartilage, neural and muscle tissue engineering.

4.13. Extracellular Vesicles for Tissue Regeneration: Integrated perspectives from Industry, Academia and Clinic

Hype and hope around extracellular vesicles (EVs) have emerged in the last decade fostered by advances in our understanding of their mechanism of action and promising results in preclinical models and clinical trials. The involvement of EVs in maintaining human health as well as driving disease progression has opened up a whole new field of research across all areas of biology, from development to host-pathogen interactions to Regenerative Medicine.

Herein, we propose the organization of a symposium where experts from different disciplines (e.g., Bioengineering, Nanotechnology, Medicine, Bioinformatics) will discuss the latest developments in the EV field. Topics of interest include, but are not limited to:

1. Cellular origins and functions of EVs in a perspective of their contribution to regenerative medicine
2. Critical bioactive molecules within EVs and their roles in tissue regeneration (proteomics, metabolomics and lipidomics)
3. Different techniques for EV engineering and their application
4. New approaches for quantitating EVs as well as analysing their biodistribution in vivo
5. Prospects and future directions of the application of EVs in tissue regeneration in particular for personalized Medicine (disease biomarkers and novel therapies)

4.14. Informing Stem Cell-Based Tissue Engineering with lessons from embryonic development

Tissue engineering is built on the three key components of cells, matrix, and signaling factors. A common practice is to design approaches and systems based on the characteristics of adult tissues to drive stem cell differentiation and development into a tissue analog with appropriate biological and mechanical properties. Developmental biology revolves around similar questions of how single (stem) cells grow to tissues, organs or even full organisms. Natural tissue formation and organogenesis follow a well-controlled temporal and spatial sequence of phenomena that prescribe the coordinated and programmed changes in the behavior of cells, the composition and spatial geometry of matrix, and the signaling repertoire of biofactors, which together complete the transformation of a community of initially undifferentiated cells into structured and functional tissues and organs. The Symposium, “Informing Stem Cell-Based Tissue Engineering with Embryonic Development and Organogenesis”, will highlight examples of tissue engineering approaches that are informed by biological and structural concepts and principles gained from the study of embryonic development, including cell differentiation, tissue morphogenesis, and organogenesis. These concepts may include, for example: (1) influence of cell shape and cytoskeletal kinetics on cell differentiation; (2) complex gradients of signaling factors over long distances and how cells decode these gradients; (3) epigenetic, physical and microenvironmental regulation of cell fate and differentiation; (4) the role of cell-cell and cell-matrix interactions in the 3D assembly of cell populations; and (5) functional tissue-tissue interactions as the basis of organogenesis. The symposium will also provide a forum to discuss novel bioengineered models of embryos and the maternal reproductive system, which present developmental biologists with unprecedented opportunities to study morphogenetic processes that are previously largely inaccessible in mammalian systems, such as implantation, gastrulation, and segmentation.

4.15. Respiratory, Reproductive, Urologic and Gastrointestinal Tissue Engineering - Different Organs, Similar Strategies?

Please note that this is a merged symposium and the final description will be available soon.

5. Process engineering

5.1. Vascularized Organoid Development

Organoid development has become one of fast moving fields in tissue engineering and regenerative medicine. Vascularization is of critical importance to creating biologically functional organoids for both in vitro and in vivo applications. The proposed symposium will bring together investigators from both academia and industry to identify grant challenges in the field and to foster collaboration between academic and industrial investigators to move the field forward.

5.2. Scaling up, maturation and nerve connection in skeletal muscle tissue engineering

Skeletal muscle tissue engineering has been pursued for various applications including transplantable grafts, tissue models, bioactuators and cultured meat. Myotube formation, tissue orientation, muscle fiber thickening and scaling up are now critical points in muscle engineering. Regarding tissue orientation, micro-patterned culture materials have been developed. Several studies demonstrated that electrical stimulation (“muscle training”) increase the diameter of myofibers. For scaling up, media perfusion technology must be introduced. Furthermore functional contraction with neuro-muscular junction formation has been also investigated. In this symposium, recent advances in skeletal muscle tissue engineering will be presented and discussed.

5.3. Advances of tissue engineering in the ear, nose & throat field

There are huge demands for the regeneration of the defects in head and neck area. Defect of bone and cartilage in the facial or cranial region, radiogenic xerostomia, severe oral mucositis or mucosal defect after chemotherapy, airway stenosis or tracheal defect after ablative surgery, parathyroid hormone deficiency after thyroidectomy, and aspiration inducing vocal fold paralysis are some representative targets in tissue engineering in ENT field. Tissue engineering approach in ENT field is considered as more difficult compared with other sites of the bodies due to 1) limited vascular supply by distal location from the heart 2) constant exposure to septic environment 3) complex shape and composite tissue required for the regeneration.

This symposium will discuss the current status and recent advances for regeneration of airway and parathyroid gland with the conventionally used stem cells as well as those mesenchymal stem cells isolated from tonsil and inferior turbinate of nasal cavity.

This symposium will also highlight the 3D cultured organoid, 3D printed scaffolds, tissue specific bioreactor, and some active biomolecular cues for better regeneration of the organ.

5.4. Human placenta material-based biomaterials for Tissue Engineering and Regenerative Medicine

The human extracellular matrix (ECM), consisting of hundreds of different proteins, having a profound impact on the behavior of all eukaryotic cells, is regarded as the perfect scaffold material for the manufacturing of medicinal products.

Although biomaterials extracted from ECM have already received significant attention for tissue engineering and regenerative medicine (TERM), numerous publications have shown that human-material based ECM goes along with a better performance in cell culture applications and in clinical applications, when compared to animal-material based ECM, because the ECM proteins are almost identical in individuals within the same species, but differ between species.

For instance, non-human collagens were frequently described to provoke immune responses in clinics. Additional drawbacks such as xenogenic disease transmissions are also often discussed. Therefore, concerns still remain regarding the safety of these materials and, as a consequence, human tissue sources such as placenta, are highly valuable for TERM.

Human placental tissue is globally available after birth and therefore a constant source for processing on industrial scales. It is free of any ethical conflicts and causes no additional harm to donors such as donor site morbidity.

In this regard, a high rate of positive consent of mothers for placental donation was reported and many relevant ECM extraction methods based on different extraction strategies and applications for TERM were published over the last decades in the scientific community.

Thus, this symposium content will cover the use of human ECM for human cell culture applications, to avoid (beside animal suffering) cell de-differentiation, change of surface receptors and false positive or negative research results caused by animal-material based ECM. Human ECM based biomaterials from placenta could open doors to an affordable personalized medicine for our society in the future.

5.5. Laser processing to support matrix repopulation

Repopulation of a dense material such as decellularized tissue is a key issue and a critical step in using allogenic or xenogeneic tissues in clinics. The purpose of this symposium is to collect the most advanced approaches in regard to laser processing of matrixes for medical application. The main focus is the perforation of tissues and biomaterials to facilitate cell invasion. We want to display the diversity of lasers available on the market (e.g. CO₂-laser, femtosecond laser, Er-YAG-laser) and their effects on tissues and scaffold materials, but also the achievable results from different approaches with a single laser type.

The key note talk (Sylvia Nürnberer Medical University of Vienna) will start with an overview of the multiple laser technologies and their possibilities for application on biological tissues. A comparative study on two different types of cartilage (articular and auricular cartilage) processed with two types of lasers (CO₂-laser and femtosecond laser) will demonstrate the potential and limitations of these methods for cartilage scaffold generation. Andrea Barbero (Universtty Basel, Switzerland) will then report on a laser treatment of tracheal cartilage for reseeding with nasal chondrocytes.

The other talks for the session will be chosen from the abstracts based on the criteria of quality and most creative and best performed studies. They should reflect the diversity of approaches currently developed for decellularized tissue, engineered scaffolds and hydrogels and also living tissues. This means that apart from different laser technologies, application strategies (e.g. holes, lamella) but also tissues (e.g. cartilage, skin, vessels) and purposes (cellular, vessel, nerve ingrowth) will be selected.

The symposium is in line with the topic of biofabrication and advanced decellularized matrices for tissue engineering.

5.6. Advanced biomaterial-based technologies in skin tissue regeneration

Skin is the largest organ in the human body. Skin injuries account for over 6 million medical procedures per year in the US, that are due to the significant skin loss, disfigurement or genetic blistering skin diseases. The bioengineered human skin constructs have been used a promising skin replacement therapy, or to recapitulate skin disorders for drug screening purposes. In particular, the biologically inspired scaffolds and dressing are promising approaches for the treatment of acute and chronic skin wounds as well as skin burns.

After successful completion of symposium in 2018 TERMIS global conference, and 2019 TERMIS-AP, we would like to have a symposium on “Advanced biomaterial-based technologies in skin tissue regeneration” for 2020 TERMIS Global Conference 2021. The symposium is to ameliorate the knowledge, awareness, and education on skin biology, stem cells, biomimetic strategies, biomaterials leading to the discovery therapies which aid to alleviate the skin diseases and injuries as one of the most significant emerging technology in the eyes of Medical, Biotechnology, Pharmaceuticals and Academia.

5.7. The tissue engineering conundrum; cell derived and engineered microenvironments.

Tissue engineers are focussing on creating new environments to guide cells and provide new regenerative therapies for patients. Researchers are working on two main avenues of research; cell derived and engineered microenvironments. Multicell population aggregates, known as cell 'spheroids' produce their own cell derived microenvironment, a combination of extracellular matrix proteins and biomolecules to support their survival and function. Microenvironments can also be created and manipulated by engineers using synthetic materials, decellularised tissue and methods such as 3D printing, electrospinning and hydrogels. These methods have advanced our understanding of cell biology immeasurably, however as of yet none accurately replace the complex in vivo environment. An intermediary approach is emerging as a possible solution for this. By harnessing features of the cell derived microenvironment through combining and controlling them with engineering to incorporate stimulus such as oxygen diffusion, shear stresses, strain and mechanical stiffness characteristics, thus advancing the field using the best of both. Such an approach can be employed for a range of tissues in the body including liver, vascular, kidney and cartilage engineering, and could be the missing link between synthetically engineered environments and the in vivo environment. This session will focus on novel approaches and developments seen in these methodologies and their future potential in regenerative medicine.

