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Supplemental figures for

"Endometrial Receptivity Defects and Impaired Implantation in Diabetic NOD Mice"

by

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Supplemental Figure Legends:

Albaghdadi and Kan Supplemental Figure S1. Blood glucose changes in the dNOD and cNOD prior to, during and after pregnancy. Diabetes started in the dNOD mice in a prediabetic stage between weeks 9-11 during which time all dNOD mice were found to have blood glucose values of $\geq$ 10.0 mmol/L. All groups of NOD mice were mated at the age of 11 weeks. Pregnancy accelerated the development of overt diabetes at week 12 and beyond, where all dNOD mice had blood glucose values of $\geq$14.9 mmol/L. Real time tracing of blood glucose beyond the post-implantation period until parturition and ten days afterwards were also recorded. Data represent mean $\pm$ SEM of three independent experiments with similar outcome. n= 5-7 per group per experiment.

Albaghdadi and Kan Supplemental Figure S2. Uterine weight changes during peri- and post-implantation in the normally mated and the ConA-pseudopregnant cNOD and dNOD mice. Decidualization and implantation failure in the dNOD mice were reflected in significantly ($p < 0.01$) less uterine weight gain at the peri- and post implantation on E4.5 and E6.5 in the normally mated and the ConA-pseudopregnant dNOD mice. Graph bars represent mean $\pm$ SEM of three independent experiments with similar outcome. Different letters represents statistical differences among NOD groups at 95% confidence where $p < 0.05$. n= 5-7 per group per experiment.

Albaghdadi and Kan Supplemental Figure S3. Morphometry of decidualized cross sectional uteri of normally mated and ConA-decidualized cNOD and dNOD dams during peri- and post-implantation. Cross-sectional areas of decidualized uteri of cNOD mice on E4.5, E4.5bid, E6.5 and E6.5bid are represented in photomicrographs A-A1, B-B1, C-C1, and D-D1 respectively. Similarly, E-E1, F-F1, G-G1 and H-H1 depict decidualization in uterine cross-sections in dNOD

mice on E4.5, E4.5bid, E6.5 and E6.5bid, respectively. Morphometry was performed using Image Pro Plus (Media Cybernetics, Inc., MD, USA). Best-fit decidualized uterine cross sections in A1-D1 and E1-H1 were highlighted in white. Empty space occupied by lumina of uteri and/or metrial glands in A1-D1 and E1-H1 were black-shaded and were excluded from analysis. The decidual (inner) margin of the uterine circular (inner layer) smooth muscles was considered in marking the outer limits of the decidualized uterine cross sectional region during morphometry. Scale bars = 200μm. Data in the bar graphs represent mean ± SEM of two independent experiments with similar results. n= 5 per group per experiment.

