

#### **49. TREATMENT OF THE PREGNANT MOUSE WITH IGF-II IN EARLY PREGNANCY ENHANCES FETAL AND PLACENTAL GROWTH**

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Gene deletion studies have shown that insulin-like growth factor-II (IGF-II) null mutation reduces both placental and fetal growth while IGF-I deficiency reduces fetal growth only. In addition, ablation of the placental labyrinth specific IGF-II transcript (P0) reduces placental growth and alters placental transport capacity resulting in fetal growth restriction. This study aimed to determine whether treatment with exogenous IGF-II during the first half or throughout pregnancy increases placental and fetal growth and alters placental structural maturation. Two cohorts of C57Black female mice of similar weight were mated with Balb/C males. On day 2 of pregnancy (day of plug = day 1), a mini osmotic pump set to deliver either 0, 12.5 or 25 µg IGF-II/day in 0.1 mmol/L acetic acid for either 8 or 16 days was inserted subcutaneously. Females were killed on day 18 of pregnancy (term = 19 days), blood was taken and placental and fetal weights were recorded. Placentas were either frozen for mRNA analyses or fixed for morphometric analyses. Plasma IGF-II in mice treated throughout pregnancy was assayed. IGF-II mRNA expression relative to 18S rRNA was assessed by real time RT-PCR. Placental weight was increased by 9.6% and 7.5% ( $P<0.05$ ) in mice treated with low and high dose IGF-II respectively from days 2-10 of pregnancy, while fetal weight was increased by 4.1% ( $P<0.05$ ) in the higher dose group. The volume of the maternal blood space in the placental labyrinth was increased by 11.8% with low dose IGF-II treatment. IGF-II mRNA expression in the higher dose group of mice treated from days 2-18 was 180% of controls following exclusion of animals in which the mini pump had ceased to deliver IGF-II ( $P=0.01$ ). Maternal net carcass weight was similar in all groups from both cohorts. In conclusion, treatment with exogenous IGF-II in the first half of murine pregnancy enhances both fetal and placental weights late in gestation but has small effects if administered throughout gestation. This suggests that IGF-II is most important in the invasive phase of placental development. IGF-II treatment of individuals with a poor capacity to synthesise IGF-II early in pregnancy may improve placental function and enhance fetal growth in pregnancies at risk.