**Protein and DNA Delivery from Fibrin Gels to Induce Nerve Regeneration**

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**Introduction**

Spinal cord regeneration is limited by inhibitory factors and the lack of stimulating growth factors. Fibrin can be harvested autologously and used to create biocompatible injectable hydrogels. Fibrin gels can be modified with fibronectin fragments that are designed to bind specific integrins [1] and growth factors, such as nerve growth factor (NGF) neurotrophin-3 (NT-3), and brain derived growth factor (BDNF). Modified gels allow for presentation of growth factors in the vicinity of the regenerating cells through integrin mediated cell binding. In addition, DNA can be delivery from fibrin gels using PPS-PEG-PEI micelles to deliver DNA or RNA after spinal cord injury.

**Materials and Methods**

A chick dorsal root ganglion (DRG) model was used to analyze neurite extension in 3D fibrin gels modified with different fibronectin fragments and neurotrophic factors. The efficiency of DNA delivery with PPS-PEG-PEI micelles inside fibrin gels to local cells was analyzed using plasmid encoding for luciferase. Transgene expression was explored in vitro with NIH3T3 cells, and in vivo within a mouse tail wound healing model.

**Results**

Fibrin gels modified with fibronectin based proteins and neurotrophic factors enhanced neurite extension of DRGs cultured inside a 3D fibrin gel.

![Fig. 1. DRG extension in gel modified with and without fibronectin fragment and BDNF.](image)

The release of DNA micelles from fibrin gels was very slow, with most of the DNA still left in the gel after one week. DNA delivery by the micelles recovered after gel degradation to cells resulted in transfection proving their bioactivity. Transfection of NIH3T3 cells inside the gel in vitro was dependent on the initial cell seeding. In vivo, fibrin gels mixed with DNA micelles were injected in a wound tail model and resulted in transgene expression after 1 week, in contrast to fibrin gels mixed with plasmid.

![Fig. 2. Transgene expression in vivo](image)

**Discussion and Conclusions**

Fibrin gels modified with fibronectin fragments and neurotrophic factors may enhance neurite extension of DRGs cultured inside a 3D fibrin gel due to the synergistic effect of integrin binding and protein presentation. Fibrin gels mixed with PEI based DNA micelles may have resulted to transgene expression in vitro and in vivo due to the reduced toxicity compared to PEI polyplexes [2].

**References**


**Acknowledgments**

This project was funded in part by the EU FP7 project Angioscaff.

**Disclosures**

The EPFL has filed for patent protection on some of the materials used in this work.