„Influence of interaction of maternal and genetic factors on offspring development and behaviour in mouse models of autism"
mgr Marta Ziętek

Autism spectrum disorders (ASD) are heterogeneous psychiatric conditions characterized by deficits in social communication and repetitive/stereotyped behaviours. Both genetic and environmental factors are known to affect neurodevelopment and the risk of developing ASD.

In the present study, the interaction of genetic and environmental factors was tested in the context of determining the occurrence of ASD. To this aim, the influences of advanced maternal age (AMA) – a known risk factor for ASD – on pregnancy outcomes and on offspring behaviour were investigated in a mouse strain genetically predisposed to develop ASD-like behaviours, BTBR T$^+$Itpr3^{tf}/J (BTBR), as well as in the normo-behaving C57BL/6J (C57BL6) strain. Furthermore, reciprocal embryo transfers between old and young females, as well as between strains, were conducted to study maternal- and embryonic-related factors influencing ASD occurrence in offspring.

Reproductive outcomes were negatively affected by AMA in both strains, while the effects of AMA on offspring ASD-like behaviours were strain-specific and depended on the offspring sex. Embryos conceived by old females had increased survival rate when transferred into young recipient, although the offspring obtained still displayed alterations in communicative and learning behavioural domains. Furthermore, development of BTBR embryos in C57BL6 recipients, and vice versa, did not change the typical behavioural phenotype characteristic of each strain.

These findings suggest that ASD-like behaviours can be reduced or exacerbated by maternal age depending on the offspring genetic background and sex, and that these effects are mainly mediated by embryonic innate predisposition to develop ASD-like behaviour, rather than to the suboptimal maternal environment provided during pregnancy by old or BTBR females.