Dr Callanan is a senior lecturer (Assistant/Associate Professor) in the Institute for Bioengineering at the University of Edinburgh. His group's research focuses on tissue engineering advanced combinatorial microenvironments and treatments for kidney, liver, cartilage and vascular applications. He also works on modelling and simulations using Finite element analysis and computational fluid dynamics. He holds a PhD in Biomedical Engineering and BEng in Mechanical Engineering, which he received from the University of Limerick, Ireland.

5.8. From phage biology to phage engineering

Bacterial infection is a major reason for large tissue defects requiring regenerative therapies. Equally, infection is one of the major risks associated with tissue engineering constructs. Novel therapies targeting infection will therefore not only protect patients, but also support the successful application of regenerative medicine in the future. Lytic bacterial viruses (bacteriophages, or phage) recognize, infect and hijack the bacterial cell to produce progeny viruses. This process has been optimized through billions of years of co-evolution between bacteria and their viruses.

This session offers a background into the basic biology of this virus-bacteria interplay and explores the principal strategies on antibacterial design and how this can be applied to TERM. To overcome intrinsic limitations of phage therapy, e.g. narrow host range, biofilm degrading properties or resistance development, genetic engineering approaches can be applied to modify these key characteristics. Yet another strategy derived from phage involves the application of cell wall degrading enzymes which lyse the cell by degrading the peptidoglycan layer of the bacterium. Recombinant expression of these enzymes and their external application was previously shown to eradicate Gram-positive bacteria including *Staphylococcus aureus*. In our research we applied an engineering approach enabling these enzymes to penetrate the outer membrane of Gram-negative pathogens including *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. These 'Artilynsins'TM show high activity and specificity towards selected pathogens, have limited resistance development and are active against persistent bacteria.

Phage derived antibacterial strategies are undergoing an intense resurgence and re-evaluation of their potential, yet still face scientific and regulatory hurdles. The introduction of recombinant engineering and molecular biology advances provide novel opportunities with regard to target discovery and enzyme-based and biotechnology-based solutions.

5.9. Novel culture technique for cell manufacturing

Cell culture is one of the most important process to realize cell therapy. This symposium covers recent development of culture techniques including not only development of a novel culture system but also construction of automation system and bioreactor as well as management of cell processing facility. This symposium will provide the facilitation of understanding concerning practical cell processing for therapy, supposing to gather the audiences from the broad fields including creators of cell therapy in basic researches, developers of cell manufacturing, operators and managers in cell processing facility.

6. Preclinical & Clinical

6.1. Veterinary regenerative medicine: Of animal models and clinical patients

Animal models are an important and compulsory component of translational research. However, they require careful selection and design to ensure they are fit-for-purpose and provide both, optimal predictive validity and ethical, animal-welfare and societal considerations. Small animals, specifically mouse and rat models, are valuable for research into mechanisms of disease and fundamental biology, but findings from such small animal models rarely translate into human clinical applications. Large animals are well-accepted, well-established and clinically relevant animal models which commonly suffer from naturally occurring disease/injuries with similar pathophysiology to the human in terms of etiology and risk factors which include over-exercise, age and genetic factors.

Among others, one special focus will be put on preclinical models for bone regeneration. A recent evaluation of the models which are currently widely used has raised significant concerns including large heterogeneity as well as a lack of reporting of sufficient experimental details. The TERMIS world conference will bring together researchers, veterinarians and clinicians and we would like to take this as a chance for an expert discussion on preclinical models with the aim to eventually come up with a consensus on a few, well defined models.

The veterinary profession has an important role to play in the translational process, offering the missing link between basic science and human clinical applications. Data obtained from animal models/veterinary clinical patients suffering from naturally occurring diseases with strong parallels to human diseases, are therefore valuable per-clinical data for the human field. The results obtained from veterinary studies may therefore benefit both veterinary and human patients. We would therefore like to apply for 2 back to back sessions (90 min each, 180 min total).

6.2. Cardiovascular tissue engineering

Cardiovascular diseases are still a worldwide leading cause of death. Therefore, revascularization to restore blood flow to ischemic organs represent a major global medical need. Furthermore, a good alternative for conventional prosthetic grafts is urgently needed to improve to poor outcome of current hemodialysis access conduits. Despite extensive research over many decades, no suitable, synthetic or biological vascular small caliber graft exists for clinical application. Many approaches to engineering biological vascular grafts have been explored and are currently under investigation with promising results.

In the proposed two symposia, we aim to provide a state-of-the-art overview of recent advances in the field of vascular tissue engineering, which ranges from basic research to regulatory aspects of product development and the latest results from clinical trials.

6.3. The vicious cycle of degeneration, inflammation, and pain – role of biological therapies in intervertebral disc disease

Low back pain is an extremely common symptom experienced by people of all ages, which is now the number one cause of disability globally. It is believed that symptomatic intervertebral disc degeneration (IDD) is the main cause of low back pain. In this workshop, we aim to explore underlying pathogenesis mechanisms and new biological therapies for symptomatic disc degeneration.

Though pharmacological and physiotherapeutic treatments relieve early symptoms in IDD, surgical intervention may be required at later stages for significant pain and/or neurological deficits in nearly 4 million patients worldwide per year. The current surgical standard to treat IDD involves the removal of the entire IVD followed by fusion of the adjacent vertebrae or the interposition of mechanical disc prosthesis to preserve motion. However, fusion presents risks for pseudarthrosis and adjacent segment disease (ASD), resulting in a higher rate

of reoperation in these patients. Prosthetic total disc replacement (TDR) devices, developed to maintain segmental mobility, are an alternative to fusion surgery. Yet recent studies have shown that not only spinal fusion, but also TDR alter spine biomechanics leading to ASD. Hence, it remains controversial whether the theoretical advantage of TDR truly translates to clinical or radiological superiority over fusion surgery. In the end, current treatment options, both conservative and surgical, fail to treat the underlying pathology; the degenerated disc remains unrepaired.

To overcome the limitations of available treatments and enhance patient care and clinical outcome, biological approaches to IVD repair or regeneration have become of increasing interest. Strategies utilized in biological IVD repair are specific to the stage of degeneration and can be classified into three major categories: biomolecular therapy, stem cell therapy, and tissue engineering-based treatment.

6.4. Bioengineering technologies for beta cell replacement

Type 1 diabetes is a chronic disease hallmarked with the loss of insulin producing beta cells due to a destructive autoimmune reaction against the patient's own cells. The conventional treatment is exogenous insulin therapy by means of regular daily injections or pumps. However, longterm insulin therapy will ultimately lead to a great number of complications such as vascular damage, neuropathy and kidney failure. The best solution would be to give type 1 diabetes patients the lost insulin producing beta cells back, which enables them to reach stable normoglycemia in a natural way.

Since the last two decades a promising cell therapy has been used in a small selected group of patients called: "clinical islet transplantation". However effective, this treatment is not very efficient, the majority of the transplanted donor islets are lost during the first two weeks of engraftment. The success of clinical islet transplantation is hampered by the intrahepatic transplantation site. Islets transplanted in the liver are prone to mechanical stress, exposure to high drug and toxin loads and strong inflammatory and immunological reactions to the allogeneic cells despite systemic immunosuppression therapy. There is a world wide effort to develop optimal beta cell replacement strategies based on combining biomaterials with stem cell derived beta cells or even xeno-derived islets using SPF islet sources. If successful this can compensate for the lack of donor tissue, by creation of a high quality sustainable unlimited beta cell source, and a more efficient way to deliver these cells to patients.

6.5. Cartilage Repair and Regeneration

This symposium aims to connect TERMIS and the International Cartilage Regeneration & Joint Preservation society (ICRS), providing TERMIS members the opportunity to present at an ICRS endorsed event. In this symposium, promising approaches for effective cartilage repair, which utilize chondrocytes, stem cells, genes, and biomaterials, will be reported.

It is generally accepted that chondral injuries usually do not heal spontaneously. Currently, several therapies exist to treat chondral injuries. However, the current cartilage repair therapies do not consistently produce hyaline repair tissue. This symposium introduces the recent attempts to use regenerative medicine principles to develop an adequate therapy for effective repair of cartilage lesions.

6.6. Tissue Engineered Therapeutic Approaches for Retinal Degenerative Diseases

Eye research has been leading the field in pluripotent stem cell based therapeutic approaches. This session will update the scientific community on most recent advances in the field of transplantation of retinal pigment epithelium, photoreceptor, and retinal cell types derived from pluripotent stem cells. Speakers will discuss scientific, manufacturing, preclinical, and regulatory challenges in developing cell-based therapies for eye diseases.

