Streszczenie w języku angielskim rozprawy doktorskiej pt. „Analysis of the role of selected exoribonucleases and poly(A) polymerases in *Mus musculus*"

Animal development is characterised by rapid and dynamic differentiation of new cell and tissue types. This requires precise gene expression regulation to control cell fate, often occurring at the transcriptomic level. For this reason, for a long time, multiple stages of animal development are considered useful models to study RNA polyadenylation and selective transcript degradation, as those two mechanisms can be deciding factors in cell differentiation pathway.

In most somatic cells poly(A) tail decides about transcript fate – a longer tail allows efficient translation to occur, while its shortening marks transcript for degradation. However, in oogenesis, maintaining short oligo(A) tail stabilizes transcripts stored in the cytoplasm until maturation initiation, when selective polyadenylation allows for their translation, a key process in oocyte's development. Yet mice deficient in GLD2, the only known cytoplasmic poly(A) polymerase in the oocyte, remain fertile, necessitating activity of other, unknown poly(A) polymerases in oogenesis.

On the other hand, RNA quality control and decay mechanisms are known to regulate cell pluripotency and differentiation through selective degradation of mRNAs. Both deadenylation and decapping (with additional uridylation between those steps) can trigger exoribonucleolytic degradation by exosome complex and Xrn1, respectively. Notably, only those exosome-bound exoribonucleases, EXOSC10 and DIS3, were shown to be essential for mouse embryogenesis.

Both of those aspects of transcriptome regulation in development were the focus of my doctoral project. I studied the roles of novel TENT5 family of poly(A) polymerases in oogenesis and the last catalytic subunit of the cytoplasmic exosome complex with an undefined role – DIS3L exoribonuclease - in embryogenesis in mice.

TENT5B and TENT5C noncanonical poly(A) polymerases play essential, but redundant, role in proper folliculogenesis and oocyte development. Knock-out of both genes leads to oocyte degeneration while GFP knock-in of *Tent5b* leads to disruption of chromatin organisation in the oocyte, also leading to infertility. Direct RNA sequencing revealed that TENT5s polyadenylate number of essential, oocyte-specific transcripts encoding secreted proteins, notably ZP3 and GDF9. RNA reporter assay showed that endoplasmic reticulum-

leading sequence can be determining factor for TENT5-mediated polyadenylation. In addition, investigation of poly(A) tail composition in wild-type animals also revealed specific overrepresentation of uridine residues close to 3'-terminus in a subgroup of spermatogenesis-essential transcripts

Meanwhile, DIS3L is essential for embryo development. DIS3L-deficient embryos produce viable embryonic stem cells but fail to develop beyond embryonic day 6,5. RNA sequencing of *Dis3l* knock-out blastocysts showed upregulation of several transcripts. Curiously, this was followed by lowered levels of proteins encoded by those transcripts caused by the overall lowered protein production in *Dis3l* knock-out embryos.