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## **DNA structure and functioning**

My lab studies the role of local DNA sequences in DNA structure and functioning. Our primary emphasis is on the effects of simple DNA repeats on such major genetic processes as DNA replication, transcription and recombination. Our main projects are:

**(1) Replication and expansion of simple DNA repeats.** Uncontrollable expansions of trinucleotide repeats lead to more than a dozen human neurological disorders, including Fragile X mental retardation, Huntington's disease, myotonic dystrophy, and Friedreich's ataxia. It has been hypothesized that these expansions are caused by replication errors. Using model bacterial and yeast experimental systems, we have obtained the first direct evidence that the replication fork progression through various repeated runs is indeed abnormal. Further, the frequency of the expansion of repeats in those systems is drastically affected by mutations in the replication apparatus. We are currently extending these observations into mammalian cell systems. Our working hypothesis is that the replication fork stalls at a trinucleotide repeat due to the formation of a very stable secondary structure in a lagging strand template. Extra copies of repeats are then added when the replication fork tries to bypass this roadblock.

**(2) Transcriptionally-dependent rearrangements in DNA.** The relationship between RNA polymerase and the DNA template is a two-way avenue. Transcription is believed to change DNA structure both upstream and downstream of the promoter. At the same time, both initiation and elongation of transcription dramatically depend on the structure

of a DNA template. We concentrate on several specific aspects of these relations in living cells. They include transcription-induced DNA supercoiling, the domain structure of transcribed DNAs, the formation of unusual DNA structures within and near transcription units, and the instability of repeated DNA mediated by transcription. We also study the influence of transcriptionally driven changes in DNA on genetic recombination.

**(3) Triplex DNA structures.** Since our discovery of three-stranded H-DNA more than a decade ago, triplex DNA has attracted very broad attention from a structural viewpoint, as a potential regulator of genetic processes and as a promising therapeutic. We have found that DNA triplexes present a steady barrier for different DNA and RNA polymerases, and we are studying the mechanisms of this phenomenon. Considerable efforts are also being devoted to detecting DNA triplexes inside living cells and elucidating their biological roles.

### **Selected Publications**

Krasilnikova, M.M., Smirnova, E.V., Krasilnikov, A.S., **Mirkin, S.M.** (2001) A new trick for an old dog: TraY binding to a homopurine-homopyrimidine run attenuates replication. *J. Mol. Biol.* **313**, 271-282.

Siyanova, E.Y., **Mirkin, S.M.** (2001) Expansion of trinucleotide repeats. *Mol. Biol.* **35**, 168-182.

**Mirkin, S.M.** (2001) DNA topology: fundamentals. In: Encyclopedia of Life Sciences, Macmillan Publishers Ltd.

Raca, G., Siyanova, E.Y., McMurray, C.T., **Mirkin, S.M.** (2000) Expansion of the (CTG)<sub>n</sub> repeat in the 5'-UTR of a reporter gene impedes translation. *Nucleic Acids Res.* **28**, 3943-3949.

Krasilnikov, A.S., Podtelezchnikov, A., Vologodskii, A., **Mirkin, S.M.** (1999) Large-scale effects of transcriptional DNA supercoiling in vivo. *J. Mol. Biol.* **292**, 1149-1160.

**Mirkin, S.M.** (1999) Structure and biology of H DNA. In: Triple Helix Forming Oligonucleotides, Kluwer Academic Publishers (Norwell, MA), C. Malvy and A. Harel-Bellan, eds., pp. 193-222.

Krasilnikova, M.M., Samadashwily, G.M., Krasilnikov, A.S., **Mirkin, S.M.** (1998) Transcription through a simple DNA repeat blocks replication elongation. *EMBO J.* **17**, 5095-5102.

Samadashwily, G.M., Raca, G., and **Mirkin, S.M.** (1997). Trinucleotide repeats affect DNA replication in vivo. *Nature Genet.* **17**, 298-304.

Cox, R., **Mirkin, S.M.** (1997) Characteristic enrichment of DNA repeats in different genomes. *Proc. Natl. Acad. Sci. USA* **94**, 5237-5242.