Laboratory of RNA Biology

Pre-mRNA splicing, spliceosome, epigenetics, nuclear architecture, retinitis pigmentosa

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Our long-term interest is to determine how cells decode information stored in the genome. We focus on the molecules called mRNAs that serve as messengers between DNA and proteins. Information for protein synthesis in our genome is fragmented and the coding sequences are joined together after transcription of DNA into RNA in a process called RNA splicing. In our laboratory, we analyse how the protein coding fragments are recognized and joined together. We mainly focus on how the nuclear environment and mainly chromatin influence RNA splicing, and the quality control mechanisms that ensure that the splicing machinery is correctly formed on proper RNA. These studies also help us to understand why mutations in proteins that catalyse RNA splicing cause retinitis pigmentosa, a human genetic disease characterized by photoreceptor cell degeneration. As we mostly study all these processes directly in living cells, we widely employ cell culture and various microscopy techniques (e.g. super-resolution fluorescence microscopy, live cell imaging, high-content microscopy, and other).

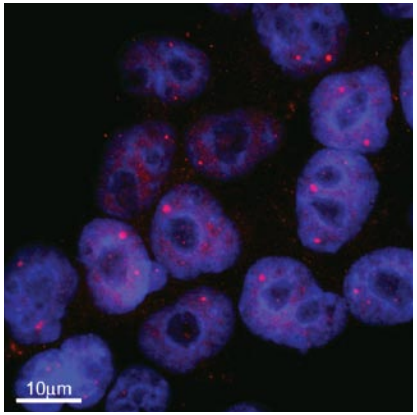

Fig. 1. Distribution of the splicing factor LSm4 (red) in cancer cells. The cell nucleus is visualized by DNA staining (blue), Cajal bodies are the bright red spots. Classical fluorescence microscopy.

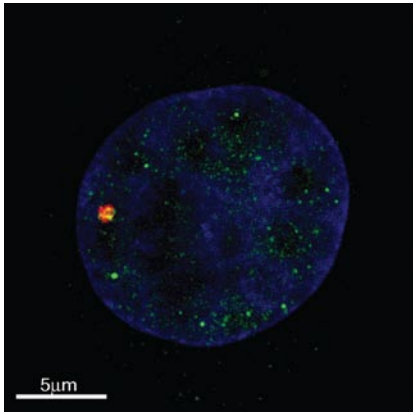

Fig. 2. Localization of the splicing factor U2 snRNA (green) in the cell nucleus (blue – DNA) and in Cajal bodies (red) using structured illumination-based super-resolution microscopy. One cancer cell shown only.

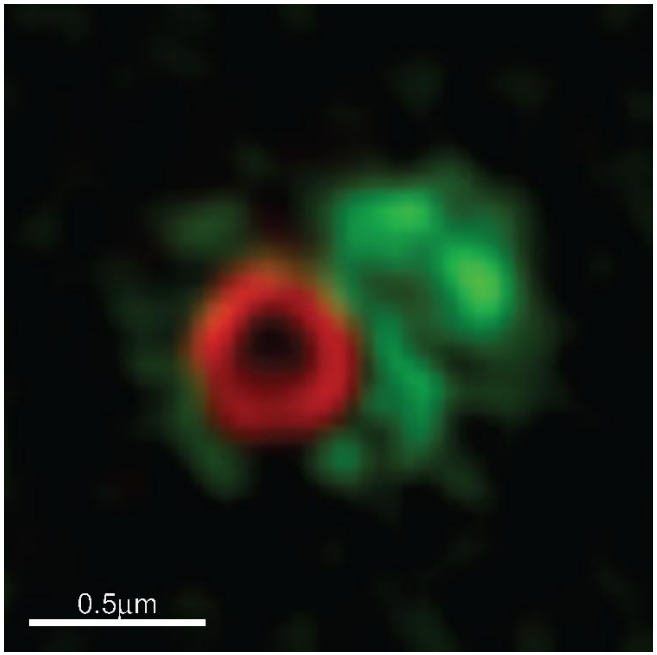

Fig. 3. Two spliceosome assembly proteins (SART3 and SMN) visualized in the Cajal body by structured illumination-based super-resolution microscopy.

- GACR, GAP302/11/1910 – Formation of splicing machinery in the context of the cell nucleus, 2011-2014, D. Staněk
- GACR, GBP305/12/G034 – Centre for RNA Biology, 2012-2018, D. Staněk, P. Svoboda
- GACR, GPP301/12/P425 – Functional analysis of hBrr2 mutations linked to retinitis pigmentosa, 2012-2014, Z. Cvačková
- ASCR, M200521206 – Functional organization of nuclear Cajal bodies with focus on the formation of ribonucleoprotein particles, 2012-2014, D. Staněk
- MEYS, LH14033 – Spliceosomal snRNP assembly and surveillance in Drosophila melanogaster, 2014-2016, D. Staněk
- GACR, GAP305/10/0424 – Regulation of alternative splicing via chromatin acetylation, 2010-2013, D. Staněk
- GAUK, 652213 – Aire, alternative splicing in the immune system, 2013-2014, S. Hozeifi/K. Klimešová
- GAUK, 460413 – SMN role during maturation of snRNPs in the cell nucleus, 2013-2015, A. Malinová
- GAUK, 320713 – Early stages of spliceosome formation, 2013-2014, E. Stejskalová

1. Stejskalová E, Staněk D: The splicing factor U1-70K interacts with the SMN complex and is required for nuclear gem integrity. **J Cell Sci 2014** 127: 3909-15.
2. Dušková E, Hnilicová J, Staněk D: CRE promoter sites modulate alternative splicing via p300-mediated histone acetylation. **RNA Biology 2014** 11(7):865-874.
3. Huang Z, Kaltenbrunner S, Šimková E, Staněk D, Lukeš J, Hashimi H (2014) The dynamics of mitochondrial RNA-binding protein complex in Trypanosoma brucei and its petite mutant under optimized immobilization conditions. **Eukaryot Cell** 13(9):1232-40.
4. Cvačková Z, Matějů D, Staněk D: Retinitis Pigmentosa Mutations of SNRNP200 Enhance Cryptic Splice-Site Recognition. **Hum Mutat 2014** 35(3): 308-17.
5. Hnilicová J, Hozeifi S, Stejskalová E, Dušková E, Poser I, Humpolíčková J, Hof M, Staněk D: The C-terminal domain of Brd2 is important for chromatin interaction and regulation of transcription and alternative splicing. **Mol Biol Cell 2013** 24(22): 3557-68.

From the left: Anna Malinová, MSc / PhD Student, Eva Kozáková (Dušková), PhD / PhD Student (until 2014)/ Postdoctoral Fellow (since October 2014), Nicole Bieberstein, PhD / Postdoctoral Fellow (since 2013), Martin Volek / Diploma Student (since 2014), Zuzana Cvačková, PhD / Research Associate, Klára Klimešová / Diploma Student, Zuzana Šándorová MSc / PhD Student (since 2014), Adriana Roithová MSc / Diploma Student (until 2014)/ PhD Student (since 2014), Eva Stejskalová (Šimková), MSc / PhD Student.

Not in the picture: David Staněk, PhD / Head of Laboratory, Samira Hozeifi, MSc / PhD Student (until 2014), Ivan Novotný, PhD / Postdoctoral Fellow (until 2013), Daniel Matějů / Diploma Student (until 2013)