LABORATORY OF

RNA BIOLOGY

RNA splicing, nuclear structures, spliceosome, retinitis pigmentosa

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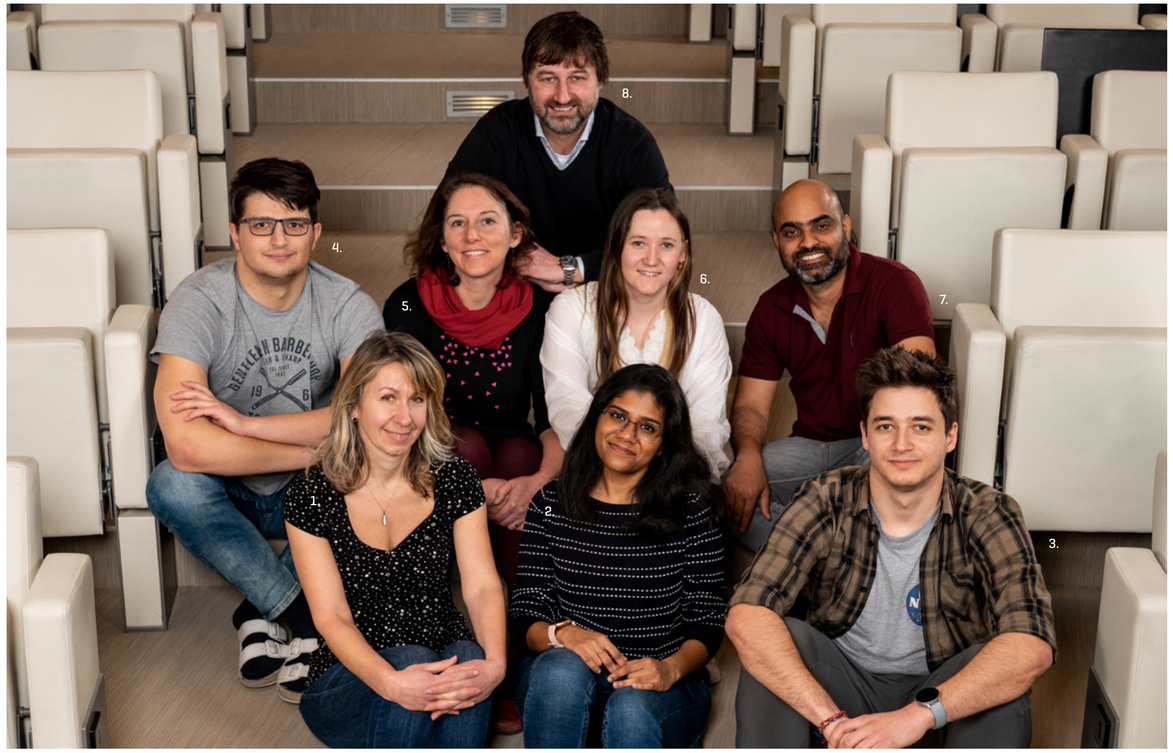
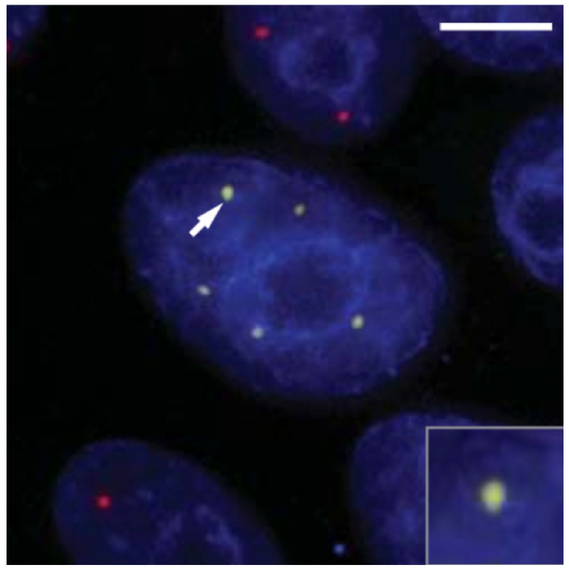


In the picture: 1. Machatová Křížová Jana | 2. Banik Poulami | 3. Radivojević Nenad | 4. Karásek Filip | 5. Cvačková Zuzana | 6. Hana Petržílková | 7. Thakur Kumar Prasoon | 8. Staněk David | Missing in photo: Felix Zimmann, Yelyzaveta Pakhomova.

Our DNA contains the information for the synthesis of all our proteins. However, this information in human DNA is fragmented and our genes contain long, seemingly "useless" sequences that need to be removed in a process called RNA splicing. The „useless" RNA sequences are removed by a large, sophisticated and dynamic molecular machine called the spliceosome. The spliceosome is one of the most complex particles in our cells, composed of several non-coding RNAs and ~150 accessory proteins. Our long-term goal is to determine how the spliceosome assembles at the right time and place inside the cell. We are investigating how nuclear architecture contributes to the correct spliceosome formation, and studying the molecular principles of the control mechanism that distinguishes correctly assembled spliceosome particles from the defective ones. We recently identified a new protein that assists in assembly and recycling of U5 snRNP - one of the essential building block of the spliceosome. We further investigated maturation process of snRNAs - crucial components of the spliceosome. We discovered a molecular mechanism that cells use to identify and eliminate defective snRNA transcripts. Finally, we seek to determine why mutations in several ubiquitously expressed spliceosomal components cause retinitis pigmentosa, a human genetic disease characterized by photoreceptor cell degeneration. We mapped how a retinitis pigmentosa-linked mutation in one of the key spliceosomal RNA helicases affects its function and RNA splicing.



In vitro transcribed snRNA labelled by Alexa488-UTP (green) was microinjected into HeLa cells snRNA localizes in Cajal bodies yellow/red (arrow). DNA was labelled by DAPI (blue). Cajal body was magnified two times in inset. Bar represents 5μm.

Selected publications:

1. Basello A.D., Matera A.G.& Staněk D.* (2022) A point mutation in human coilin prevents Cajal body formation. Journal of Cell Science. 135 (8): jcs259587.
2. Cihlářová Z., Kubovčiak J., Sobol M., Krejčíková K., Sachová J., Kolář M, Staněk D., Bařinka C., Yoon G., Caldecott K.W. & Hanzlíková H.* (2022) BRAT1 Links Integrator and Defective RNA Processing with Neurodegeneration. Nature Communications 13(1):5026
3. Obuca M., Cvačková Z., Kubovčiak J., Kolář M. & Staněk D.* (2022) Retinitis pigmentosa-linked mutation in DHX38 modulates its splicing aktivity. PLoS ONE. 17(4):e0265742
4. Klimešová K., Vojáčková J., Radivojević N., Vandermoere F., Bertrand E., Verheggen C. & Staněk D.* (2021) TSSC4 is a component of U5 snRNP that promotes tri-snRNP formation. Nature Communications 12:3646.
5. Roithová A., Feketová Z., Vaňáčová Š. & Staněk D.* (2020) DIS3L2 and LSm proteins are involved in the surveillance of Sm ring-deficient snRNAs. Nucleic Acids Research. 48(11):6184-6197