

# Preface

This year the RNA technologies are celebrating two very important anniversaries. The first one is the 60th anniversary of the founding of the RNA Tie Club and the other one is the 40th anniversary of the successful crystallization and structural determination of the phenylalanine-specific tRNA from yeast.

The 60th anniversary of the RNA Tie Club is indeed a very important date to remember! The 20 members of this club, among them Sydney Brenner, Erwin Chargaff, Francis Crick, Max Delbrück, Paul Doty, George Gamow, Leslie Orgel, Alexander Rich, Gunther Stent, and James Watson, had realized to the surprise of everyone, only 1 year after Watson and Crick had determined the double helical structure for DNA (Watson and Crick 1953), that there seems to be much more to RNA molecules than anticipated.

Indeed, Watson and Crick had surprised everyone with the statement in their DNA paper concerning RNA molecules: “It is impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact” (Watson and Crick 1953). It was therefore not expected when 1 year later the RNA Tie Club was founded with the goal to “to solve the riddle of the RNA structure and to understand how it built proteins”.

The members of the RNA Tie Club had selected the guide slogan “Do or die, or don’t try”. Thus, very intensive RNA structural and functional studies were initiated, in which Alexander Rich played a key role. Indeed, Rich could demonstrate in the following years that RNA may form Watson and Crick base pairs, that an RNA strand could base pair with a DNA strand and that even triple strand nucleic acid structures were possible (Rich personal communication; Rich 2009). With the determination of the three-dimensional tRNA structure 40 years ago by the research groups from Alexander Rich (Kim et al. 1973) and Aaron Klug (Robertus et al. 1974), the unforeseen diversity of RNA structural potentials became apparent for the first time, and it can be safe to assume that we are still lacking the complete knowledge of all structural possibilities of the RNA molecules.

Parallel to the structural activities, studies were initiated in which the chemistry of nucleic acids was developed, so that oligonucleotides could be chemically

synthesized. It was the knowledge of the chemical synthesis of nucleic acids which turned out to be the key to unlock the secrets of the genetic code.

Clearly these early RNA studies required the significant involvement of nucleic acid chemistry, which later on with the rapid developments of molecular biology and molecular genetics seemed to be less and less important. But now in the last few years there has been a unique revival of the employment of nucleic acid chemical methods in the natural sciences, so that we are currently speaking of the new field of chemical biology.

We, as the editors of this volume in the *RNA Technologies Series*, are very happy to present to the reader 29 of the world leading research groups in the area of chemical biology. You will see that the exiting research carried out by these groups will introduce us to new ideas how chemistry can add new elements to the areas of nucleic acids in biotechnologies, nanotechnologies, and, very importantly, in the areas of diagnostics and therapy in the field of molecular medicine.

This new volume of *RNA Technologies* starts with a contribution devoted to the newly defined field named *pre-biology*. The majority of papers address in a new way the fundamental questions: how the early genetic code was developed, how stable and prone to isomerisation RNAs are, and how stable nucleobases in RNAs are. The search for alternative and modified nucleobase systems has both a sense of basic questions and also applicational aspects in the fields of new approaches in therapies and technologies. In a similar context one can view the questions discussed in papers dealing with structural aspects of nucleic acids. The coped knowledge is very rich, yet it seems that still many possible structural features of nucleic acids are to be discovered. For example, the dynamic structures of nucleic acids and their analogs, with their ingenious modifications in the sugar moiety, which for example, determine their biological functions in processes such as DNA replication. But also very interestingly, their extra- and intracellular transport are the subject of several papers. This includes, for example, the important G-quadruplex motifs as potential therapeutic targets and still double-stranded nucleic acids as important molecular tools.

The development of technologies suitable to modify the level of gene expression is remarkable as well. The possibility of exon skipping by chemically modified RNAs brings again a new element to RNA functions. These technologies include editing of therapeutic genes, using modified riboswitches and approaches that are based on modification of Cap regions of the mRNAs. Not overlooked should be the developments of new powerful approaches to detect nucleic acids and the applications of appropriately modified RNAs by electron paramagnetic resonance (EPR) spectroscopy. One very interesting contribution, as a representative of these techniques, is also presented in this book.

And finally, we would like to bring the readers' attention to new approaches to study structure and interactions of nucleic acids and other biomolecules in an environment that is offered by ionic liquids. This field widens the range of observations of the most important biological molecules and might be considered as a step towards studying their structure and interactions under the conditions of molecular crowding, which is otherwise hardly accessible for detailed analysis.

The order of the chapters in the book could perhaps also be a different one. But this is more a personal opinion, because the areas covered in the field of chemical biology are so diverse that it should tempt the reader to just go through the book and read the chapters which interest him at that time the most.

In summary, we hope that this new volume of *RNA Technologies* will be of interest for chemists, biochemists, and life scientists and that it will not only stimulate their research but also our future research.

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