Molecular and Cellular Genetics

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Research

The RNA World

In the early eighties Sid Altmann (Yale) and Tom Cech (Boulder, Colorado) surprised the world with their observations of catalysis by RNAs. This led to a dramatic change of our thinking about how reactions in a cell are being catalyzed and on the nature of the catalysts that helped to establish the first self-replicative systems at the beginning of biological evolution. These two researchers won the Nobel prize in chemistry in 1989 for their most original work.

R Schroeder and U von Ahsen
Group I Introns and Bbinding of Antibiotics to RNA

This work started a few years ago with the surprising observation that self-splicing of group I introns can be inhibited by antibiotics which previously had only been recognized as inhibitors of the ribosome.Current projects concern the mechanisms underlying the mode of binding and of function-interference of aminoglycoside and peptide antibiotics with group I intron RNA as well as with in vitro selected small RNAs.

A second topic of this group concerns the role of divalent metal ions in RNA catalysis. Depending on the nature of the metal ion occupying certain pockets in group I intron RNA, different reactions are catalyzed.

MW Mueller, M Hetzer and RJ Schweyen
Self-splicing andTransposition of Group II Introns

Introns of this class are known to occur in bacteria and in organelles of eucaryotes. They are assumed to be the ancient forms of RNAs from which the abundant nuclear mRNA introns and the snRNAs were derived during evolution of eucaryotic genes.To further investigate this hypothesis studies are being undertaken which aim at the structural and functional characterization of domains of group II introns in comparison with nuclear snRNA.

Group II intron RNAs catalyze a series of transesterifications in vitro. These can be directed towards other RNAs to perform various nucleotidyl transfer reactions. Thus, group II intron RNAs are 'ribozymes' which, among other reactions, can catalyze editing-like insertion and deletion of nucleotides and RNA or DNA polymerization reactions.

Group II introns also can reverse splice, i.e. the lariat intron RNA can insert into other RNAs at specific sites. Intron encoded reverse transcriptases may generate DNA copies of these 'recombinant' RNAs and thus help them to find their way into genomic DNA. Thus, group II introns are mobile

elements, invading various gene sequences with relatively high frequencies.

A Ragnini, RJ Schweyen
Yeast as a Model System for the Study of Eukaryotic Genes

During the last decade we have learned that basic functions at the cellular level are highly conserved among eucaryotes. Human genes or plant genes can substitute for the respective genes in a simple unicellular organism like yeast. This organism with a haplontic and a diplontic phase is ideally suited for genetics and gene technology. Therefore, it became a favourite organism world-wide for studies on the basic functions of genes and genomes.

This research group is particularly interested in genes directly or indirectly involved in the biogenesis of mitochondria. One gene which presently attracts most of our interest, MRS6, is the homolog of a human gene which in mutant form causes a rare hereditary disease called choroideraemia. It is involved in the control of protein sorting in all eukarotic cells. Mrs6 mutant cells of yeast are severely disturbed in vesicular systems of the cell and in mitochondrial morphology. Making use of the excellent genetics of yeast we hope to elucidate the spectrum of cellular defects and, hopefully, to define the critical one which causes the choroideraemia phenotype in humans.

Teaching

Members of this section teach molecular genetics from introductory to highly advanced courses. Laboratory courses deal with microbial genetics, particularly with yeast as a model organism and with work on nucleic acids, cloning and gene analysis.

International Cooperations

All research projects of this section are performed in collaboration with other groups, mostly in Europe. Two researchers (Schroeder, Schweyen) are presently participants of European programs, others are planning to participate in such programs. Collaboration in these programs is in the form of networks involving scientists in at least three European countries

Selected References

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