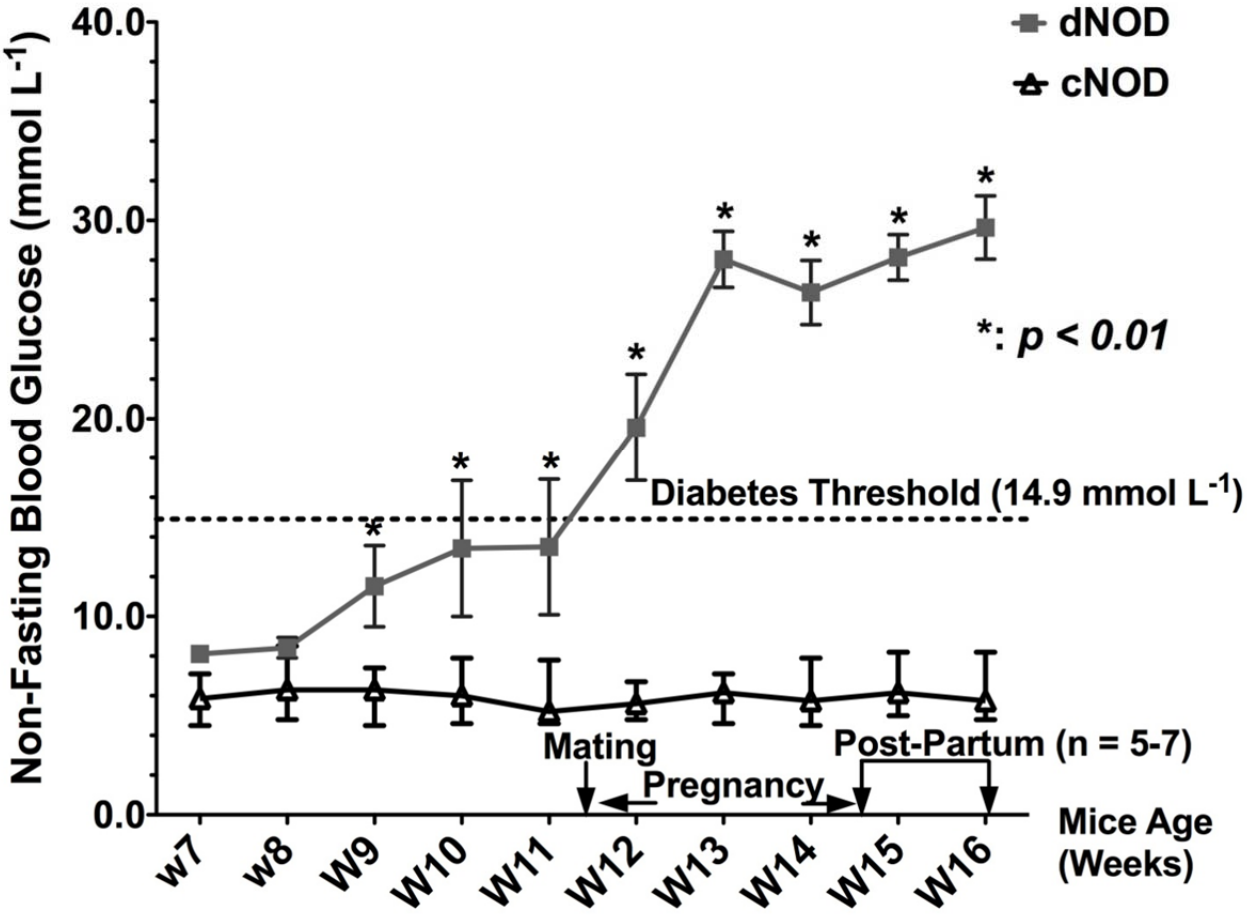
Albaghdadi and Kan Supplemental Figure S4. Expression of Leukemia Inhibitory Factor (LIF) in the uteri of normally-mated cNOD and dNOD mice at the peri and post-implantation periods. Reduced LIF expression accompanied uterodome maturation failure in the uteri of dNOD mice at the time of embryo implantation. WB detection of LIF on E4.5 and E6.5 in the uteri of cNOD is expressed in lanes 1 and 2, whereas lanes 3 and 4 are representative of LIF expression in dNOD on E4.5 and E6.5, respectively. Graph bars represent mean values of LIF/GAPDH chemilumiscence ± SEM obtained in three independent experiments for all lanes within the respective WB as measured by Image J analysis with background subtraction. Statistical differences among data represented in the graph bars are indicated by different alphabets where $p < 0.05$. n= 5-7 per group per experiment.

Albaghdadi and Kan Supplemental Figure S5. Levels of serum progesterone (P4) during peri- and post-implantation in cNOD and dNOD mice. Significantly ($p<0.01$) high level of serum P4 in dNOD mice was measured on E4.5 and E6.5, respectively. Unexpectedly, a dramatic reduction in the serum level of P4 was measured on E8.5 in the normally-mated dNOD mice.

Data shown in the graph represents mean ± SEM of three independent experiments with similar outcome. n= 5-7per group per experiment.

Albaghdadi and Kan Supplemental Figure S6. Linear regression analysis between levels of MUC1 mRNA expression as a function of percentage of co-localization of PIASy and PRs in early pregnancy in the normally-mated and the pseudopregnant cNOD (A and B) and dNOD mice (C and D) NOD, respectively. Correlation was significant ($p < 0.001$) during implantation in mated cNOD and dNOD mice. Significantly low ($p < 0.01$) PR A and B expression in the pseudopregnant dNOD mice resulted in lack of correlation. The Spearman correlation "r" values indicating significant correlations in different experimental groups are the following: Normal early pregnancy: 0.7845, Normal pseudopregnancy: 0.6929 and Diabetic early pregnancy: 0.7533. Diabetic pseudopregnancy has a square root value of 0.4352 ($p = 0.196$).