6.7. Cardiovascular ageing and regenerative medicine

Cardiovascular disease is the leading cause of death worldwide. Progresses have been done in the last 10 years in the development of in vitro models¹ to study cardiovascular diseases and ageing. Here, in vitro and in silico models have been proposed to mimic the physiological conditions of heart and vasculature, and in vitro models of aged blood vessels and cardiac tissue have been developed for the study of ageing biology and identification of new therapeutic targets. In addition, progresses have been done in the development of advanced therapies such as gene-, cell-, extracellular vesicle-, biomaterials-based therapies². Some of the disease targets include cardiac and peripheral ischemia, heart failure, vein graft failure, among others. The symposium will focus in nanomedicine-based therapies such as nanoparticles and extracellular vesicles. Indeed, recent advances have been done in the use of nanoparticles that may simultaneously act as vehicles of drugs and imaging payloads³. In the area of extracellular vesicles, advances have been done in better understanding the composition of EVs, their role in the communication between cells of the same or different tissues in the body, and how the content of EVs secreted by stem/progenitor cells or other cardiac populations is affected by disease⁴. As consequence of these progresses, there are 2 observational and 2 interventional clinical trials actively running.

6.8. Tackling tendon disease: updates on tendon degeneration, injury and repair with innovative tissue engineering

The biggest compartment of the musculoskeletal system are tendons and ligaments. They are dense connective tissues critical for the integrity and function of this system. They are mainly composed of collagen fibers and tendon-resident cells that lie embedded in parallel rows in a well-ordered extracellular matrix (ECM). The tissue hierarchical internal structure delivers a high tensile force and resilience. The tendon-resident cell population is composed of approximately 90 - 95% of tenocytes, whilst the remaining 5 - 10% of cells are tendon stem/progenitor cells and tenoblasts.

Due to the increasing age of our society and a rise in engagement of young people in extreme and/or competitive sports, both tendinopathies and tendon ruptures present a major clinical and financial challenge in modern medicine. So far, there is no reliable method to detect early tendinopathy and no strategy to ameliorate its progress. Inevitably, tendinopathies lead to tendon rupture and once this happens, tendon natural healing is slow, often poorly responding to treatments and requires prolonged rehabilitation in most cases. Therefore, improving our understanding on tendon biology, biomechanics, degenerative and healing processes and identifying ways, with the help of innovative tissue engineering, to augment and steer their repair to more satisfactory outcomes is of critical importance.

In this symposium, an overview of tendon basic and translational research will be provided along the following points: (1) Keynote speaker Prof. H. Screen (UK): Tendon structure function relationship with focus on the role of interfascicular matrix in tendon injury and tendon biomechanics; (ii) Invited speakers 1 Prof. A. Traweger (Austria) and 2 Prof. T. Sakai (UK): Tendon healing process with focus on the involvement of “tenophages” (endogenous macrophage-like population) and tendon progenitor cells; (iii) Invited speaker 3 Dr. R. Domingues (Portugal): Tendon tissue engineering with focus on recreating the complex biophysical and biochemical tendon niche.

6.9. Progress and Challenges Associated with Translation of Regenerative Medicine Therapies

Advances in tissue engineering and regenerative medicine have provided new therapeutic opportunities for repairing damaged tissues and organs. However, the actual delivery of regenerative medicine therapies to the clinic has shown to be difficult due to the complex processes involved with the translation. In fact, the translational process is often complicated by various unforeseen factors that lead to a delay in delivering commercially viable therapies capable of addressing unmet clinical needs. This session will provide a better understanding of the translational processes that facilitate safe and accelerated delivery of clinical therapies to patients. These include, not only addressing the scientific challenges but understanding the regulatory processes

and requirements that ensure safe and effective delivery of therapies, as well as manufacturing approaches that permit delivery of consistent and reliable therapeutic products in a timely and cost-effective manner.

6.10. Clinical bone regeneration for maxilla-facial surgery and trauma/orthopedics

Bone defects, be it in long bones, the skull or in the maxilla-facial area, are still a medical challenge. Especially, large defects are difficult to heal and regeneration is highly depending on several systems such as osteogenic inducing cells and factors, angiogenesis as well as mechanical stability. Based on autologous bone replacement, which is still regarded as gold standard, new technologies in reconstructive bone surgery have been developed within the last twenty years. During the last decade bone surgeons achieved a break through concerning reconstructive techniques in bone. The approach to new methods in bone surgery is urgently required due to risks concerning bone transplantation.

The newly developed techniques have been adapted for different medical indications. They work with mesenchymal stem cells (MSCs) from different sources, smart scaffold technologies (including 3D-printing), growth factors (recombinant, DNA, mRNA, miRNA), and clinical know-how procedures especially in minimal invasive techniques. Which techniques and which combinations to use is depending on the patient in a personalized medicine way. Hereto an intensive collaboration between researchers, clinicians, industry and governmental bodies is very important. Preclinical research on the newest developments and clinical (case) studies treating bone defects with regenerative approaches will comprise this symposium. The emphasis is on the biology part (MSC, growth factors) in the surgical treatment of large bone defects. The keynote speaker will provide many different approaches to treat long bone defects with the “diamond concept”, which was development by him. This symposium will demonstrate examples of the translation of these new techniques for bone regeneration in maxilla-facial and trauma/orthopedic surgery.

6.11. Preclinical and clinical non-viral gene therapy

Ex vivo or in vivo genetic manipulation of suitable target cells offers effective avenues to achieve true functional regeneration of tissues in vivo through induced auto-regeneration. The augmentation or down-regulation of endogenous effectors of cell behaviour through the delivery of nucleic acids offers a targeted and fine-tuned approach for biomimetic approaches to manipulate cellular behaviour. Non-viral, transient genetic manipulation in regenerative medicine is a field particularly amenable to accelerated translation and deployment for patient benefit due to its safety and cost-effectiveness. Such approaches have been demonstrated to be feasible and useful in preclinical studies for regeneration. They could become viable alternatives or supportive therapies to current clinical standards if the current limitations of efficacy and control of delivery can be improved.

This symposium aims at providing a comprehensive and current overview of preclinical systems in development and currently deployed state of the art clinical systems for regenerative medicine. These include ex vivo gene therapies that involve in vitro stem cell manipulation as well as approaches for direct in vivo genetic manipulation. Technologies should cover non-viral nucleic acid delivery in preclinical in vivo models or clinical studies, aimed at addressing a clinical challenge in regenerative medicine. Submissions covering systems to improve efficacy through novel agents or combinations with biomaterials are encouraged as are innovative strategies for advanced spatiotemporal control of delivery and new avenues to transient endogenous gene regulation/reprogramming.

6.12. Repairing and regenerating organs for transplant purposes: the standard of care in transplant medicine

Organ preservation represents a formidable example of organ bioengineering. The development of organ preservation strategies has been fundamental for the success of solid organ transplantation, a therapy that, in the past four decades, has become the standard of care for a myriad of clinical settings characterized by end stage organ failure. This symposium will illustrate to the TERMIS audience the state of the art of organ preservation, and will propose three speakers who are acknowledged by their peers as leader in the field. The symposium will also present the extraordinary, cutting edge concept of the Organ Repair Center, where marginal

lungs that would otherwise be discarded, are repaired using regenerative medicine technologies, in order to come to fruition for transplantation. This idea was conceived, developed and implemented by the University of Toronto.

6.13. Treatment of liver diseases, venturing beyond organ and cell transplantation

The symposium will focus on a regenerative medicine approach for treatment of liver disease utilizing cellular transplantation, gene editing and tissue engineering of liver tissue. Dr. Robert Fisher, Transplant surgeon, Professor Emeritus at Harvard and a pioneer in Clinical Hepatocyte transplantation, will open the symposium with a lecture that will introduce the field and future direction. Dr. Fisher will also illustrate the mission and current scientific focus of the CTRMS society.

Dr. Stephen Strom, Professor of Cell Transplantation and Regenerative medicine at Karolinska Institute, Sweden, also a pioneer in Clinical Hepatocyte transplantation will present his work on Correction of Liver-based Monogenetic Disease: Current Strategies, Future Developments. The third speaker, Dr. Giuseppe Mazza from the Institute for Liver and Digestive Health at University College London will present his work on tissue engineered Liver and possible clinical applications.

6.14. Regenerative Rehabilitation – Functional Translation of Biologically Inspired Regenerative Technologies

The field of tissue engineering has long integrated fundamental principles of stem cell biology, biomaterials and mechanical engineering to better design new tissues. As regenerative technologies become more prevalent in the clinic, it is becoming increasingly apparent that the rehabilitation regimen and management of the intervention after the delivery/implantation is just as critical to the success of the implant as the fundamental technology itself. This recognition has generated the new integrative field of Regenerative Rehabilitation. In affiliation with the TERMIS thematic group on Regenerative Rehabilitation we propose this symposium session to foster dialogue and collaboration between the various disciplines.

This session will first present an introduction on regenerative rehabilitation and the importance of considering rehabilitation for the translation of biologically inspired tissue engineering and regenerative therapies. There will be then be a keynote talk and invited short talks which will highlight research that has integrated rehabilitation principles to enhance the efficacy and translation of regenerative and tissue engineering therapies.

6.15. Biophysical Therapies in Regenerative Medicine

Chronic wounds, non-healing fractures, and many other conditions impose a significant burden to the individual and the healthcare system. Biophysical treatments can be brief in duration, incur low costs and have a high level of efficacy. Points of use include stand-alone treatment or support of standard care which may be required to complete healing. In response to this clinical need, advanced technologies are being developed to improve tissue regeneration. These treatments may involve application of mechanical energy, light, or electrical energy to the wounded tissue. Such biophysical energy - tissue interactions have already been shown to re-stimulate the natural healing pathways but a joint multi-disciplinary effort involving physics, biology, and medicine is required to fully understand underlying mechanics and to optimize treatment strategies. Slowly, a more nuanced understanding of the pathways stimulated by these treatment modalities is emerging as the scientific community is embracing the potential of these therapies.

Although scientific evidence supports the clinical usage of such therapies, routine treatment protocols have yet to be established and often rely on the personal experience of individual physicians. Importantly, variations of equipment and technique may introduce variations at the wound surface that influence healing and personalized, custom tailored treatment protocols are still in concept phase.

