FEBS Lecture

**FL**

The discovery of Spiegelzymes and their potentials in molecular biology and medicine

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The last 30 years we have seen a very rapid development of the field of RNA technologies. The developments to this extent were surely not for seen by the members of the RNA Tie Club 57 years ago. As a matter of fact, it was at that time that the scientists in the field discussed whether or not RNA molecules could form such structures as Watson-Crick base pairs. It was Alexander Rich, who predicted that Watson-Crick base pairs would take place in RNA and he even predicted that antisense mechanisms could regulate protein synthesis. When Thomas R. Cech and Sidney Altman discovered that RNA molecules were able to catalyze biological reactions, the idea was born that all life most likely originated from an RNA world. We in Berlin were able to found in 1998 the Berlin Network for RNA Technologies, with the goal to further pursue the structural and functional potentials of RNA molecules. In my presentation I will summarize the work we have done in my group within this RNA Network, which will cover RNA structures, as determined by x-ray analysis, at high resolution from crystals grown under micro gravity conditions in seventeen different space missions. Also the development of high affinity mirror image nucleic acids will be described, which are like aptamers, except that their nucleic acids do not consist of the natural D-form nucleotides, but the L-form. These L-form aptamers we are calling Spiegelmers and they have a number of advantages when compared with aptamers. First, they are very stable in human sera and cells, because since nature does not make L-nucleic acids, there was no need to develop any enzymes hydrolyzing the L-form of nucleic acids. Thus, Spiegelzymes are extremely stable when compared with other forms of nucleic acids. Second, Spiegelmers can be compared with protein antibodies, and indeed Apatamers and Spiegelmers can assume very similar functions to antibodies. Third, Spiegelmers are considerably smaller than antibodies and they are easily synthesized by nucleic acid synthesizers. And fourth, Spiegelmers are not toxic or immunogenic and therefore most likely ideally suited for the development of new types of pharmaceutical drugs. As a matter of fact, the Noxxon Pharma AG in Berlin is currently entering the clinical test phases IIA with several of their Spiegelmers. After we had developed the Spiegelmers, we have recently been able to develop, also on a mirror image basis, ribozymes, which we call Spiegelzymes, and which can hydrolyze sequence specifically the high affinity Spiegelmers. The Spiegelzymes developed are on the basis of hammerhead ribozymes. Since there are no medications known to be entirely free of side reactions, our Spiegelzymes may actually be potentially the perfect antidote against Spiegelmers in case that they would cause in patients unwanted side reactions. The development of Spiegelzymes also opens up new possibilities in basic research and in the area of molecular evolution. Some of these possibilities will be discussed during this presentation.

Plenary Lecture

**PL**

Perspectives of Nucleic Acid Biosensors for medical applications; Electrically readable biochips for rapid RNA analysis

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Transduction of biochemical events arising from nucleic acid hybridisation to electrically readable signals is the objective of the presented research. The aim is to develop analytical devices (biochips) for use in diagnostics, biotechnology and environmental analysis.

In our approach, nucleic acid hybridisation directs a thermostable esterase [1] for binding to gold electrodes where an electrochemically detectable p-aminophenol is enzymatically synthesized and detected as a redox reaction — dependent current.

All reactions are performed directly on CMOS chips presenting 128 electrodes in a volume of about ten microliters, or less. Technical solutions and optimized biochemical procedures improving the sensitivity and specificity will be discussed. Applications for detection of bacteria and microRNA will be presented [2, 3].

References


Acknowledgements

Supported by German Federal Ministry of Education and Research in frame of “The Medical Valley, Europäische Metropolregion Nürnberg”.

47th Congress of the Polish Biochemical Society, 2012