

# Foreword

## The history that brought it all alive

It began with an interesting conversation between Richard Giegé and Uttam L RajBhandary (Tom). The conversation took place at the exciting and successful 20th International tRNA workshop in Banz, Germany in October 2003. ‘t’ or ‘transfer’ RNAs are the central players in the transfer of the information contained in the language of genes, which are usually DNA molecules, to the language of proteins. More correctly, tRNAs interpret the information present in messenger RNA, whose sequence is derived from that of the gene. tRNA molecules function as adaptors that bring amino acids to the protein synthesizing machine, the ribosome, in an orderly fashion and in a way that mirrors the array of base triplets (the codons) specified on messenger RNA. Richard and Tom thought how important it would be to get together people who had worked on tRNA, especially in the early days, in order to exchange personal recollections about the history of the field. That discussion has led to this special issue of *Journal of Biosciences*.

Fired by the success of the meeting in Banz, and with the thought of doing something out of the ordinary, I – as the organizer – jumped on the opportunity to propose a session on the history of tRNA research in the 21st workshop which was held in Bangalore in December 2005. In such meetings where the focus is on “state of the art” issues, a history session may have struck many as risky. Nevertheless, while the idea to hold a history session was relatively straightforward, shouldering the responsibility of organizing such a session was by no means simple. Fortunately, both Richard and Tom agreed to take it on themselves jointly. Thus they became the first two session chairs for the meeting in Bangalore – long before any thing else about the meeting was decided. However, I knew that this was a good start. From the number of e-mails and telephone calls that followed, it became clear how much work needed to go into organizing the History session. Hard work is said to always pay; I trust readers will agree that the returns from this piece of hard work were commensurate with the efforts that went into it.

Besides the two session chairs, the other speakers in the history session were Sidney Altman, Brian Clark, Tamara Hendrickson, Dieter Söll, Mathias Sprinzl and Kimitsuna Watanabe. A fairly comprehensive set of themes was covered. Among them were the discovery of tRNAs, their purification, sequence analysis, three-dimensional structure, base modifications, aminoacylation and its chemistry, editing of the misacylated tRNAs, discovery and mechanism of action of RNase P (the 5’ ends of tRNAs are processed by this enzyme), and – it goes without saying – the genetic code. When it comes to supposedly well-known facts in science, it is often the case that one has doubts and would like to get them straightened out, but the opportunity does not arise. Even when it does, the awe with which one views historical facts makes one hesitate. Our History session was ideal for “Everything you wanted to know but were too afraid to ask” about tRNA. The session may well have been the pick of the workshop. No wonder it turned out to be a super-hit – with the speakers enjoying it no less than the audience.

In turn, that success led to the idea of publishing the proceedings of the history session as a special issue of *Journal of Biosciences*...once again, a great idea that I could not let go. Getting everything together was a slightly tricky business, but we are now happy to bring out this special issue with six articles. These articles make a substantial contribution to the history of tRNA research. They present a lively picture of the early days and show that two common assumptions about ‘ancient’ science are false. One assumption is that doing science in those days must have been relatively easy because so little was known: almost any finding would have been of interest. The other assumption is that not just the conceptual underpinnings, but also the methods of the science of yesterday are out of date today. A journey through these articles is bound to arouse admiration for the heroic nature of the advances that we see as part of history. Often the starting materials for experiments were not in kilogram or tens of kilograms but in hundreds of kilograms

for getting that final precious little! One derives inspiration from these articles and realizes that the methods used then are relevant even today.

Tom and Caroline get the history of the tRNA research going in this volume; to me it is a good reminder of my student days, of solving the questions given by the biochemistry instructor on building the sequences of oligonucleotides from their fingerprints. At the time, I never realized that the images used in these assignments were probably all from Tom's lab. The article by Brian brings alive the intense race between the groups at MRC, UK and MIT, USA in getting to the three-dimensional structure of tRNA. And it shows that there is some merit in retaining crystals for as long as 20 years! The genetic code is universal ...is it? We need to unlearn some of that. As Dieter and Tom point out, we need to realise that codons can have different meanings in different biological systems, and that termination codons can have utility in coding newer amino acids. If you thought that the modifications on nucleosides were not important, you could not be more wrong; and to see why, read the discourse by Susumu Nishimura and Kimi on the discovery and the importance of modified nucleosides. There is a great deal of art in the science of identifying the modified nucleosides, especially when it comes to the mitochondrial tRNAs. Richard takes us through the remarkable history of tRNA aminoacylation, misacylation and the strategies used in specific recognition of the tRNAs or tRNA-like structures by the aminoacyl-tRNA synthetases. Importantly, while doing this, he does not omit to highlight the importance of native tRNA preparations, which have become rare commodities these days. Finally, Mathias adds a chemist's perspective in his article. He tells us about the importance of the 2' and the 3'-OH groups of the ribose sugar of the 3'-terminal A in the tRNA in the various reactions it participates in, whether on or off the ribosome, including the substrate-assisted catalysis of peptide bond formation. His article is as stimulating to read as his talk was to listen to. I can't help mentioning that while Mathias delivered his energetic talk at the meeting, we all wondered – a few of us rather nervously – why some of his slides were turning yellow all of a sudden. We realised only later that every time he emphasized something, the energy that he exuded on the dais caused the connector from the computer to the LCD projector to get loose.

In ending with that anecdote, let me take this opportunity to thank all the authors who have contributed to this special issue of *Journal of Biosciences*. A special welcome to Caroline Köhrer who has co-authored an article with Tom. Also, while we missed Susumu at the meeting because of an unfortunate last minute emergency, we have an article from him in this issue co-authored with Kimi. I have thoroughly enjoyed working on these articles. Every time I went through them, I found something more to admire. Also, I would like to say that we wished to invite many more of the pioneers of the tRNA research to speak at the meeting. However, the inevitable constraints of time meant that we had to limit an already extended session on the history of tRNA research. My earnest wish is that the beginning that we have made will be continued in future tRNA workshops. Let us hope we have initiated a trend of talks on historical aspects, so that the rest of us can learn, enjoy and appreciate the past. A word of thanks to the *Journal of Biosciences*, which made it possible for me to bring out this Special Issue of the journal that I am happy to offer.

The cover of this special issue shows Professor Zamecnik with a representation of the tRNA structure in the background (taken from the cover page of the volume of *Abstracts* of the 16th tRNA workshop organized by W H McClain). Born in 1913 in Cleveland, Ohio, USA, Paul C Zamecnik was trained to be a medical doctor. His interest in fundamental research led him to make a number of seminal contributions in the area of basic biology. Among these was the discovery, along with Mahlon Hoagland, Elizabeth Keller and Mary Stephenson, of aminoacyl-tRNA synthetases and soluble RNAs (now tRNAs, shown in the background on the cover page), which carry amino acids to the ribosome. Paul C Zamecnik continues his research at the Massachusetts General Hospital and is Professor Emeritus at the Harvard Medical School in Boston.

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