Ongoing basic research helps define the wound system, establish primary energy-tissue interactions, and develop optimized protocols for specific wound healing needs leading towards broader adoption into clinical practice for improved care of chronic wounds.

This symposium aims to elucidate applications of biophysical applications in regenerative medicine, seeks to fully characterize such treatment approaches, and unravel the interaction between applied physical triggers and tissue reactions. Basic research as well as clinical applications will be discussed.

6.16. Corneal tissue engineering and regenerative medicine.

The cornea represents a translational opportunity for tissue engineering and regenerative medicine. The cornea is an avascular surface tissue, existing lamellar surgeries transplant component layers of the cornea individually to treat disease. A shortage of donor corneas creates a demand for alternative treatments. To translate corneal tissue engineering and regenerative medicine treatments from the bench to the clinic cooperation between academic disciplines, clinicians, and industry is essential. This session's keynote speaker and chairs are leaders in the field who have promoted translation of advanced therapies through this necessary cooperation. The keynote speaker Prof Griffith (University of Montreal, Canada) has developed multiple tissue-engineered products to treat corneal blindness. Among them, she reported the first successful regeneration of the cornea using cell-free pro-regeneration recombinant human collagen hydrogels applied in more than 10 patients. Co-chair Prof. Connon's approach is based on the balance and the proper spatial and temporal presentation of cells, signaling molecules, biomaterials, and mechanical stimulation. He is a co-founder of Atelerix Ltd, CellulaREvolution Ltd and 3D Bio-Tissues Ltd, and Faculty Director of Business Development, Newcastle University. Assoc. Prof Mark Daniell (Centre for Eye Research Australia) collaborates with researchers at the University of Melbourne and Eversight (USA) to develop tissue engineered therapies incorporating a novel synthetic polymer scaffold. He has had successful collaborations at the Mawson Institute (Australia) and L.V.Prasad Eye Institute (India), developing methods to transfer limbal stem cells to the patient. Assist. Prof Gonzalez-Andrades' (University of Cordoba, Spain; and Harvard Medical School, USA) research focuses on: fibrin-agarose and collagen scaffolds, decellularized porcine corneas, keratoprosthesis, biointegration of synthetic materials and bioadhesives. He was the coordinator for a multi-centric clinical trial, which is still in progress, for the evaluation of artificial human corneas based on fibrin-agarose with corneal cells after carrying out the preclinical research.

7. Enabling technologies: imaging, modeling, fluidics

7.1. (Degradable) biometals for tissue regeneration

Bio-metals are employed in various forms to substitute for damaged structural components and to restore lost functions within the human body for the purpose of tissue engineering/regenerative medicine. A favorable combination of tensile strength, fracture toughness, and fatigue strength warrant their application in orthopedics, as artificial joints, plates, and screws, in orthodontics and dentistry, as braces and dental implants, and as cardiovascular and neurosurgical devices, such as artificial heart, staples, stents, wires, and coils. Compared to polymer and ceramic biomaterials, metals are characterized by higher electro-conductivity, and as such have been employed to enclose electrodes in artificial electronic organs.

Lately, biodegradable metals emerged as a new generation of medical implants for regeneration. Although bio-inert biomaterials show a great performance especially in fixation applications, they bring an important problem into the play: they remain in the body forever or require additional surgery to remove them. Biodegradable materials do not have this problem, and especially in the case of metallic biomaterials, they also provide a dynamic (i.e. time-varying) mechanical stability profile, but taking advantage of them requires tuning the mechanical and electrochemical parameters.

This symposium is meant as a venue to communicate the latest developments in the experimental investigations and practical applications as well as the computational modeling of (degradable) biometals with special emphasis on the integration with tissue engineering products. Developing mathematical and computational models of

mechanical behavior and the degradation processes is a proper approach for addressing the issue of tuning the behavior of the material. Combining such models with computational models of mechanobiology/tissue engineering phenomena enables the researchers to study not only the electrochemical behavior of the biomaterial but also the response of the surrounding cells/tissues prior to conducting any in-vitro or in-vivo experiments.

7.2. [Engineering, quantifying, understanding, and modelling cellular geometry for controlling cell function and artificial intelligence-supported outcome prediction](#)

Strategies for implanting autologous cells and biomaterial-assisted strategies for controlling the patient's cells after biomaterial-implantation hold substantial interest for developing regenerative therapies that focus on controlling disease mechanisms and on improving patient outcome. In this context, multiple approaches exist that create artificial cellular microenvironments and/or target specific disease characteristics. A promising yet largely unexplored strategy is the intentional engineering of cellular geometry for controlling cell functions in regard to expression profiles relevant for better understanding and controlling disease states. This symposium will introduce the concept of the intentional engineering of cellular geometry and will present selected biophysical methods used in controlled in vitro systems used for this task. Moreover, the symposium will relate crucial aspects of cellular geometry to the expression profiles of human chondrocytes in the context of degeneration such as seen in osteoarthritis (OA). Furthermore, this symposium will provide the necessary knowledge in terms of cellular and subcellular mechano-biology to aid mechanistic understanding of this process. General mechanisms of cell shape-associated alterations in cell adhesions, cytoskeletal structures and signal transduction pathways will be discussed, as they provide a rationale for cell function modulation for a targeted cell shape engineering in regenerative medicine and disease modelling. Finally, this symposium will explore strategies for quantifying, modelling and analysing cell geometry for artificial intelligence-supported outcome prediction and will provide "real-life" applications in academia and industry. These topics not only have ramifications for our pathophysiological understanding of cell function, but they are also important in the context of degenerative diseases, novel clinical evaluation strategies and therapeutic approaches.

7.3. [Mass spectrometry in regenerative medicine](#)

Mass spectrometry technology is particularly interesting to obtain a global understanding of cell-material molecular interactions. MS-based applications in the field of regenerative medicine will be discussed during this symposium including mass spectrometry imaging, lipidomics, proteomics and metabolomics and how they can provide a better knowledge of key molecular processes for cell fate determination.

7.4. [Multiscale Engineered Biomimetic Systems for Stem Cell and Tissue Engineering](#)

This session aims to collect efforts for the development of multiscale engineered biomimetic systems for biomedical applications. Such systems usually combine physiological tissue-level complexity with a controlled environment, thus constituting an ideal environment for clinically relevant in-depth studies. This session will be divided into two sub-sessions. We will open the first sub-session with the EU-funded project B2B (Silvia Scaglione, CNR-IEIT, Italy), which is developing a first-of-a-kind 3D model of spontaneous breast cancer metastasis to the bone. The device features two organoids of clinically relevant dimensions (cm³) connected with a fluidic network made of self-assembled micro-sized capillaries merged with bioprinted macro-sized vessels. The second sub-session will introduce a series of advanced multiscale patterned platforms inspired by the unique architectures of native tissues and ECMs that can provide cells the in vivo-like topographical stem cell environment. Such platforms enable the understanding of the function of living stem cells and tissue regeneration without the need for complex surgical treatments or tissue transplantation. Together with the other selected talks, we aim to give an overview of the most innovative and challenging aspects of multiscale engineered biomimetic systems and of devices that enable the crosstalk between tissues.

7.5. TE tools to speed up the discovery and preclinical testing of vaccines for SARS-CoV-2 and therapeutic agents for COVID-19

We would like to update the TERMIS research community on the cell modeling tools in 3D, already used in virology and vaccinology, that could accelerate the understanding of SARS-CoV-2 infection mechanisms and could speed up the development of relevant vaccines and therapeutic agents against COVID-19.

Cell morphology, virus penetration and cell damage are replicated similarly to in-vivo in 3D cell and organoid static culture models, which are impressively more permissive to viral infection than cell monolayers: cell expression of viruses receptors, antiviral genes, antigens to viruses and inflammatory markers is more similar, in time and space, to in-vivo. Moreover, in 3D models, the sensitivity to antiviral drugs is significantly lower and highly comparable to in vivo conditions.

Perfused cell models allow to extend infection studies even up to several months, on stable cell cultures of highly differentiated cells, at higher infection efficiency and at lower multiplicity of infection, compared to non-perfused models. This potentially enables to extend to in vitro systems the study of the life cycle and genetic stability of new viruses like SARS-CoV-2, even if derived in minimal doses from patients, and also to test sequential antiviral drug treatments. Most importantly, perfused cell models allow to reproduce dynamic interactions between tissue-resident cells and circulating ones, including the response to pathogens of innate and adaptive lymphocytes, thus, to extend to in vitro some aspects of vaccines testing.

Key advantages of intravital imaging are largely present, with respect to conventional histopathological inspections, that can speed-up the preclinical evaluation of vaccines and novel antiviral therapies. Dynamics of infection progression and the effect of vaccines and drugs can be appreciated and quantified in real time with a resolution up to the sub-cellular scale. Also, the sensitivity and robustness of intravital imaging to assess immunization is greater than in vitro assays.