Albaghdadi and Kan Supplemental Figure S1:



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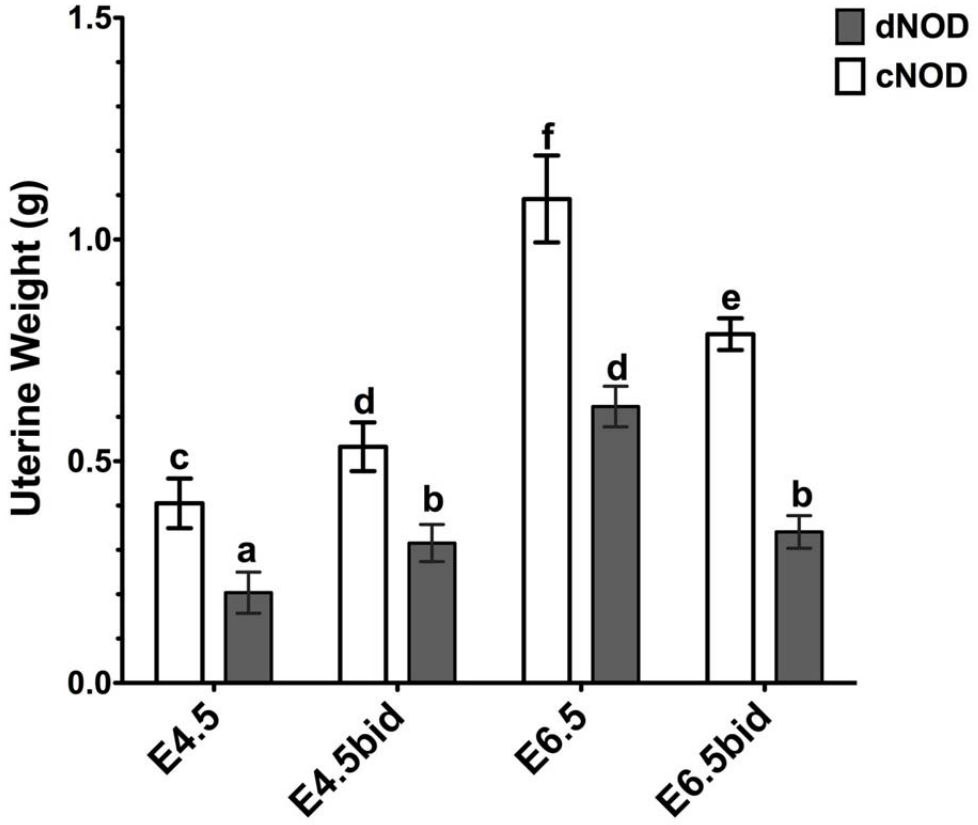
Albaghdadi and Kan Supplemental Figure S2:



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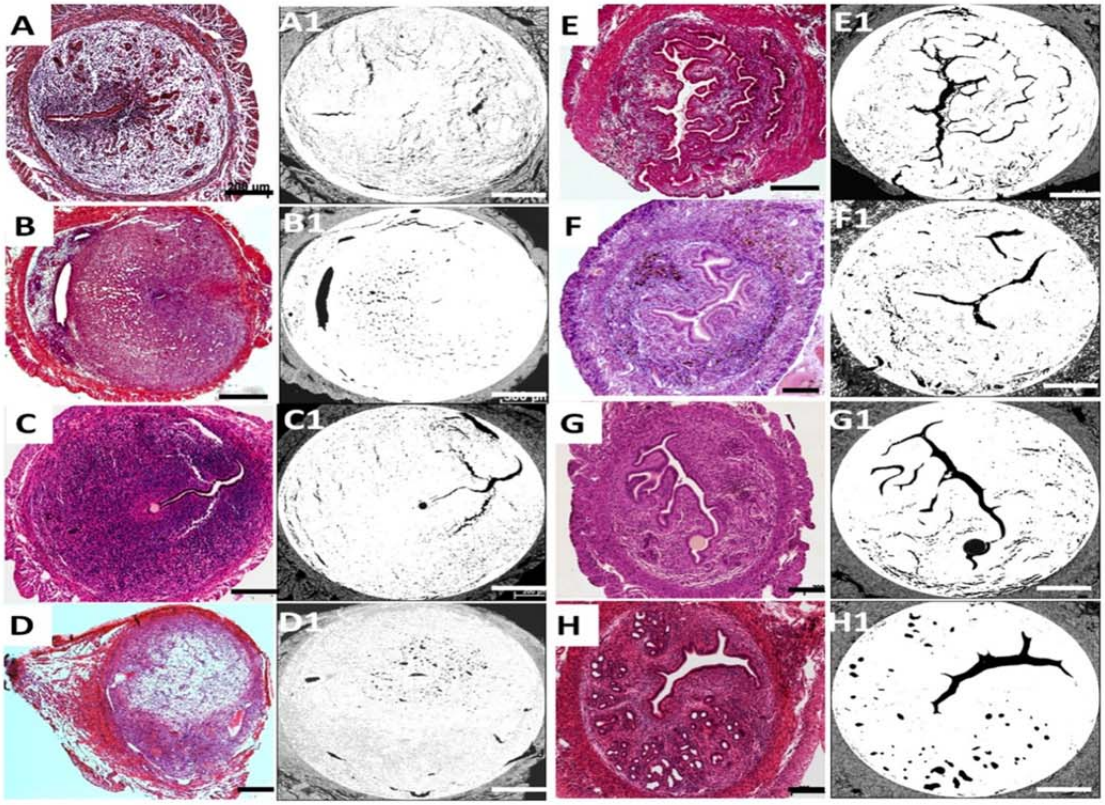
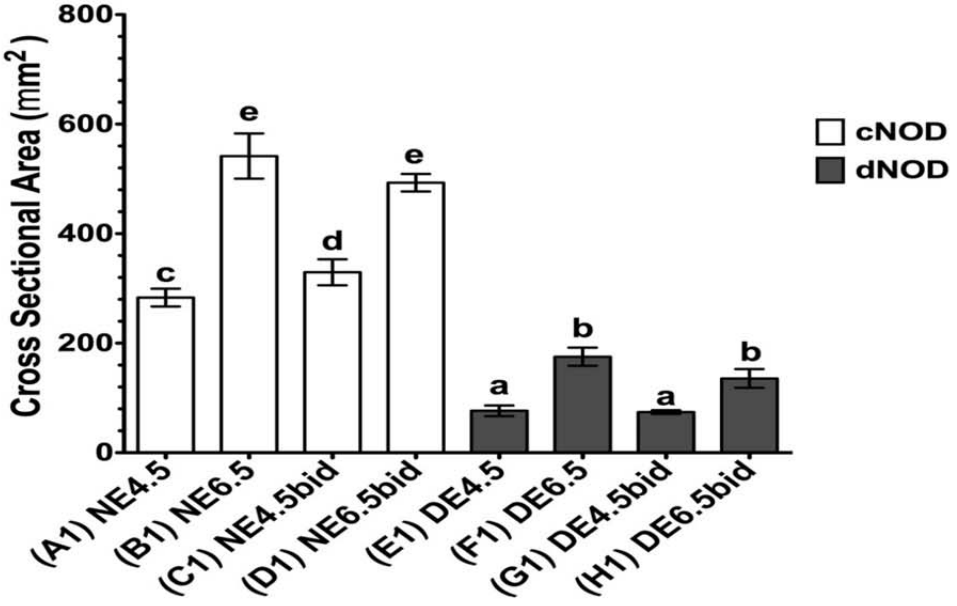
Albaghdadi and Kan Supplemental Figure S3:





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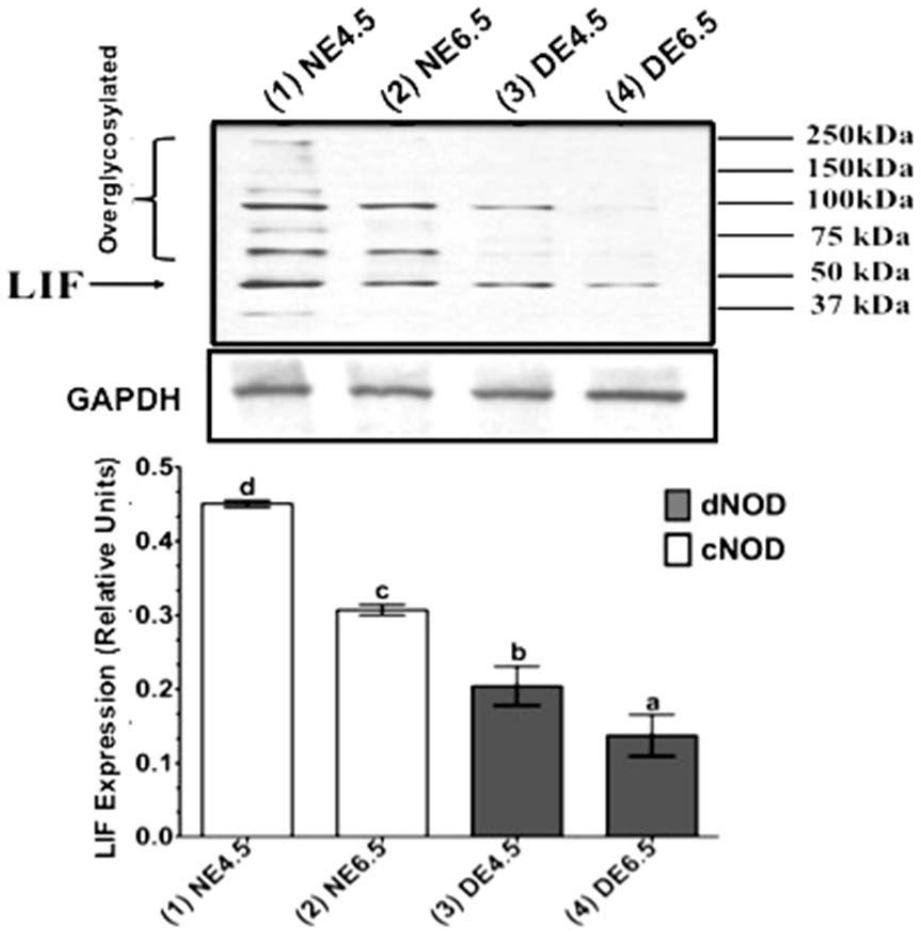

