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Autor(en) des Beitrags: Adler, K; Krause, S; Fuchs, YF; Foertsch, K; Ziegler, AG; Bonifacio, E


Abstract: The impact of gestation and fetal-maternal interactions on pre-existent autoimmune beta cell destruction is widely unknown. The aim of this study was to investigate the influence of gestation per se and fetal mismatching on the onset of autoimmune diabetes in female non-obese diabetic (NOD) mice. We examined cumulative diabetes frequencies of NOD dams mated to syngeneic NOD, haploidentical CByB6F1/J and fully mismatched C57BL/6J male mice. Pregnancy from NOD males neither increased nor accelerated the diabetes onset of NOD dams (71% by age 28 weeks) compared to unmated female NOD mice (81% by age 28 weeks; P = 0.38). In contrast, delayed diabetes onset was observed when NOD dams were mated at 10 weeks of age with major histocompatibility complex (MHC) haploidentical CByB6F1/J male mice (38% at age 28 weeks; P = 0.01). Mating with fully MHC mismatched C57BL/6J male mice (72% diabetes by age 28 weeks; P = 0.22) or mating with the haploidentical males at the later time-point of age 13 weeks (64% versus 91% in unmated litter-matched controls; P = 0.13) did not delay diabetes significantly in NOD females. Because infusion of haploidentical male mouse splenocytes was found previously to prevent diabetes in NOD mice we looked for, but found no evidence of, persistent chimeric lymphocytes from haploidentical paternal origin within
the dams' splenocytes. Gestation per se appears to have no aggravating or ameliorating effects on pre-existent autoimmune beta cell destruction, but pregnancy from MHC partially mismatched males delays diabetes onset in female NOD mice.