

Polymerized peptide-amphiphile microstructures for cell-based microsystems

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INTRODUCTION: Biomimetic interfaces that allow interactions with biological cells in a specific desired way are forming a core area of research in bioengineered materials¹. Cell-based microsystems are becoming increasingly important in diagnostics and therapeutics. We have recently described the synthesis of polymerizable peptide-amphiphiles that can be used to form planar as well as 3-D architectures^{2,3}. The well known "RGD" peptide linked to a polymerized diacetylenic lipid monolayer is shown to promote cell-adhesion in a controlled way. These biologically active structures are stable, and can be organized on conventional solid substrates. We also introduce a design principle for the development of cell-based microarrays by using surface-immobilized polymerized vesicles that expose a bioactive ligand at the outer surface.

METHODS: Peptide synthesis was done on solid-phase using standard F-moc chemistry protocols. Peptide amphiphiles were purified on RP-HPLC and characterized by ESI-MS, NMR and FTIR. Self-assembled Langmuir monolayers were polymerized on the water-air interface and transferred subsequently to a substrate, which is coated with a surface-attached polymer gel. The monolayer was fixed to the polymer by photochemical⁴ means [Fig. 1A]. These monolayers were studied with respect to the phase-behaviour and topography using LBK techniques, BAM and AFM, respectively. Vesicles were prepared in water and studied by UV-Vis spectroscopy, FTIR and TEM. Microarrays were prepared by microcontact printing of the polymerized vesicles on a cell-inhibiting hydrogel with a subsequent photochemical immobilization of the polymerised vesicles.

RESULTS: Several parameters have been mapped out with respect to the phase-behaviour and polymerization in order to produce highly stable bioactive surfaces. The surface concentration of the polymerized peptide-amphiphile monolayer was controlled by addition of an analogous polymerizable amphiphile that carried no peptide head-group. The monolayers having various amounts of peptide exposed at the surface were found to influence the adhesion of human microvasculature endothelial cells in a concentration dependent manner [Fig. 1B].

Polymerized vesicles were prepared using the same peptide-amphiphiles mixtures. The polymerized vesicles were printed on a polymer hydrogel that does not promote cell-adhesion, and subsequently, the vesicles are covalently linked to the underlying surface by photochemical means. The microarrays were characterized with respect to the surface-morphology, immobilization efficiency, and the possibility to direct the cell-adhesion in a spatially controlled manner.

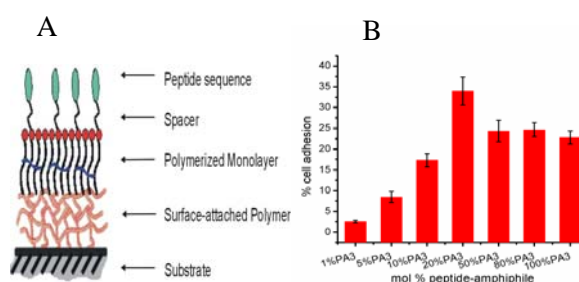


Fig. 1:[A] Scheme of a polymer supported peptide amphiphile monolayer,[B] Amount of adherent cells as a function of the molar concentration of ligand in the peptide-amphiphile monolayers.

DISCUSSION & CONCLUSIONS: 2D and 3D architectures composed of polymerized peptide-amphiphiles have been prepared. Supported polymerized monolayers show enhanced stability and promote the adhesion of microvasculature endothelial cells in a concentration dependent manner. Polymerized vesicles can be used to design microarrays that consist of cell-adhesion promoting areas (i.e. spots) surrounded by a hydrogel layer that does not support the attachment of cells.

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ACKNOWLEDGEMENTS: Financial support through the Emmy-Noether Program of the DFG under grant number BI738/1-2/1-3, and the Fonds der chemischen Industrie is gratefully acknowledged. We thank Dr. Ralf Thomann for TEM measurements, A. Kopyshv and Dr. S. Santer for AFM measurements, Dr. J. W  rth and C. Warth for ESI-MS.