7.6. Organoids and Advanced Models for Cancer and Disease Investigations

For many years, researchers used cells cultured in vitro on tissue culture plastic dishes for basic research applications. Cell culture is a poor analogue of tissue growth in vivo, in part because it doesn't replicate the tissue microenvironment, a complex space typified by stromal cells, ECM components, and a cocktail of signaling factors. Newly developed bioengineered tissue platforms, such as 3D organoids, open new opportunities for better tissue modeling, especially incorporating the complex cellular and physical aspects of the microenvironment that are known to have a major role in regulation of function. In this symposium, researchers will get an opportunity to know about the current methodologies and technologies for the development and uses of biomaterial-based matrices for 3D organoids, cellular and cancer disease models. Advances in 3D cancer organoids, bioprinting, micro patterning, and microfluidic devices will permit to study the cell migration (e.g. tumor cell invasion, intravasation, and extravasation) and tissue growth. Highly realistic 3D in vitro tumor models that include the tumor microenvironment and cell migration enable us to study and manipulate cancer and other diseases for anticancer therapies screening and disease microenvironment dynamics. This symposium will also comprise researchers working in the specific areas like tissue engineering and regenerative medicine applied to cancer diseases and/or development. In particular, those working with natural and micro-nano composite biomaterials, 3D in vitro microenvironment modulations, cell-based bio-inks, 3D tumor disease modeling, nanoparticle-based delivery vehicle, micro-patterning, spheroids, micro-tissues and drug screening using latest emerging technologies like microfluidics, bio-printing, tumor lab-on-a chip, cancer organoids, and cancer stem cell.

7.7. Spatiotemporal imaging, modelling, and mimicking of tissue microenvironments

Engineered models of normal and abnormal tissue are emerging clinical products for the biomanufacturing of therapies and drug testbeds, respectively. However, most translational models remain critically limited to small and basic (homogeneous) tissue architectures, unable to capture the spatial complexity which is necessary to

recapitulate niche environments and all their essential building blocks. For instance, tissue distribution of biochemical molecules, matrix proteins, cell types, and cell differentiation states are frequently striated into gradient zones to simultaneously harbour immature cell types (eg stem cell niche zones) while driving differentiated tissue production (eg perivascular zones).

Over the last 4 decades, tissue engineering has championed the replacement of traditional cell culture systems with 3D platforms to better mimic the in vivo microenvironment. This longstanding belief is frequently validated only by process outputs (resultant cell proliferation, differentiation, function) and supernatant by-products (nutrients, metabolites, growth factors) and rarely a direct spatial inspection of the microenvironment replica in situ. In these symposia we discuss studies which spatially detail biomimicry accuracy, spatiotemporally monitor and control microenvironment performance, and optimise microenvironment features toward improved biomanufacturing process outputs.

Recent advances in spatially heterogeneous biomaterials fabrication and tissue engineering, quantitative imaging techniques, and spatiotemporal mathematical modelling are promising to faithfully recapitulate natural tissue morphogenesis and functional or dysfunctional native architecture. We propose this session to showcase promising (1) biomaterials, tissue culture, or animal model experimental techniques to model spatially zoned or gradient tissues, as well as (2) microscopy and mathematics-based computational techniques to assess, predict, and optimise spatially-heterogeneous tissues for (a) normal tissue biomanufacturing and (b) abnormal tissue modelling.

7.8. [Developing \(multiorgan\) Microphysiological Platforms to model diseases](#)

Multi-organ microphysiological systems (MPS), also known as "Body-on-a-Chip", provide human surrogates to test potential drug treatments for efficacy and off-target effects in preclinical studies and assist in the interpretation of clinical trials, as well as increasing our understanding of tissue functions and pathophysiology. Human surrogates may speed drug development by assessing, in preclinical trials, those drugs and drug combinations most likely to be both safe and efficacious for humans. MPS systems can test not only efficacy - either directly or through a model output such as binding a receptor - but also side effects on non-target organs and interactions with other drugs a patient may be taking. In the scenario of a pandemic, the rapid development of safe treatments is critical.

The symposium also focuses on new research in the design and development of new microfluidic physiological platforms that work as tissue models with a range of applications, from testing hypotheses that stem from a systems biology approach to evaluating new therapies. The understanding of the mechanisms of tissue function, which requires a detailed study of the behavior of cells and their interaction with the microenvironment (e.g. the extracellular matrix – ECM) is now feasible. Recently, advances in micro- and nanofabrication have enabled tissue engineers to construct extremely accurate biological microenvironments in vitro that closely mimic what happens in the body.

7.9. [Human musculoskeletal Organoids and Microphysiological Systems for disease modelling and personalized therapies](#)

The direct translation of human therapies from bench-to-bedside remains a challenge. Human musculoskeletal organoids and microphysiological systems are emerging approaches to accurately model human musculoskeletal diseases. They are characterized by the ability of cells to organize themselves into three-dimensional structures that recapitulates the musculoskeletal functions and processes from molecular to the cellular, or organ level. Musculoskeletal organoids and microphysiological formations are regulated by biochemical and biomechanical signals; cell-cell cross-talk. High fidelity and reliable bioengineering approaches are needed to enhance control of organoid development and further modulate the system for downstream applications. To this end, biological and biochemical factors, biofabrication technologies and micro-machined devices are investigated and used in combination or alone, to create systems that resemble the native musculoskeletal tissues structures and activities. In this symposium, we will discuss the current state and limitations of musculoskeletal organoid and

microphysiological system approaches. Biofabrication technologies and methods used to assess the development and functionality of the generated musculoskeletal organoids and microsystems will also be addressed. Furthermore, the relevance of generating musculoskeletal disease organoids using patient-derived cells to understand the exact disease pathomechanisms, and to facilitate the implementation of personalized therapies will be discussed.

7.10. Biomechanics of 3D (Bio) printed materials

More than 100 years ago, thanks to the unique collaboration between the anatomist Georg von Meyer and the civil Engineer Karl Culmann, the physician Julius Wolff proposed his famous law of bone microarchitecture adaptation in response to mechanical loads, and the biologist Wilhelm Roux intuited the likely importance, during this process, of biophysical self-regulation mechanisms at the cell level. The bases of modern mechanobiology were set, allowing improved understanding of tissue development and regeneration. Mechanobiology concepts are now employed to apprehend multifactorial biological processes like cell-extracellular matrix interaction, tissue growth, disease progressing, as well as in the development of materials and fabrication strategies for tissue repair and regeneration.

In this symposium we will explore the biomechanical issues associated with biofabricated materials. Biofabrication is a relatively recent multidisciplinary field that focuses on using a large tool box of 3D Printing based and biological building blocks assembly fabrication strategies to engineer living tissues and organs. The success of bioprinting draws from numerous parameters including composition, dynamic cell-cell and cell-material interactions and in particular biophysical cues. A particular focus of this symposium will be on research that targets the development of more complex and biomimicking solutions for tissue manufacturing, by understanding the fundamental mechanobiological pathways at the base of (bio) fabricated tissues development and maturation.

This Symposium will be jointly chaired by Dr. Miguel Castilho and Dr. Jérôme Noailly, that have vast experience in 3D printing, biofabrication, biomechanics and mechanobiology. This is the first symposium co-organized by the European Society of Biomechanics and the International Society for Biofabrication, that recently started a strategic alliance.

7.11. Biomagnetic approaches for tissue engineering and regenerative medicine

An area of expanding interest in our community is into the use of magnetic biomaterials in biomedicine. A key feature allignable with tissue engineering and regenerative medicine applications is that the properties of these materials can be controlled in a remote fashion enabling non-invasive (noncontact) forms of actuation. The use of MNPs, especially superparamagnetic iron oxide nanoparticles (SPIONs), in biomedical and tissue engineering applications has exceeded expectations, mainly because of their superparamagnetic behavior which relies on a magnetic field to be present for actuation to take place. SPIONs are composed of a magnetic core e.g. magnetite (Fe_3O_4) or maghemite (Fe_2O_3) and often polymer coated to improve their biocompatibility, structural and colloidal stability, while providing functional groups for bioactive molecules and/or ligands conjugation for targeting cells or tissues. Polymeric composites incorporating superparamagnetic iron oxide particles are one of the strategies for remotely actuatable biomaterials, using magnetic fields as exogenous mechanical triggers to exert forces over seeded cells. Another feature is their multi-modal characteristics for use with cells enabling SPIONs to be used for imaging as contrast agents, for targeting and cell delivery as well as actuation via particle movement delivering forces to receptors or heating to deliver stress to cells. In this mini symposia, we will present and discuss this growing field with speakers from our global community.

7.12. Regenerative Medicine meets Mathematical Modelling: Discovering Symbiotic Relationships

To bring new approaches to the clinic, many facets of the field must be determined and defined to the standards and rigour of the scientific, regulatory and clinical communities. With the increase in innovative technologies and cell-based therapies aiming for the clinic, there are key quantitative challenges in metrology, modelling, data

throughput, multivariate approaches for the characterisation of products, inferential monitoring of products during manufacture, technology integration and automation. In this minisymposium, we will highlight how quantitative mathematical and computational approaches can be exploited alongside state-of-the-art tissue engineering and regenerative biomedical research to address these challenges, leading to novel therapies that can more rapidly be translated to the clinic. This quantitative approach to regenerative therapies requires close interdisciplinary collaboration between mathematicians, bioengineers, biologists and clinicians to address the uncertainties, complexity and multidisciplinary challenges, and accelerate the clinical translation of new therapies from bench to bedside.

The proposed symposium will demonstrate the transformative potential of interfacing mathematical modelling and computational approaches with experimental research. Predictive mathematical models are faster and cheaper than performing numerous time consuming and expensive experiments and also go beyond the usual trial-and-error experimental approach. Mathematical modelling can be exploited to guide experimental design, enable quantitative assessment of the cellular microenvironment, integrate multiple quantitative data and hence "bridge the gap" between in vitro and in vivo models, generating experimentally testable hypotheses leading to new treatment strategies, optimise cell therapy protocols, underpin regulation via safety assessment and inform successful clinical translation. Key challenges for Regenerative Medicine have been identified, and indicate how the integration of mathematical and computational approaches into the regenerative medicine pipeline can offer a major shift towards translational outputs.

