

LABORATORY OF MOLECULAR BIOLOGY

Head: Dr. Mitsuru Takanami

This laboratory was established to expand researches of molecular biology in the late Hayaishi laboratory in 1968, and Dr. M. Takanami has since been in charge of this laboratory. Until March 1976, Dr. O. Hayaishi who is professor of Faculty of Medicine also supervised activities of this laboratory as a concurrent professor.

The major project of this laboratory has been focussed on analysis of DNA information required for initiation and termination of transcription. DNA of a small bacteriophage, named fd, was chosen for this purpose, since this DNA is only 6,200 nucleotides long and contains information enough to code eight proteins. The first several years the effort was concentrated to characterize the transcription system, and the transcription units on fd DNA as well as the positions of transcription start (promoter) and stop (terminator) were consequently determined.

The next step of research was the isolation of DNA segments containing promoter and terminator regions. For this purpose, attempts were made to cleave fd DNA into unique segments by the use of restriction endonuclease, which is not known to cleave double-stranded DNA by recognizing a unique sequence. At that time, however, only one species of restriction endonuclease was available, and that enzyme introduced only a single cut in fd DNA. Accordingly, a number of bacterial strains were surveyed to find other such enzymes but with different specificities. In 1972, three new enzymes which specifically cleave fd DNA into smaller pieces were isolated. By the discovery of these enzymes, a cleavage map of fd DNA was constructed, and as a consequence, short DNA segments containing promoter and terminator regions were isolated. In the meanwhile, the method for sequencing DNA was introduced, and in 1974, the sequence of a promoter region was successfully determined. In 1975, more sequence information about promoter and terminator regions was obtained. As of October 1976, research work is being concentrated to define the structure essential for promoter and terminator function in fd DNA, and also to gain sequence information on promoter and terminator of other DNA molecules.

Publications

1. M. Sugiura, T. Okamoto, and M. Takanami: The Starting Nucleotide Sequences of RNA Synthesized on the Replicative form DNA of Coliphage fd, *J. Mol. Biol.*, **43**, 299 (1969).
2. T. Okamoto, M. Sugiura, and M. Takanami: Length of RNA Transcribed on the Replicative Form DNA of Coliphage fd, *J. Mol. Biol.*, **44**, 101 (1969).
3. M. Takanami, T. Okamoto, and M. Sugiura: The Starting Nucleotide Sequences and Size of RNA Transcribed on Phage DNA Templates, *Cold Spring Harbor Symp. Quant. Biol.*, **35**, 179 (1970).
4. T. Okamoto, M. Sugiura, and M. Takanami: Characterization of RNA Transcribed *in vitro* on Phage 80 DNA, *Biochemistry*, **9**, 3533 (1970).
5. M. Sugiura, T. Okamoto, and M. Takanami: RNA Polymerase Sigma Factor and Initiation Site Selection, *Nature*, **225**, 589 (1970).

6. M. Takanami, T. Okamoto, and M. Sugiura: Termination of RNA Transcription on the Replicative Form DNA of Coliphage fd, *J. Mol. Biol.*, **62**, 81 (1971).
7. T. Oda and M. Takanami: Observations on the Structure of the Termination Factor Rho and Its Attachment to DNA, *ibid.*, **71**, 799 (1972).
8. T. Okamoto, M. Sugiura, and M. Takanami: RNA Polymerase Binding Sites of Phage fd Replicative form DNA, *Nature (New Biol.)*, **237**, 108 (1972).
9. M. Takanami, and H. Kojo: Cleavage Site Specificity of an Endonuclease Isolated from *Haemophilus influenzae* H1, *FEBS Letters*, **29**, 267 (1973).
10. M. Takanami: Specific Cleavage of Coliphage fd DNA by Five Different Restriction Endonucleases from *Haemophilus* Genus, *ibid.*, **34**, 318 (1973).
11. M. Takanami and T. Okamoto: Physical Mapping of Transcribing Regions on Coliphage fd DNA by the Use of Restriction Endonucleases, *Symp. Control Transcription*, **12**, 145 (1973).
12. H. Sugisaki and M. Takanami: DNA Sequence Restricted by Restriction Endonuclease AP from *Haemophilus aphrophilus*, *Nature (New Biol.)*, **246**, 138 (1973).
13. T. Takeya and M. Takanami: Isolation of DNA Segments Containing Promoters from Bacteriophage T3 DNA, *Biochemistry*, **13**, 5388 (1974).
14. M. Takanami: Restriction Endonucleases AP, GA, and HI from Three *Haemophilus* Strains, *Methods in Mol. Biol.*, **5**, 113 (1974).
15. M. Takanami, T. Okamoto, K. Sugimoto, and H. Sugisaki: Studies on Bacteriophage fd DNA. I. A Cleavage Map of the fd Genome, *J. Mol. Biol.*, **95**, 21 (1975).
16. T. Okamoto, K. Sugimoto, H. Sugisaki, and M. Takanami: Studies on Bacteriophage fd DNA. II. Localization of RNA Intiation Sites on the Cleavage Map of the fd Genome, *ibid.*, **95**, 33 (1975).
17. K. Sugimoto, T. Okamoto, H. Sugisaki, and M. Takanami: The Nucleotide Sequence of an RNA Polymerase Binding Site on Bacteriophage fd DNA, *Nature*, **253**, 410 (1975).
18. K. Sugimoto, T. Okamoto, H. Sugisaki, and M. Takanami: Studies on Bacteriophage fd DNA. III. Nucleotide Sequence Preceding the RNA Start-Site on a Promoter-Containing Fragment, *Nucleic Acids Research*, **2**, 2091 (1975).
19. M. Takanami, K. Sugimoto, H. Sugisaki, and T. Okamoto: Sequence of Promoter for Coat Protein Gene of Bacteriophage fd, *Nature*, **260**, 297 (1976).
20. A. Oka and M. Takanami: A Cleavage Map of Colicin El Plasmid, *ibid.*, **263**, 193 (1976).
21. A. Wada, H. Tachibana, and M. Takanami: Long Range Homology of Physical Stability in Double Stranded DNA, *ibid.*, **263**, 439 (1976).