High Complexity Peptide Libraries on a Microchip

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We present a novel approach for the combinatorial synthesis of high complexity peptide arrays utilizing amino acid particles. These microparticles comprise the activated, proteinogenic amino acids and can be charged by friction. This allows the consecutive addressing of monomer packages by means of electrostatic charged patterns generated on a solid support, where they are melted to release and couple the amino acids to the surface. Charge patterns are generated on CMOS microchips equipped with an array of individually triggered pixel electrodes. Resolution of synthesis is only restrained by the size of the chip structures and the particles employed. Our new method circumvents the limitations of solvent-based combinatorial peptide synthesis (e.g. spotting and printing methods) and should allow to increasing the peptide density from about 20 to 40.000 spots/cm^2.

In proof-of-principle experiments we have synthesized chessboard like patterns of two different peptides with a resolution of 10.000 spots/cm^2. Peptide synthesis was done on microchips which have been modified with poly(ethylene glycol) methacrylate grafted polymer films. These films are stable under usual Merrifield conditions and allow NH_2-loading up to 10 nmol/cm^2. Furthermore, films show appropriate swelling properties for peptide synthesis and prevent unspecific protein adsorption with respect to immunoassays.

In future applications, we aim at producing diagnostic chips for biomedical research and at developing a functional tool for proteome analysis.