7.13. Bioelectronics - Neural Interfaces and Neurostimulation

The field of bioelectronics is poised to usher in a new paradigm in the way we diagnose and treat neurological disorders. Bioelectronic devices such as ECoG arrays and biosensors have revolutionised our understanding of neural systems and neuropathologies, while devices such as deep brain stimulators, cochlear implants, and closed-loop prosthetics have fundamentally altered the way in which we approach treatment. A significant development within bioelectronics over the past five years has been the shift away from traditional engineering approaches and the incorporation of tissue engineering & regenerative medicine considerations in the design and implementation of bioelectronic devices and systems. At the core of this approach is a fundamental appreciation for the complexity of host-device interactions which is reflected in the design of devices and systems which interact with these complex biological environments. In particular, the use of electrical stimulation to control or modulate cellular activity has been shown to be efficacious in controlling pathological neural activity, halting neurodegeneration, regenerating damaged neural tissue, and promoting wound healing. This symposium will examine applications of bioelectronics within tissue engineering and regenerative medicine including the use of soft biomaterials for neural interfaces, the incorporation of living components such as stem cells and neural progenitor cells within bionics and neural interfaces, the control of stem cell fate and neural interfaces through the use of electrical stimulus, electrical stimulation for accelerated wound healing, wide scale monitoring and modulation of neural activity in the study and treatment of neuropathologies such as dementia, and translation of diagnostic and therapeutic strategies within the field of bioelectronics.

7.14. Topography and Curvature for influencing cell behaviour

It is commonly accepted that the microenvironment surrounding cells has an influence on their survival and behaviour. Biochemical composition and mechanical characteristics such as substrate stiffness can be manipulated to regulate cell fate. However, researcher's knowledge of how cells respond to 3D geometric cues such as topography and curvature is limited, despite its potential for helping researchers advance their understanding of stem cell differentiation, disease development and regenerative medicine. 3D geometric cues are capable of influencing cell behaviour, and are a key factor in the design of biomaterials and an increasing subject of tissue engineering research. This symposium will focus on the influence of 3D cues such as topography and curvature, including manufacture and materials, and their influence on cell behaviour.

Dr Kurniawan is an Assistant Professor in the Department of Biomedical Engineering at the Eindhoven University of Technology (TU/e). His research focuses on understanding why and how cells behave the way they do in different physical environments. To answer this question, he creates biomimetic cellular environments at

multiple scales—from 2D micropatterns to 3D extracellular matrices and bioreactors—where every physical and mechanical cues to the cells can be precisely controlled. Dr Kurniawan received his PhD in 2012 from the National University of Singapore, for studying the role of matrix viscoelasticity in cancer metastasis. In 2015, he joined TU/e as an Assistant Professor in the research group Soft Tissue Engineering and Mechanobiology. He is also a member of the Institute for Complex Molecular Systems.

7.15. Biomimetic 3D models of cardiac tissue: for tissue engineering, drug testing and patient specific drug screening

Cardiovascular diseases (CVD) are the most common causes of death and serious morbidity. According to WHO, in 2030, almost 23.6 million people will die from CVDs. Myocardial infarction (MI) is one of the most common causes of heart disease. Biomaterial based solutions are the best way forward for cardiac repair, post MI, since most purely cell-based therapeutics have not successfully created new cardiac muscle. However, the current clinical materials have many problems including tissue shrinkage, retraction aneurysm and fibrosis; immunogenic reactions, extensive calcification and thrombogenicity. Also, cardiac tissue is highly anisotropic from both the perspective of mechanical behaviour and cardiomyocyte morphology, with a complex overall 3D architecture. Hence, for the development of a functional biomimetic 3D model, all these aspects need to be taken into consideration.

In this Symposium we will aim to address all these aspects in relation to the development of truly biomimetic 3D cardiac tissue models that can be used as functional cardiac patches, post MI, suitable models for the testing of novel drugs and for patient customised drug screening. The topics covered in this Symposium will include the design, processing and characterisation of a range of Biomaterials, natural and synthetic, that can be used to create the 3D models, including thermoplastics, hydrogels and hierarchical multimaterial structures, in combination with a range of cell types including induced pluripotent stem cells; and innovative processing methods such as 3D printing, 3D bioprinting and melt electrospinning. Bioreactor development and activation using mechano-stimulation, active factors- including exosomes, growth factors, miRNAs will be also part of this symposium. Modelling work required to inform the development of such a Biomimetic model will also be considered. Overall, the Symposium will aim to showcase the need of truly interdisciplinary approaches in order to achieve a fully functional and biomimetic 3D model of cardiac tissue.

7.16. Advanced imaging Technologies for Regenerative Medicine

Regenerative medicine aims to re-establish the normal function of cells, tissues or organs via cell therapy, tissue engineering or stimulation of endogenous repair. These approaches have shown great promise to improve healthcare and to promote healthy aging in the coming years. With several clinical trials underway worldwide, there is a pressing need for non-destructive label-free technologies to assess quality control criteria of cell-based therapies for clinical translation and manufacturing. Clinicians need to assess that the readiness of the cellular implants for implantation without interfering with their therapeutic potential as well as implant integrity. Similarly, the development of cell-based products in the regenerative medicine industry will benefit from non-destructive monitoring for production and quality assessment.

The need for novel non-destructive label-free technologies is also driven by the translation of 2D cell biology research to 3D regenerative medicine applications where optical assessment is not straightforward. Current imaging methods for cell-based constructs in tissue engineering and regenerative medicine are based upon a combination of different techniques, the majority of which are destructive end-point tests, such as histology, scanning electron microscopy, immunohistochemistry, and other biochemical assays. They also require the use of staining agents and sample processing, which should be avoided to limit safety issues. We invite researchers to present original research that will stimulate the ongoing effort to develop novel or translate existing monitoring technologies to assess cell distribution, viability, identity and function in three-dimensional delivery vehicles for cell-therapies and/or to establish quality control of cell-based-products.

Potential research topics include, but are not limited to:

- Optical coherence tomography
- Bioimpedance
- Multispectral imaging
- Raman spectroscopy
- Ultra high-resolution ultrasound
- Photoacoustic imaging
- Non-linear optics – second harmonic
- Diffuse optical tomography
- Auto-fluorescence

7.17. Tissue Organoids for cartilage and joint disease Modeling

The proper functioning of the articular joint depends on the maintenance of joint homeostasis, a dynamic equilibrium between anabolic and catabolic processes within all the components of the joint. The intricate interaction between these different components and cell types makes it quite challenging to recapitulate both healthy and pathological joint physiology in a model.

Recent advances in engineering and biology have resulted in the development of more physiologically relevant models that are able to recapitulate human diseases, accurately mimicking the in vivo situation. These microphysiological systems (MPS) enable the analysis of biophysical and biochemical cues in a controlled environment, thus eliminating the variability found in animal models. Further, they allow to recreate the physiological response to different stimuli, including mechanical stimulation such as load bearing. In this respect, the articular joint represents a unique challenge, due to its multi-tissue composition with each tissue being exposed to different types of mechanical stimulation. To date, organs-on-a-chip have been reported for tissues in the cardiac, musculoskeletal, nervous, respiratory, endocrine, gastrointestinal, reproductive systems, and cancer. These systems have been created using tissue-specific cells, tissue-derived adult stem cells, or combination thereof. More recently, there is a push for generating these MPS and OC from iPSCs, due to their inherent broader differentiation potential. The primary rationale for the development of a platform that uses human tissues is to apply them to evaluate the efficacy, safety, and toxicity of promising therapies.

7.18. Tissue organoids for renal disease modeling

Worldwide, the chronic shortage of kidney donors has created an urgent need for tissue-engineered alternatives. A number of tissue engineering strategies combine three-dimensional (3D) culture systems with developmental biology principles to generate de novo kidney tissue. These approaches start with embryonic kidney fragments or kidney progenitor cells that are induced stepwise to develop into 3D kidney tissue. Other strategies use scaffolds obtained from human or animal kidneys through decellularization as a template for reconstructing a kidney graft, which is then seeded with stem or progenitor cells or living membranes capable of active transport of uremic toxins. Although these approaches have provided very promising results, many challenges must be overcome before engineered kidneys become clinically useful, including size, sufficient vascularization, immunological issues, and proper connection to the host vascular and draining system. In parallel, the use of advanced kidney-on-a-chip as disease modelling platforms could bring further insight in understanding the mechanism of diseases progression and the development of new therapeutics. Despite being often considered in isolation, kidney disease typically appears alongside with other comorbidities, highlighting a complex pathophysiology. There is mounting evidence supporting the ongoing inter-communication between the kidneys and other organs. this symposium will aim at showcasing the recent developments in understanding kidney disease and the inter-organ communication in the context of kidney disease.

8. Regulatory, Business, Consortia, Patients, SYIS, Sister societies

8.1. Regenerative strategies and surface tailoring of implantable prosthesis for their better integration.

The benefits provided to patients by biomedical implants in terms of pain reduction, mobility and quality of life are incommensurable. Additionally, with the increasing life expectancy and the aging of world population, the number of implanted prosthesis increases every year. A variety of surface modifications/coatings are currently used to enhance the short- and long-term performance of implants. In the orthopedic field, this can be achieved by encouraging bone in-growth and enhancing fixation. Nevertheless, despite their overwhelming success over the long term (> 7 years), the implantation of an orthopedic device is usually associated with adverse local and remote tissue responses, which often result in loosening phenomena and implant instability, requiring revision surgery with replacement of the loosened components. However, revision surgeries show a higher morbidity and a higher complication rate than primary implantation surgery, thus increasing costs and the risk of adverse side effects. Research groups and leading companies in the field are currently focusing their efforts on the design of a new generation of implants with the potential to reduce the risk of undesired tissue responses while promoting tissue integration and regeneration and increasing patient quality of life. Moreover, with the advancement of biomedical research and the development of a new generation of implantable devices, the set-up of standardized, highly-controllable preclinical characterization tools is becoming an urgent need. In this regard, the design and optimization of three-dimensional (3D) bioengineered models of the bone tissue represent a significant advancement, overcoming the limitations of already used *in vitro* and *in vivo* models (e.g., lack of repeatability and standardization, difficult comparisons among already published works), with additional advantages in terms of ethical and economic issues.

