

MRNIP Interacts with Sex Body Chromatin to Support Meiotic Progression, Spermatogenesis, and Male Fertility in Mice

Samina Kazi¹, Julio M. Castañeda², Audrey Savolainen¹, Yiding Xu³, Ning Liu³, Huanyu Qiao³, Ramiro Ramirez-Solis⁴, Kaori Nozawa⁵, Zhifeng Yu^{5,6}, Martin M. Matzuk^{5,6}, Renata Prunskaitė-Hyyryläinen¹

¹Faculty of Biochemistry and Molecular Medicine, University of Oulu, Oulu, Finland

²Research Institute for Microbial Diseases, Osaka University, Suita, Japan

³Department of Comparative Biosciences, University of Illinois at Urbana-Champaign, Urbana, Illinois, USA

⁴University of Texas Health Science Center, San Antonio, Texas, USA

⁵Department of Pathology & Immunology, Baylor College of Medicine, Houston, Texas, USA

⁶Center for Drug Discovery, Baylor College of Medicine, Houston, Texas, USA

The MRN complex interacting protein (MRNIP) was initially identified as a protein involved in maintaining genome stability by playing a role in DNA double-strand break repair processes in mitosis. It has also been shown that MRNIP is an important factor for the protection of the replication fork during mitosis and is involved in promoting DNA double-strand break repair sensing by liquid-liquid phase separation. Our and other (PMID: 33689881) research works have established a central MRNIP role in male meiosis using *Mrnip* knock-out mouse models.

We show that *Mrnip* is ubiquitously expressed in multiple tissues both in mice and humans and that the gene expression in mice testes begins postnatally. Our analysis demonstrates that MRNIP is specific to male, not female meiosis. It is expressed during the first wave of spermatogenesis and becomes specific to meiocytes from mid-pachytene until the diplotene stage in prophase I. The deletion of *Mrnip* leads to a four-fold reduction in testes size and weight but normal body weight in mice. The histological and sperm motility analysis revealed seized spermatogenesis. Deeper studies showed that deletion of *Mrnip* leads to reduced sex body formation, impaired meiotic sex chromosome inactivation, and defective retroposition of X-linked genes to autosomes. Furthermore, we observed the formation of droplet-like accumulations of MRNIP that coalesce to create a distinct sub-nuclear compartment resembling nucleoli through meiotic progression. The analysis demonstrates that MRNIP droplets within the nucleus closely associate with the sex body during diplotene.

Taken together, the loss of *Mrnip* causes meiocyte apoptosis at the diplotene stage leading to a failure in the formation of mature and motile sperm cells causing male mice infertility.

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