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Laboratory of RNA biology

pre-mRNA splicing, small nuclear ribonucleoproteins

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Research topics

RNA molecules are not just messengers acting between DNA and proteins but rather required factors that play an active role in the expression of genes encoded in our genome. An RNA processing step called splicing can dramatically increase the diversity of proteins in human cells and tissues. RNA splicing is catalyzed by a large macromolecular complex, the spliceosome, which is formed from several RNA-protein complexes called snRNPs. In our group we are interested in spliceosome assembly and the organization of RNA splicing in the cell nucleus. Using advanced microscopy techniques (e.g. live cell imaging, FRET, FCS) we explore where and when the spliceosome assembles in the cell nucleus. Experimental data are then used for modelling spliceosome assembly in the 3D space of the nuclear landscape. We identified the conserved nuclear compartment, the Cajal body, as the site of snRNP assembly and recycling, and we proposed a model stating that the presence of Cajal bodies increases the efficiency of snRNP formation. We also aim to determine how mutations in splicing factors can cause *retinitis pigmentosa*, a human genetic disease characterized by photoreceptor cell degeneration.

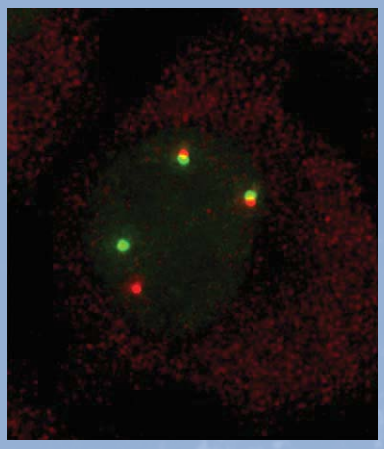
Current grant support

GA CR (301/05/0601, 204/07/0133) MPI-partner group 2006-2008: Pre-mRNA splicing and organization of the cell nucleus

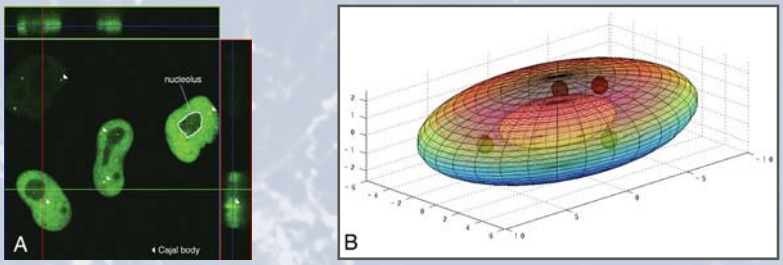
Selected recent papers

A new group, so far no papers from IMG; below papers of D.S. from the previous laboratory are shown:

1. Staněk D, Rader SD, Klingauf M, Neugebauer KM. Targeting of U4/U6 small nuclear RNP assembly factor SART3/p110 to Cajal Bodies. **J Cell Biol.** 2003;160:505-516.
2. Staněk D, Neugebauer KM. Detection of snRNP assembly intermediates in Cajal bodies by FRET. **J Cell Biol.** 2004;166:1015-25.
3. Dundr M, Hebert MD., Karpova TS, Staněk D, Xu H, Shpargel KB, Meier TU, Neugebauer KM, Matera AG, Misteli T. In vivo kinetics of Cajal body components. **J Cell Biol.** 2004;164: 831-842.
4. Klingauf M, Staněk D, Neugebauer, KM. Enhancement of U4/U6 snRNP association in Cajal bodies predicted by mathematical modeling. **Mol Biol Cell** 2006;17:4972-81.
5. Staněk D, Neugebauer KM. Cajal bodies: a meeting place for snRNP in the nuclear maze. **Chromosoma** 2006;115:343-54.



Localization of two proteins involved in spliceosome assembly in a human HeLa cell. Green – SART3 distributed throughout the nucleus and concentrated in Cajal bodies; red – SMN localized in nuclear gems and in the cytoplasm.



Modelling of nuclear space. Distribution of a splicing factor in the nucleus of live cells (A) and a derived mathematical model of the nucleus used for mathematical analysis (B).