In the end, we expect that this symposium will elucidate how newly developed knowledge will enable clinical translation and commercialization of a new generation of implants.

8.2. Cardiac repair

REGMEDXB CV moonshot on cardiac repair is the starting point

8.3. Translational Aspects of 3D

The adoption of 3D printing, bioprinting, and other advanced techniques are increasingly used in new development of biologically inspired reparative and regenerative products. In addition to advantages they may offer, these technologies have their own specific properties and limitations. While many of these processes use the same synthetic and biologic materials already used in a variety of marketed products, process-based risks must be reasonably determined and reduced to a safe level.

There are notable examples of 3D printed products both in the in different countries, with early adoption mainly in the creation of surgical guides and models. The ultimate promise for many is the potential to build biologically inspired engineered tissue structures, up to full organ replacements, to advance biomedical products well beyond the current limits.

This special symposium comprises a two-part discussion focused on various translational considerations of 3D printed constructs, including (1) advancing technology out of the lab, and (2) translating technologies into products for broad clinical use. This will include also discussion of safety, regulatory and funding aspects.

8.4. Orthopaedic therapies- Biologically inspired reparative therapies- translational hurdles from bench to clinic

Advances in our understanding of stem cells, innovative biomimetic materials, natural biological factors and their role in skeletal repair, have advanced apace in the last decades. However, the translation of therapies to restore the function of traumatised or lost skeletal tissue as a consequence of age or disease still remains a significant challenge. In essence, the route to clinical adoption is fraught with technical and translational obstacles. A wealth of promising academic approaches have failed to cross from exciting preclinical bench science to clinical reality, in the so-called “valley of death.”

This workshop will focus on bench to clinical translation and industrial challenges therein with a focus on the clinical, regulatory, market and, critically, safety, including immune responses of any therapeutic product for patient application. The workshop will explore, outlining the pitfalls in clinical development, first hand, from two biotechnology companies using two exemplars; i) clay-based nanomaterials for biologics and drug delivery, with a particular focus on low dose bone morphogenic protein delivery for bone repair, as well as their exciting possibilities for hard and soft tissue regenerative medicine and ii) Blood serum - an underutilised but well-researched therapeutic tool with unique regenerative properties. The importance of clinical involvement and the need for multidisciplinary will be covered.

8.5. SINERGIA H2020 project - Advanced technologies for drug discovery and precision medicine: in vitro modelling human physiology and disease

Discovering new therapeutic compounds is a fundamental branch of current biomedical research with immediate and substantial impact on society, health systems and economy. Subsequent to the discovery of lead compounds, a key step in the drug development process (DDP) is to predict information on safety, efficacy and mechanisms of action of a candidate molecule in physiological and pathological preclinical models that approximate the human body (lead optimization). However, a large gap exists between current in vitro strategies, representing the cheapest and easiest drug screening tools with the drawbacks of low-precision, and in vivo animal experimentation that provides higher resemblance to native complexity at high running costs and raising ethical issues and uncertainty due to inter-species differences.

Chances of clinical trial success are currently about 10% and the total time-to-market of a candidate drug compound is estimated to be around 12 years. There is general consensus that reasons for this critical scenario are to be found in the limited predictive capabilities of most of the existing preclinical screening tools.

The SINERGIA project targets the urgent need for efficient and predictive in vitro preclinical drug screening tools. SINERGIA aims at establishing new in vitro models enabling for drug discovery by taking advantage of cutting-edge technologies that are currently emerging as extremely promising and innovative, either alone or through their possible combinations: i) organs-on-chip, ii) bioreactors for advanced 3D cell cultures, iii) 3D Bioprinting, iv) induced Pluripotent Stem Cells (iPSCs).

SINERGIA was financed by the EU-H2020 in the framework of MSCA-ITN-ETN. SINERGIA Consortium is composed by academic sector, contract research organizations (CROs), Biotech companies, hospitals.

8.6. ESAO @ TERMIS 2021

The European Society for Artificial Organs (ESAO) is a scientific society joining scientists and medical professionals with an interest in developing artificial life-supporting devices for many clinical conditions in which organ failure causes severe health limitations such as cardiac, liver, kidney or lung. This society is also affiliated at the International Federation for Artificial Organs (IFAO) joining the European society with other intercontinental colleagues.

The large experience of many members of ESAO in developing artificial organs over the last 50+ years is a strong asset that can bring together the knowledge developed in complimentary fields for the benefit of patients desperately in need of clinical solutions. The past experience of successes and failures in developing artificial organs provides an invaluable repository of information and experience that should be widely shared with the international scientific community and has obvious interest for the community of Tissue Engineering and Regenerative Medicine.

8.7. Ethics Parallel Research in Regenerative Medicine

Emerging technologies in Regenerative Medicine – such as iPS cell applications, 3D bioprinting and supramolecular material design – pose new and challenging questions of ethics, governance and societal impact. We may now ask: How can we arrange stem cell research in a responsible manner? How could choices in biomaterial design (unintendedly) impact the final clinical product?

Moreover, the new reality of these technologies might not fit existing regulation and ethical guidelines, and could affect the practice of healthcare and its context: We no longer only aim to repair what was broken, but to regenerate the body to its original state of health.

These questions require the involvement of ethicists and other relevant stakeholders during the technological development. In this session our approach of Ethics Parallel Research is presented. It aims to involve ethics in emerging biomedical technologies starting from the early phases of development to the final stages of clinical translation and societal implementation. This is done by ‘thinking with’ rather than ‘thinking about’ research practice and engaging different stakeholders in order to anticipate and guide ethical and societal challenges in a timely manner.

The session is chaired by two experienced ethicists, who will present the six ingredients of Ethics Parallel Research in the context of emerging technologies in Regenerative Medicine. Two early stage researchers will exemplify the method by presenting their own approaches in the ethics of stem cell and biomaterial research. Our keynote speaker is an expert in kidney development and regeneration and will present her view on ethical issues in biomedical practice. The session will end with a plenary discussion, offering the participants an opportunity to reflect on their own role as moral actors in the regenerative field.

8.8. Bridging the translation: Clinician, Researchers and Industry.

Over the last two decades, musculoskeletal tissue engineering and regenerative medicine have been one of the most fast-growing fields. Thousands of biomaterials have been developed. However, there are still big gaps between scientific research, commercialisation and clinical translation. Therefore, it is the time for the researchers to meet the clinicians and industry partners for stimulating communication across the different sectors and promoting knowledge transfer.

This symposium will invite keynote/invited speakers from academia, industry and clinician to talks about current advance and challenges in stem cells/tissue engineering ‘pre-clinical research’, the routes to ‘commercialisation’ and ‘clinical translation’.

The chair, Dr Yang (University of Leeds, UK), has over 15 years of expertise in clinical orthopaedics and 20 years in bone and cartilage tissue engineering research, in particular in pre-clinical testing. The co-chair, Professor Zhongyu Li (Wake Forest University, USA), has expertise in clinical orthopaedics and research on peripheral nerve tissue engineering and regeneration.

The organiser, Dr Yang has successfully organised/chaired several symposia on bone/osteochondral tissue engineering topics for TERMIS-WCs 2012/2015, TERMIS-AP 2013/2014/2016/2017, TERMIS EU 2019 and the forthcoming TERMIS AP 2020. Previously, he invited clinicians from Japan, USA and UK to give talks at these symposia. He has very wide contact/collaboration with clinicians in the UK, USA, China, Japan, Malaysia and industry partners in the USA, UK and China.

8.9. Soft and hard tissue adhesives: managing the challenges of translation from lab to clinical application

The goal is to enable researchers developing tissue adhesives to focus on the issues of translating from laboratory to patient use. The new MDR (2017) mandates an evidence-based approach that will make innovation in adhesive biomaterials hard to achieve as there are very few established predicate materials in clinical use.

Tissue adhesive candidates fall broadly into two groups: synthetic chemically engineered and bioinspired biomimetic adhesives. Example of the former are n-butyl cyanoacrylates and novel polyurethanes whilst the latter includes adhesives derived from biology such as fibrin glues and adhesive proteins from a range of animal and plant sources. The mechanisms of adhesion differ and some may fall into drug regulation and others may be considered devices.

Despite the advances in surgical techniques there are many unmet clinical needs where an adhesive technology would either augment or replace current standard treatments. Examples in soft tissue are meniscal tear repair and cartilage scaffolds where sutures are the main attachment strategy and an effective adhesive technology would transform procedures. Bone fractures close to joints have osteochondral bone fragments that standard implants cannot fixate. The diversity in tissue types and properties will not enable a single adhesive to bond all tissues and it is necessary to engineer tissue specific adhesives/joining mechanisms ideally in the same way that the body does.

Key tissue adhesive properties are bio-stimulation that choreographs appropriate tissue formation, some form of delivery and immediate support for the biomaterial, and the ability to selectively form bonds only with the target tissues. The tissue engineering opportunity is often when the desired functionality has to be improved. For example, attaching hydrogels to soft internal tissues for the development of various biomedical devices. Tough, highly adhesive, hydrogels may lack injectability and require contacting surface conditioning to realise the full bonding strength with soft tissues. On the other hand, in osteochondral fragment fixation injectable bioceramics may lack the interconnected porosity and cellular biostimulation needed for rapid osteointegration in hard tissues. Adopting a bioinspired design approach strategy opens a broader window of physicochemical properties in both soft and calcified tissue applications. An example of this is the substitution of Phosphoserine for the Dopa in adhesive formulations. Phosphoserine plays roles both in cellular adhesion and in extracellular signalling transactions and in combination with structural bioceramics can be biostimulative to a degree usually associated with growth factors. This enables faster and more complete healing and regeneration of fractured cancellous bone than seen with current bioceramics approved for orthopaedic use.

