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MHC GENES DETERMINE FETAL SUSCEPTIBILITY IN A RAT MODEL OF CONGENITAL HEART BLOCK

Vijole Dzikaite,¹ Maja Jagodic,² Vijay K Kuchroo,³ Tomas Olsson,² Marie Wahren-Herlenius¹ ¹Rheumatology Unit, Department of Medicine, Stockholm, Sweden; ²Neuroimmunology Unit, Department of Clinical Neuroscience, Stockholm, Sweden; ³Center for Neurological Diseases, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA

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Objective Congenital heart block (CHB) develops in fetuses of anti-Ro52 antibody positive women. A recurrence rate of 12–25%, despite the persistence of maternal autoantibodies indicates that there are additional, yet unidentified, factors critical for development of CHB. The authors hypothesised that fetal susceptibility to the maternal autoantibodies could be determined by fetal genes.

Methods A passive antibody transfer model was used in several different rat strains and MHC congenics (DA.AV1; Lew.1AV1; Lew.L; Lew.N). Two-four mg of a Ro52 monoclonal antibody (7.8C7) was injected intraperitoneally before day 7 of gestation. On the day of delivery, three-lead ECG were recorded from conscious pups.

Results After maternal passive antibody transfer, significant PR prolongation was induced in the DA.AV1 pups by Ro52-p200 specific antibodies at the dose of 4 mg. In Lew.1AV1 rats, PR prolongation was induced in the pups already at 2 mg injections, indicating that fetal non-MHC genes can increase susceptibility to CHB. In Lew.L rats, PR intervals were significantly more prolonged after 2 mg injections, indicating that fetal L MHC genes conferred to highest susceptibility to CHB. In Lewis.N rats however, no difference in the PR intervals were observed between the PBS-injected control group and groups injected with 2 or 4 mg of Ro52 monoclonal antibody, suggesting that specific fetal MHC genes can confer the resistance and play a protective role in the development of the CHB.

Conclusions Our findings show that both fetal MHC and non-MHC genes regulate susceptibility to CHB and determine the fetal disease outcome in anti-Ro52 positive pregnancies. Different fetal MHC alleles can either render the fetus susceptible or play a protective role in the disease development.