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Preface

In Vitro Selected Nucleic Acids

Ever since it was first shown in 1990 by three independent research groups, those of Larry Gold, Jack Szostak and Jerry Joyce, that functional nucleic acids can be selected from randomised sequence libraries entirely in vitro, the field of nucleic acid selections has grown impressively. Aptamers and artificial ribozymes are increasingly being applied as useful tools in research, diagnostics and medicine. This Symposium-in-Print entitled 'In Vitro Selected Nucleic Acids', comprising the first 11 articles in this issue, is an effort to introduce these fascinating and useful molecules to the audience of Bioorganic and Medicinal Chemistry. All contributed manuscripts are original research papers that mainly cover the areas of aptamer- and ribozyme research.

Combinatorial selection of nucleic acids has led to the discovery of novel ligands ('aptamers') and catalysts ('ribozymes') that have important implications for both chemistry and medicine. By methods of combinatorial chemistry, random syntheses of nucleic acid libraries rapidly generate up to 10^{15} different molecules in which a tiny fraction exhibits the desired functional properties. A decisive advantage of nucleic acid combinatorial chemistry is that the genotype directly determines the phenotype and function. The sequence of single stranded nucleic acids in concert with certain buffer conditions, temperature and concentration of divalent metal ions determines its folding into defined tertiary structures resulting in interesting activities. Iterative selection and amplification result in one of the highest throughput screens conceivable whereby each molecule encodes its own activity permitting parallel sampling of multibillion different molecules.

While many of the contributions in this symposium provide interesting examples of novel nucleic acids selected to specifically recognize diverse molecules, such as tetracycline, tyrosineamide, or moenomycin some of the papers provide examples of aptamer and ribozyme applications for advancements of the in vitro selection technology.

For example, **Cox** and **Ellington** show that selection for specific-ligand-binding RNA- or DNA-molecules can now also be performed in an automated fashion. This bears the potential to perform many aptamer-selections in parallel and thus to isolate aptamers in only a fraction of the time required for manual selections.

Two examples of aptamers that act inside cells are presented in the contributions by **Grate** and **Wilson** and by **Homann** and **Göringer**. These studies provide further important examples that show that aptamers may serve as useful tools to modulate a biological target within an in vivo context or to modulate gene expression in a controlled fashion. **Brunel** et al. even used a pool of genomic RNAs to screen for biologically relevant aptamers, whereas **Ryu** and **Rando** investigated the interaction of a low-molecular weight molecule with sequence motifs found in natural RNAs.

An important area of nucleic acid selections is devoted to the isolation of novel catalytic nucleic acids. **Levy** and **Ellington** have selected deoxyribozymes that can catalyze the formation of phosphorothioester internucleotide linkages from a random sequence pool. **Frauendorf** and **Jäschke** have designed an allosteric aptamer/ribozyme chimera that cleaves a fluorescence labelled substrate in response to a small molecule that is specific for the aptameric portion of the catalyst. **Carmi** and **Breaker** characterized the features of a catalytic single-stranded DNA that is able to cleave DNA substrates.

I hope that this Symposium-in-Print will convince the uninitiated reader that the field of nucleic acid selections is an exciting, stimulating, and highly dynamic research area and that it will provide a cumulated source of interesting and useful new data for the experts in our field.

Michael Famulok
Kekule Institut für Organische Chemie und Biochemie,
Gerhard-Domagk Str. 1,
53121 Bonn,
Germany
E-mail: m.famulok@uni-bonn.de

PII: S0968-0896(01)00156-0