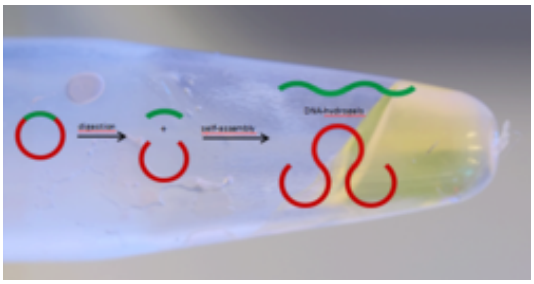
Technology Offer

DNA hydrogels from linear building blocks

Reference Number 99-00075

Challenge
Hydrogels play an important role as research tools as well as in biomedical applications. The desired properties of a gel are determined by the chemical properties of its constituents. As a biopolymer, DNA has specific properties which are particularly advantageous for the formation of hydrogels. DNA is hydrophilic, biocompatible, forms predictable secondary structures by sequence-specific hybridization, under certain conditions forms hydrogels spontaneously, and can be incorporated into synthetic polymers. Accordingly, DNA hydrogels are applicable in many biomedical fields (e.g. tissue culture, drug delivery, cell-free protein production). Presently, available preparation methods are based on branched DNA building blocks (X, Y or T-shaped) or use chemical cross-linkers. However, these methods have significant drawbacks such as that the synthesis of the required branched DNA oligomers is expensive, chemical cross-linkers may have unwanted side-effects and such hydrogels are not biodegradable. Accordingly, processes are required that allow cost-effective production of homogenous pristine DNA hydrogels with advantageous properties.



DNA hydrogel self-assembly from dsDNA building blocks

Technology
The present invention relates to a method for producing pristine DNA hydrogels from linear dsDNA building blocks. The method uses base DNA as starting point that may be any DNA that is available at large scale, preferably from biological or biotechnological sources, e.g. plasmid DNA which can be generated in extraordinary large scale by fermentation. The bulk DNA is digested enzymatically to obtain linear dsDNA building blocks which subsequently are assembled by hybridization and/or ligation. Moreover, the plasmid DNA may be manipulated to contain repetitive elements that allow obtaining several dsDNA building blocks of identical sequence from a single plasmid copy upon enzymatic digestion. While the DNA hydrogel can be generated entirely from linear DNA building blocks, non-linear DNA building blocks may be added in minor amounts for modification of its physical properties, for example to adjust the rheological properties (stiffness) of the hydrogel. Depending on the enzyme used for digestion,dsDNA building blocks comprising single-strand DNA (ssDNA) overhangs (sticky ends) can be obtained. These hydrogels are formed solely by hybridization and are thus thermo-responsive. In addition, one or more types of functionalized DNA, LNA or PNA oligomers can be added during self-assembly or post hydrogel formation to obtain functionalized DNA hydrogels. The inventive DNA hydrogels can be applied in the field of cell transplant therapy, biomineralization, tissue engineering, gene therapy, drug delivery, wound healing, cell culture, cell-free protein biosynthesis, bio-sensing, cosmetics, 3D printing, biocatalysis or biofuel cells.

Commercial Opportunity
The technology is offered for co-development and/or licensing

Development Status
First thermoreactive DNA hydrogels were obtained. Further prototypes for specific 3D cell-culture applications and cell-free protein production are in preparation.

Patent Situation
Priority was filed in April 2016 at the EPO, an international PCT-application was filed in April 2017 (WO2017178594).

Further Reading
Nöll et al. 2017. Pristine DNA Hydrogels from Biotechnologically Derived Plasmid DNA. Angew. Chem. Int. Ed. 10.1002/anie.201705001

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