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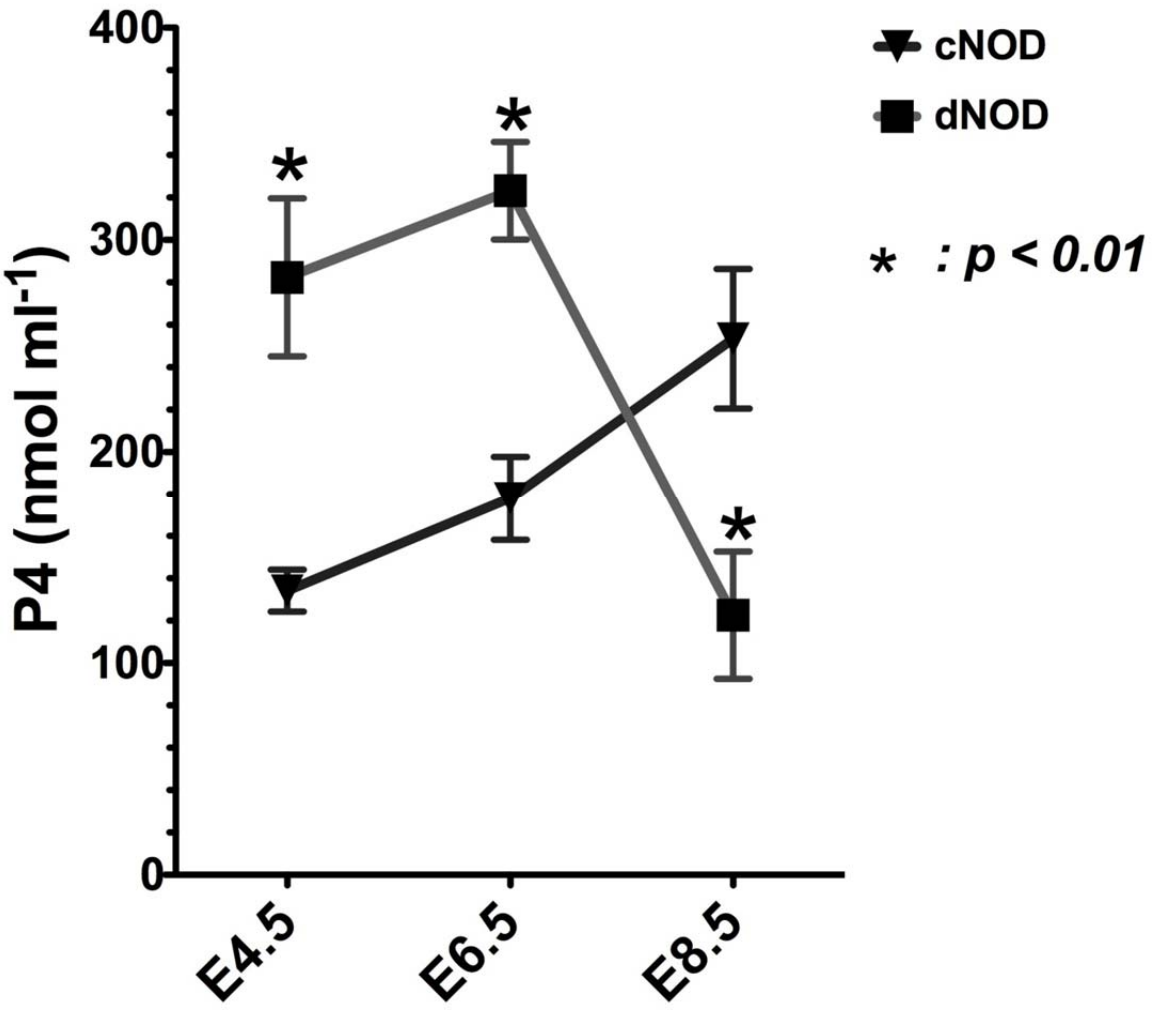

Albaghdadi and Kan Supplemental Figure S6: