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EPIGENETICS OF THE CELL NUCLEUS

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Identification of new players affecting meiosis during gametogenesis is clearly a very important, timely endeavour as the chromosomal dynamics and possible complications during meiotic divisions still remain incompletely understood. Yet, inaccuracies during meiotic stages are connected to chromosomal aberrations leading to severe genetic disorders as well as to male infertility.

In our experiments, we showed that vinculin/DEB-1 participates in meiotic prophase progression. Depletion of DEB-1 impacts chromosomal pairing stabilization, attachment of chromosomes to cytoskeletal forces, and formation of synaptonemal complex during prophase I, resulting in meiosis delay and increased presence of chromosome univalents. Our study thus revealed an unsuspected role of DEB-1 in the progression of meiotic prophase, including chromosome dynamics and pairing that have been shown to be essential meiotic components.
So far, nuclear functions of vinculin/DEB-1 have not been described at all, and we suggest accomplishing a systematic study using a panel of structural, molecular and genetic methods in order to reveal details about its biological functions in the cell nucleus, and in meiosis in particular. We plan to achieve two main aims: 1/ Mapping of vinculin at meiosis-specific structures in cell nuclei; 2/ Deciphering the meiosis-specific roles of vinculin and associated proteins.
Meiosis is a key process in sexual reproduction contributing to the genetic variability of organisms. Deciphering the roles of novel components of the synaptonemal complex would therefore significantly contribute to our understanding of the molecular mechanisms and dynamics of meiotic events, and may possibly also help to explain some of the fertility deficiencies, which are a prominent medial problem affecting 10 % of humans.

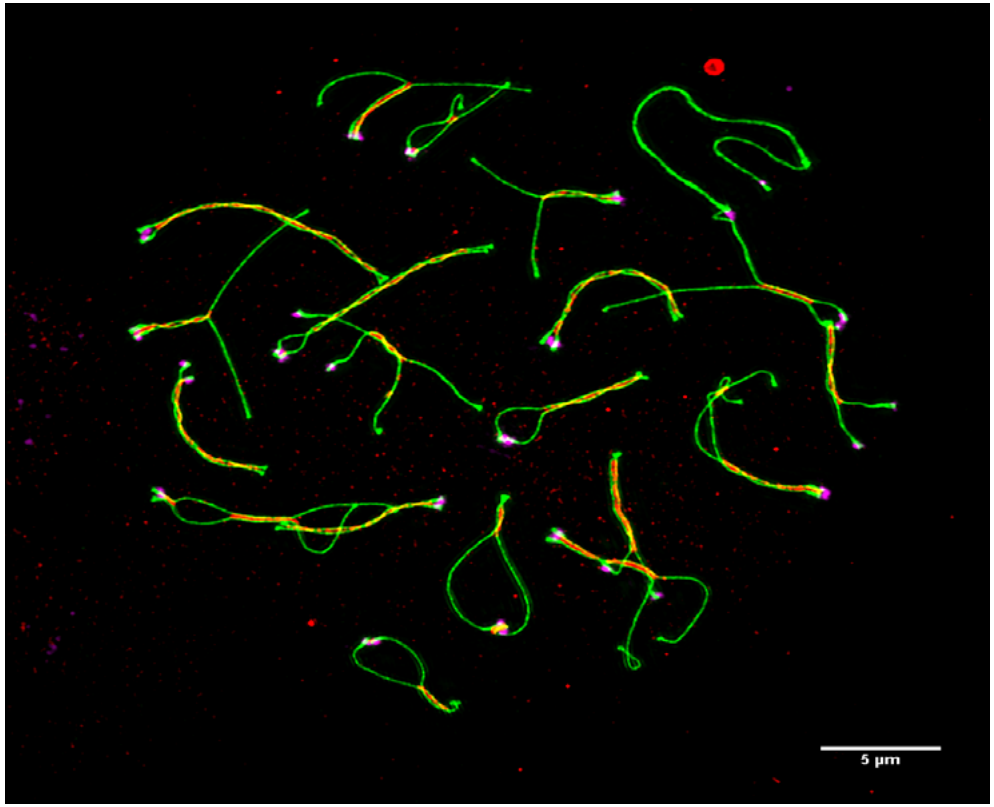

Figure 1. Spread mouse primary spermatocyte of an adult fertile male in the diplotene stage of meiotic cell division. Meiotic synaptonemal-complex (SC) proteins of the pairing chromosomes are marked by indirect immunofluorescence technique. SYCP3 – the lateral element of SC in green colour; SYCP1 - the central element of SC in red colour; in magenta, centromeres – the structural part of chromosomes essential for the proper pairing and segregation of homologous chromosomes.

Selected publications:

1. Rohožková J, Hůlková L, Fukalová J, Flachs P, Hozák P* (2019) Pairing of homologous chromosomes in C. elegans meiosis requires DEB-1 – an orthologue of mammalian vinculin. *Nucleus*, **10**:93-115. doi: 10.1080/19491034.2019.1602337
2. Fišerová J, Maninová M, Sieger T, Uhlířová J, Šebestová L, Efenberková M, Čapek M, Fišer K, Hozák P* (2019) Nuclear pore protein TPR associates with lamin B1 and affects nuclear lamina organization and nuclear pore distribution. *Cell Mol Life Sci*, **76**:2199-2216. doi: 10.1007/s00018-019-03037-0

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