Biodegradable Polypeptide-Based Hydrogels for Soft Tissue Regeneration
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Introduction
Biodegradable hydrogels based on poly(α-amino acid)s (PAA) have been investigated as potential scaffolds for soft tissue implants, such as scaffolds for neural tissue regeneration. PAAs, due to their polypeptide backbone are prone to enzymatic hydrolysis, which can be controlled through copolymerization or modification of PAA side chains. This contribution is focused on the feasibility of preparing soft, highly swollen covalently crosslinked hydrogels based on biodegradable PAAs. The effect of biomimetic modification of hydrogels with RGDS and YIGSR peptides on the seeding efficiency of porcine mesenchymal stem cells will be studied in vitro.

Materials and Methods
Covalently crosslinked hydrogels were formed by radical polymerization of methacryloylated macromonomer poly[\(N^2\)-(2-hydroxyethyl)-L-glutamine-stat-L-alanine-stat-methacryloyllysine] poly(HEG-stat-Ala-stat-MALys) with minority of 2-hydroxyethyl methacrylate (HEMA) and with/without adhesive peptides (methacryloyl-GGGRGDSG-OH and methacryloyl-GGGYIGSR-OH) in water. In this system, the polypeptide macromonomer serves as a biodegradable crosslinker.

Results
Mechanical stability of gels with different ratio of solids/water and co-polypeptide/HEMA was tested by swelling. Equilibrium water content of hydrogels ranged from 85-95 % depending on hydrogel composition. Two types of porosity were formed in gels. Primary porosity (channels of 100-150 µm in diameter) was prepared by leaching solid organic porogen. Orientation of porogen makes it possible to provide oriented porosity in the gel. Secondary, isotropic interconnected macropores (5-30 µm) formed by phase separation of small fraction of polyHEMA in presence of water are shown as well. Our cell culture experiments proved that biomimetic modification with RGD and YIGSR sequences enhanced MSCs ability to attach, survive and form proper cellular morphology on the hydrogel surface.

Discussion and Conclusions
Crosslinked high-water-content hydrogels based on biodegradable poly(α-amino acid)s can be prepared from methacryloylated PAAs through copolymerization with HEMA. Modification of hydrogels with biomimetic peptides was achieved through copolymerization with methacryloylated peptides during gel formation. Different porous morphology of gels can support flow of nutrients and oxygen through soft material during cell cultivation. While the highly hydrophilic gels are rather resistant to unspecific protein adsorption and, therefore, are expected to exhibit low affinity to cell adhesion, the effect of modification with adhesive peptides, which does not significantly change gross physical properties of gels, revealed the feasibility of controlling specific biomaterial/cell interactions through cellular adhesion receptors binding. Short synthetic adhesive peptides in gels can be more practical in real use than the whole protein of extracellular matrix (ECM), with demanding production and purification. Also the cells seeded to the hydrogels will eventually produce their own ECM and, in this context, the most important thing is to enable the initial cell attachment and scaffold colonization.

Acknowledgments
Support from the Grant Agency of the Academy of Sciences of the Czech Republic (grant No. KJB400500801) and Ministry of Education of CR Research Centers Program (grant no.: 1M0538) is acknowledged.

Disclosures
Authors have nothing to disclose.