Cologne Seminar Series on Ageing

Speaker: Karla M Neugebauer
Yale University, New Haven (USA)

Tuesday, 18 June, 2019, at 16:00

CECAD Research Center
Joseph-Stelzmann-Str. 26
Lecture hall, ground floor

Host: Andreas Beyer
(CECAD)

Scientific Background:

- 2013 – present Professor of Molecular Biophysics and Biochemistry and of Cell Biology, Yale University (USA)
- 2001 – 2013 Research Group Leader, Max Planck Institute of Molecular Cell Biology and Genetics in Dresden (GER)
- 1999-2001 Assistant Professor, Department of Neurology, University of Washington Medical School, Seattle (USA)
- 1998-1999 Staff Scientist at Fred Hutchinson Cancer Research Center, Seattle (USA)
- 1996-1997 Postdoc at EMBL in Heidelberg (GER)
- 1991-1996 Postdoc at Fred Hutchinson Cancer Research Center, Seattle (USA)

Title: Nascent RNA and the coordination of transcription with splicing

About Prof Neugebauer's talk:

Our goal is to understand how gene expression is controlled in living cells, using a combination of fluorescence imaging, biochemistry and molecular biology, as well as custom-designed RNA-Seq methods to observe dynamic nuclear functions *in vivo*. How is gene regulation achieved through pre-mRNA splicing, transcription, chromatin and the 3D organization of the cell nucleus? The use of budding yeast, mammalian tissue culture cells and zebrafish embryos as model systems has allowed us to investigate how transcription and splicing are coordinated. We have recently shown that the spliceosome completes exon-exon ligation as the 3' splice site emerges from Pol II. The proximity of the spliceosome and Pol II suggests physical and/or temporal cross-regulation among these machineries. Indeed, splicing feeds back to transcription by affecting elongation rates and or pausing; splicing also feeds forward to mRNA export by guiding mRNA export factors to mRNA binding. I will present unpublished data using long read sequencing of full length nascent RNAs in *Schizosaccharomyces pombe* showing the coordinated removal of introns within single transcripts as well as a dependency of polyadenylation cleavage on splicing. The findings that nuclear Cajal bodies (CBs) are sites of efficient spliceosomal snRNP assembly and essential for zebrafish embryogenesis are reflective of the propensity of the gene expression machinery to segregated – possibly through liquid-liquid phase separation – within the cell nucleus. I will discuss several models of nuclear function that could lead to the coordination of gene expression, which are suggested by the combination of these insights.

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