For industry to translate a tissue adhesive candidate it would require GLP level preclinical evidence of safety and efficacy in animal models that adequately mirror the clinical situation. It would need to address an unmet need area of sufficient size to make the investment attractive and that would have a clear path to reimbursement. Any new paradigm of treatment with an adhesive has to have a well thought out patient journey that clearly demonstrates the clinical benefit to patient, surgeon and ultimately the healthcare providers.

8.10. [Mechanobiology and risk assessment of biomaterials for musculo-skeletal tissues regeneration](#)

Biomaterials along with engineered tissues and implants are essential part of any operations for tissue repair and regenerations. Besides biological and chemical properties, mechanical properties are of equal importance for tissue engineered applications, including inter alia hydrogels, organoids, composites and scaffolds. Biomechanical properties are also critical to consider a proper cell culture system, and they need to be evaluated in a correct and physiologically relevant way. When cell culture systems become more specific, there are also more scientific, technical, and regulative demands to quantify the properties.

Many different methods of biomechanical testing are being used for this purpose but, unfortunately, they are often lacking consistency and details as well as giving rather different outcomes. It creates a difficulty to justify required properties and performance of the biomaterials for practical applications, so it is not easy to obtain realistic, true properties. From translational point of view, proper biomechanical characterization is also required for regulative approval, suitability for the purpose and for risk assessment.

This symposium focuses on practical biomechanical characterization of biomaterials for musculo-skeletal tissue engineering and adjacent ATMP and medical devices. It comprises mechanobiology phenomena, biomechanical features and integrated biomechanology. Topic will cover also essentials of proper experimental methods, ways of data processing and possible sources of errors and misinterpretation of these experimental data. Several cases will be presented, and the considerations of the correct biomechanical characterization and risk assessment are discussed.

8.11. Strategies To Enhance Bone Regeneration

Bone regeneration consists of a well-orchestrated series of biological events of bone induction and conduction, involving a number of cell types and intracellular and extracellular molecular-signalling pathways, with a definable temporal and spatial sequence, aiming to optimise skeletal repair and restore skeletal function. There are several clinical conditions that require enhancement of bone regeneration either locally or systemically, and various methods are currently used to augment or accelerate bone repair, depending on the healing potential and the specific requirements of each case. This symposium will be chaired by two top clinicians with many years of clinical experience in bone defect treatment: Prof. Elias Panagiotopoulos (ecpanagi@med.upatras.gr) who is also the coordination for a H2020 Project on Smart Bone Regeneration, and Prof. Peter Giannoudis, with many years of experience in clinical testing of new devices (pgiannoudi@aol.com). In this symposium strategies to enhance bone repair will be discussed by the chairs and invited speakers covering all the currently approaches used in the experimental and clinical setting by a faculty of experts (as seen below).

The key-note presentation will be related to state-of-the-art Drug Delivery and Targeting approaches for enhancing bone and in general tissue regeneration; “Novel Drug Delivery and Targeting Approaches for Tissue Regeneration” by Prof. S.G. Antimisiaris (santimis@upatras.gr), an expert in the field with >25 years of research experience and participation in many large collaborative research programs.

8.12. H2020-MSCA-RISE BAMOS project session: Biomaterials and Additive Manufacturing for early intervention of osteoarthritis

Osteoarthritis (OA) is a degenerative joint disease, typified by a loss of quality of cartilage and changes in bone at the interface of a joint, resulting in pain, stiffness and reduced mobility. H2020 BAMOS project aims to establish and embed a new collaboration between seven internationally leading research organisations (four universities, two healthcare provider and one manufacturer with expertise in additive manufacturing) in addressing the challenges in OA treatment by providing novel cost effective osteochondral scaffold technology for early intervention of OA to delay or avoid the joint replacement operations by develop new materials and manufacturing technologies for the fabrication of custom-tailored osteochondral scaffolds. This session is to share the updated achievement of the BAMOS project within TERMIS community, and interact with colleagues who have the same interest in early OA intervention.

8.13. Biomaterials for Tissue Engineering and Regenerative Medicine

The symposium is a combined effort by different biomaterial and tissue engineering related societies within Europe. Biomaterials play a key role in medicine and these have made a major impact on the field of Tissue Engineering and Regenerative Medicine. This symposium introduces various speakers from the different societies and illustrate how biomaterials are used across Europe with a global impact. The focus is on engineering tissues for clinical and preclinical applications using different manufacturing approaches and a wide range of materials suitable for high-end fabrication methods. The interface with materials and cells is a fundamental aspect in tissue engineering as cells are highly susceptible towards their microenvironment and need both biochemical and biophysical stimuli to direct them into a functional construct. The final functionality of the tissue is only as good as the complex organization of cells within the tissue. Hence, close collaboration between tissue inherent cells is of utmost importance and combining different cells is still a highly challenging endeavor. The symposium will shed light on these complex aspects and just as cells need each other to function, the various national societies need each other in order to bring together the scientific disciplines needed to advance the field of Tissue Engineering and Regenerative Medicine.

8.14. Transition of bio-based TE products to market: processing scalability, quality control, sustainability, regulatory aspects

Nature-derived polymers like silk, collagen, elastin, chitosan have become a powerful platform for innovative medical devices. The great interest in the biomedical field is due to their general non-toxicity, renewable nature,

enzymatic degradation, presence of cell-instructive sequences, tunability and processability. Biopolymers can be isolated from natural sources, industrial waste (ex. Textile), or food waste (ex. Chitin), or from advanced genetic engineering procedures (ex. Bacteria). Several methods for advanced manufacturing and nanotechnology were defined providing the specific required properties to the final construct and validated in vitro and in vivo. Scientists involved in new biomaterials for biomedical applications, are considering nature-derived product commercialization and their use in clinics.

With a keen eye on the commercialization of biopolymers-based products, the symposium will cover the value chain of nature-derived products for use in biomaterials and tissue engineering/regenerative medicine contexts. Specifically, will be focused on regulatory aspects and needs, formulations reproducibility and processing quality control, process scalability, and on design of more successfully TERM products based on biopolymers.

The symposium focus will be on: Scalability of new manufacturing methods to fabricate advanced biopolymers-based systems for medical needs; Aspects of constructs behavior in vivo: considering clinical perspectives; Regulatory aspects and needs; Biopolymers on the TE market: analysis of products already on the market.

8.15. 3D thyroid gland models to screen the influence of endocrine disruptors.

The endocrine system of the human body consists of a group of ductless glands which produce and release substances (hormones) to control a number of essential physiologic functions. Examples of endocrine glands are the thyroid and parathyroid gland located in the neck region, the hypothalamus and pituitary gland located in the brain, and many others. Research on glands is performed to a large extent in animal models which, due to interspecies differences, clearly limits the relevance of the results gained. This includes the possibility of disease modelling and advancing regenerative approaches but also using these in vivo models to screen chemical compounds for their potential to act as so-called endocrine disruptors. Novel and more complex in vitro models, such as stem cell-derived organoids, are for these reasons of utmost importance and gradually researchers are devising new innovative strategies. Beyond this, these models may help to better understand the role of sexual dimorphism in relation to endocrine disruptors. The thyroid gland, as part of the central hypothalamic-pituitary-thyroid axis, plays a vital role in development, differentiation and maturation but also in energy homeostasis and metabolism. Thyroid hormones, synthesized and stored in the thyroid follicles, target multiple organs and have organ-specific effects. Because of its central role, the development of 3D thyroid gland models, e.g. to efficiently screen the influence of endocrine disruptors in high-throughput, is one of the major goals in the field. Recently, important progress has been made towards realising protocols to derive thyroid progenitor cells and generate follicles from pluripotent stem cells. Researchers have also investigated the extracellular matrix composition of different endocrine glands including the thyroid. These building blocks are converging with bioengineering approaches to develop novel 3D in vitro models, to mimic the complex function of these glands for long periods of culture with fluidics and bioreactor-based approaches.

8.16. TERMIS-SYIS meets FIRM and yESAO: The next generation of research leaders

Young scientists across the world and multiple disciplines form organized societies such as TERMIS Student and Young Investigator Section (SYIS), Future Investigators of Regenerative Medicine (FIRM) and young section of The European Society for Artificial Organs (yESAO) to gather together and to further develop their professional and scientific skills. These societies provide a unique niche and enable the formation of the next generation of leaders in science. Typically, these societies arrange annual meetings to discuss the most burning questions, to meet today's leading experts, to exchange knowledge, network and to support each other. In this symposium, we would like to bring together young scientists from all around the world and promote the activities of TERMIS-SYIS, FIRM and yESAO societies. This joint symposium will provide opportunity to showcase the latest developments in tissue engineering, regenerative medicine, artificial organ technology, regulatory and clinical translation to achieve the ultimate goal – help patients. This joint symposium, chaired by the representatives of TERMIS-SYIS, FIRM and yESAO will feature one keynote speaker - Prof Nuno Neves from the 3B's Research Group at the University of Minho, Portugal. Prof Neves main area of research is the development of biomaterials from natural origin polymers that are used for a range of biomedical applications in combination with stem and



progenitor cells for tissue engineering and regenerative medicine strategies for bone, cartilage, kidney or thymus and drug delivery devices.