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Design of COMT-Knockout mouse as a preeclampsia mode

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Preeclampsia is a multisystem pregnancy disorder that occurs after 20 weeks of gestation, leading to e.g. preterm labor. It is characterized by hypertension, proteinuria, edema, and multiple organ dysfunction. Up to 8% of pregnancies are complicated by preeclampsia, which is one of the most serious causes of maternal and perinatal mortality [1]. For research of pregnancy disorders and development of therapy for it, a mouse model can be used due of the fact that pregnancy development in mice, especially at early stages, is somewhat similar to human and is well-studied, in particular, in terms of molecular biology [2]. One of the possible options for creating mouse models of preeclampsia is considered to be a mutation in the *COMT* gene encoding catechol-O-methyltransferase [3]. This enzyme plays an important role in the catecholamines conversion and it also catalyzes the O-methylation of hydroxyestradiol producing methoxyestradiol. *COMT* gene knockout results in a phenotype similar to preeclampsia with elevated blood pressure and proteinuria [3]. The previous model was obtained through classic transgenesis methods with Neomycin cassette insertion in the *COMT* locus potentially influencing the results of the experiments. The development of the genome editing systems and its active utilization at Saint Petersburg State University made it possible to obtain a *COMT*-KO mouse line using CRISPR/Cas9 technology which had not been done in Russia before. This model will allow to effectively study the development of preeclampsia and ways to prevent and treat it.

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REFERENCES

1. Sibai BM. Preeclampsia As a Cause of Preterm and Late Preterm (Near-Term) Births. *Semin Perinatol.* 2006;30(1):16–19. DOI: 10.1053/j.semperi.2006.01.008

2. Wu SP, Emery OM, DeMayo FJ. Molecular Studies on Pregnancy with Mouse Models. *Curr Opin Physiol.* 2020;13:123–127. DOI: 10.1016/j.cophys.2019.10.018

3. Kanasaki K, Palmsten K, Sugimoto H, et al. Deficiency in catechol-O-methyltransferase and 2-methoxyoestradiol is associated with pre-eclampsia. *Nature.* 2008;453(7198):1117–1121. DOI: 10.1038/nature06951

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