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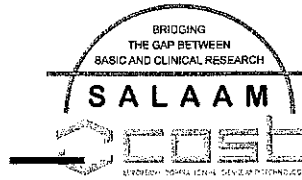
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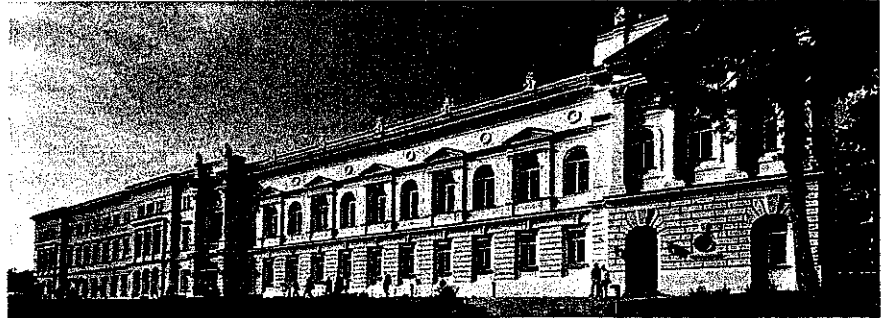
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FINAL CONFERENCE

**ADVANCES ON LARGE ANIMAL MODELS: BRIDGING THE GAP BETWEEN
BIOMEDICAL RESEARCH AND CLINICAL TRANSLATION**

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PROGRAMME AND ABSTRACTS

Is maternal diabetes causing a delay in embryo development through hypoblast underdevelopment?

Grybel KJ¹, Canon E², Knelangen J¹, Kradolfer D³, Pendzialek M¹, Schindler M¹, Seeling T¹, Gürke J¹, Blachère T⁴, Godet M⁴, Obeid R⁵, Ulbrich S³, Fischer B¹, Duranthon V² and Navarrete Santos A¹

Department of Anatomy and Cell Biology, Martin Luther University Faculty of Medicine, Halle, Germany¹;

INRA, UMR 1198, Department of the Reproductive Biology, F-78350 Jouy-en-Josas, France²;
Institute of Agricultural Sciences, LFW B 57.1, Universitätstrasse 2, 8092 Zürich, Switzerland³
Stem-cell and Brain Research Institute, Inserm U846, 69500 Bron, France and University of Lyon, Université Lyon I, 69003, Lyon, France⁴;

Department of Clinical Chemistry, University Hospital of the Saarland, 66424, Homburg, Germany⁵

In early pregnancy maternal diabetes leads to delay in embryo development and changes in nutritional and hormonal signals of the uterine environment. The current study focuses on consequences of maternal diabetes on embryonic tissue formation and its DNA methylation.

We have investigated the expression and promoter methylation of epiblast lineage specifier Oct4 in 6 day old rabbit blastocysts at early gastrulation stage. The expression of Oct4 was higher in epiblast of diabetic blastocysts, accompanied by upregulation of Nanog and Sox2, suggesting that epiblasts were less differentiated. Moreover the hypoblast differentiation factors Cer1 and Dkk1 were downregulated, what is a mark of underdevelopment.

Specific methylation of the POU5F1 (Oct4) promoter region was investigated by bisulfite sequencing. The Oct4 promoter was hypomethylated in hypoblasts and trophoblasts of diabetic rabbits, implying also a mark of delay in differentiation.

The global DNA methylation of male and female blastocysts from diabetic and healthy rabbits was examined, employing embryoblast and trophoblast tissue separately, using Luminometric Methylation Assay (LUMA). No significant changes in global DNA methylation were observed between embryonic tissues from healthy and diabetic embryos.

Furthermore we verified that the methyl group donor S-adenosyl methionine (SAM) and the product of the methylation reactions S-adenosylhomocysteine (SAH) were changed in diabetic pregnancy. Concentrations of SAM and SAH were measured by use of a modified liquid chromatography-tandem mass spectrometry in rabbit blood plasma collected at the day 6 *post coitum*.

Oct4 methylation was not caused by global methylation changes. Our data showed that maternal diabetes mellitus affects the Oct4 promoter methylation in a specific way with consequences for Oct4 gene transcription and embryo development. A possible reason for this could be delay in differentiation of the hypoblast tissue what has a consequence on signaling between the hypoblast and epiblast.

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