Abstract

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Title of the thesis: Study of ontogenesis of enzymes involved in *de novo* synthesis and salvage pathways of nucleotides in the placenta

The placenta is a highly complex, multifunctional organ, whose proper growth and development are crucial for an uncomplicated pregnancy, fetal development, and programming. Nucleos(t)ides play a fundamental role in various cellular processes, including biosynthetic reactions, the structure and function of coenzymes, and signaling mechanisms. These mechanisms are particularly significant in tissues with high proliferative activity, such as the placenta. However, our understanding of these dynamic processes, even during trophoblast differentiation, remains limited. In this study, we investigated the expression of genes involved in the *de novo* synthesis and salvage pathways of purines/pyrimidines, adenosine metabolism, and signaling in first-trimester placentas, placentas from spontaneous preterm births, term placentas, and in vitro cell models – isolated primary trophoblast cells and the BeWo cell line. To determine the expression of defined gene groups, we used the qRT-PCR laboratory method. Our results showed increased expression of genes encoding enzymes involved in *de novo* synthesis and salvage pathways of purine and pyrimidine nucleos(t)ides, as well as adenosine metabolism, in term placentas. An interesting finding was that placentas from spontaneous preterm births exhibited increased expression of genes involved in pyrimidine *de novo* synthesis, purine salvage pathways, adenosine metabolism, transport, and adenosine receptors. In differentiated primary trophoblast cells, we observed a shift in the expression of genes particularly related to adenosine metabolism. Our results suggest that nucleos(t)ide metabolism is regulated during placental development and that dysregulation of this dynamic process may be associated with preterm birth mainly with the compensatory mechanism. Furthermore, the changes in adenosine metabolism and signaling observed in our study point to the critical physiological role of this nucleoside. Further research is needed to fully elucidate the mechanisms of nucleos(t)ide metabolism in the human placenta and how placental nucleos(t)ide metabolism is influenced by commonly ingested methylxanthines (e.g., caffeine) or nucleos(t)ide-derived antiretroviral drugs (e.g., abacavir) used in HIV pharmacotherapy during pregnancy.