Organized by the European Union project RIGHT (6th framework) and by the Nucleic Acid Center, a research center founded by the Danish National Research Foundation

Perspectives on Nucleic Acid Chemistry for Therapy

June 17-20, 2008
Sesimbra, Portugal

Tuesday, June 17, 2008

Arrival day — Registration

Wednesday, June 18, 2008

9.00 – 12.30 — Theme 1

Do we need new methods for oligonucleotide synthesis?

Chair: *C. Reese*

Discussion: After more than 50 years of research, it remains difficult to produce large amounts of oligonucleotides (especially RNA) in high yield and purity. What is the reason for this and how may progress be made? Is it possible to develop methods to synthesize longer oligonucleotides and to synthesize them faster?

Lecturers:

- *W. Pleiderer : Oligonucleotide synthesis on a chip.*
- *S. Beaucage :* Challenges in the solid-phase synthesis of RNA oligonucleotides.
- *J.-J. Vasseur: Alternatives to solid-phase synthesis of oligonucleotides.*
- *M. Damha: The adventures in DNA/RNA synthesis.*

14.30 – 18.00 Theme 2

Do we need new chemical modifications to make nucleic acids therapy a reality?

Chair: *J. Wengel*

Discussion: Oligonucleotides have been designed with modifications in the backbone, the sugar part and the base moiety, with the idea to increase thermal stability and protect them against enzymatic degradation (playing around with conformational restriction, base pairing strength, charge neutralization, stacking interactions). What are the main properties needed to use modified oligonucleotides in biology? Are we still missing something to move modified oligonucleotides in therapy? Which new oligomers should be designed?

Lecturers:

- *M. Damha : Decorating RNA through novel conjugation chemistry.*
- *J.M. Escudier : Constrained nucleic acids : synthesis and first evaluation.*
- *F. Seela : Base-modified nucleic acids, synthesis, molecular recognition and application.*

Thursday, June 19, 2008

9.00 – 12.30 Theme 3

Conjugate chemistry versus formulations: what is the best way for nucleic acids delivery?

Chair: *P. Herdewijn*

Discussion: Oligonucleotides need to enter the target cell and their intracellular target in sufficient amounts. Despite some success *in vitro*, the parallel *in vivo* data are lacking. What could be the best delivery approach for pharmacokinetics, cellular uptake and cellular targeting? Will it be possible to escape from the approach of local delivery? Is peroral delivery a way to go or are we happy with IV administration, like done with antibodies?

Lecturers:

- *M. Gait: Peptide conjugates of DNA for cell delivery and biological activity.*
- *H. Loennberg: Glycoconjugates of oligonucleotides*
- *M. Antopolsky: Peptide-Oligonucleotide Conjugates. Chemical ways of preparation, investigations on Tat-related optimal sequence, studies on hybrid molecules design.*

14.30 – 18.00 Theme 4

Oligonucleotide-based drug development strategies: which way to go?

Chair: *J. Engels*

Discussion: Many approaches are available to intervene with gene expression using oligonucleotides. Some of them are rather artificial (antisense, aptamers), others make use of natural mechanisms (siRNA, ribozymes, CpG). What are the most powerful approaches? Which one is the easiest to develop? What are the pitfalls and promises? Can we design other principles?

Lecturers:

- *E. Uhlman: Nucleic acids as key regulators of innate and adaptive immunity.*
- *K. Fluiter: Testing oligonucleotide chemistry in vivo: Considerations for preclinical development.*
- *G. Sczakiel: Intracellular transport of siRNA and RNA interference.*

Friday, June 20, 2008

9.00 – 12.30 Theme 5

Biophysical and biochemical studies of nucleic acids: which information is needed to improve our understanding of the biology of nucleic acids?

Chair: *J. Chattopadhyaya*

Discussion: Plenty of biophysical and biochemical techniques are available to analyze structure and function of nucleic acids. Which information do we need to answer questions in biology, i.e. siRNA? How can we generate this information and make this transfer of knowledge more successful? What are the key biophysical and biochemical experiments that need to be done to better understand this biology?

Lecturers:

- *D. Patel: Small RNAs: mediators of gene regulation, catalysis and silencing.*
- *M. Sattler: Structural biology of RNA structure and molecular recognition in the regulation of gene expression.*
- *O. Plashkevych: In silico elucidation of the cleavage mechanism by RNA cleaving 10-23 DNAzyme.*