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Molecular pathology of diabetic embryopathy in mouse models

Claudia Kappen

Pennington Biomedical Research Center, USA

Maternal diabetes during pregnancy is a well-known risk factor for a spectrum of structural birth defects in the offspring, collectively addressed as diabetic embryopathy. Heart defects and neural tube defects are the most common malformations, but craniofacial defects, caudal growth defects and either small or large-for-gestational-age are also characteristic outcomes. It is believed that the latter two conditions also constitute risk factors for cardiometabolic disease later in life. Using mouse models, my research program investigates the underlying molecular mechanisms for abnormal development in utero, with particular focus on neural tube defects. Embryos exposed to maternal diabetes in utero are smaller, which is associated with placental abnormalities and altered gene expression. Microarray and in situ hybridization studies identified abnormalities in proliferation and migration of spongiotrophoblasts, which are a source of intrauterine nutrition. The exposure also alters gene regulatory programs in the developing embryo, particularly affecting the expression of known genes that have a role in neural tube closure. Evidence from chromatin-immunoprecipitation, followed by nextgeneration sequencing, implicates epigenetic changes as the underlying molecular mechanism. We have recently shown that the neural tube closure defects in the diabetic models are preceded by impairments in gastrulation, the critical process during which cells for all three germ layers are specified. These early abnormalities, for the first time, provide a unifying molecular and cellular explanation for the seemingly unconnected phenotypic defects in diabetic embryopathy.

Biography

Claudia Kappen received her doctorate from the University of Cologne, Germany, followed by postdoctoral training at Yale University. She since directed independent research laboratories at Mayo Clinic Arizona and University of Nebraska Medical Center, rising through the ranks to Full Professor, and currently holds the Peggy M. Pennington Cole Endowed Chair in Maternal Biology at Pennington Biomedical Research Center in Baton Rouge, Louisiana. She has 60 publications listed in PubMed, received the James G. Wilson Publication Award from the Teratology Society in 2009, co-edited a special issue "Neural Tube Defects" for the journal Birth Defects Research, and serves as Associate Editor for the journals Reproductive Toxicology and PLoS One.

Claudia.Kappen@pbrc.edu

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