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Plenary Lecture I

# I. Structural Biology of RNA-binding Domains

## II. The Present Status of the Japanese Structural Genomics Project (the NMR Park)

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### I. Structural Biology of RNA-binding Domains

We are studying the structures of ribonucleoprotein (RNP) domains [or RNA-recognition motif (RRM) domains] and their RNA-binding mechanisms. This type of RNA-binding domain usually binds a single-stranded region of RNA. Many proteins have two or more RNA-binding domains. The Sex-lethal (Sxl) protein from *Drosophila* has two tandemly repeated RNA-binding domains, and recognizes polyuridine sequences with no secondary structure for regulation of sex-specific alternative splicing. We have determined the solution structures of the first and second RNA-binding domain fragments of Sxl by NMR spectroscopy, and found that the first domain has a characteristic arrangement of aromatic residues on the surface of the  $\beta$  sheet. We have determined the crystal structure of a didomain fragment of Sxl complexed with the tra pre-mRNA polyuridine tract. The two RNA-binding domains bind the RNA with no base pairs between the two  $\beta$  sheet surfaces forming a deep, positively charged cleft. The RNA molecule is characteristically extended.

## II. The Present Status of the Japanese Structural Genomics Project (the NMR Park)

The RIKEN Institute (The Institute of Physical and Chemical Research) has started the Genomic Sciences Center. The 15-year program consists of four national projects, the Human Genome Sequencing Project, the Mouse Full-length cDNA Project, the Protein Folds Project, and the Mouse Mutants Project. The Protein Folds Project is to contribute to making the complete catalog of protein folds, the number of which has been proposed to be about one thousand or more, as well as the domain functions. The protein fold catalog is expected to be useful for functional genomics. The structure determination of functional domains will be done by NMR spectroscopy and X-ray crystallography. The construction of a new NMR facility ("the NMR Park") has been started, and 16 NMR instruments (600 and 800 MHz) will be installed by the end of fiscal 1999 (March 2000). The institute has also been involved in the construction and operation of the synchrotron radiation facility, SPring-8.