Regulation of Mouse Uterine Aquaporin Expression in the Preimplantation Period and the Impact of Ovarian Superovulation

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Uterine fluid level in early pregnancy is a critical determinant of fertility and aquaporins (AQPs), selective bidirectional transporters that move water along a concentration gradient, are major regulators of water homeostasis. The expression of mouse uterine AQP genes and proteins in early pregnancy has been studied but these studies yielded inconsistent results. To better understand their roles in regulating luminal fluid levels in the preimplantation period, we conducted a multi-pronged analysis of uterine Aqp/AQP expression on the morning of D1 and D4 of pregnancy in ovarian superovulated and non-superovulated WT C57 Bl/6 mice. Expression was also determined in ovariectomized mice that received E2, P4 or E2 + P4 and in D4 pregnant RU486-treated mice. Our analyses revealed that in the non-superovulated females, Aqp3, Aqp4, Aqp5 and Aqp8 exhibit greater expression on D1 and are induced by E2 while Aqp1 and Aqp11 exhibit greater expression on D4 and are induced by P4. Interestingly, Aqp9 is constitutively expressed. We also observed that P4 inhibits the E2-induced expression of Aqp3 and Aqp4 (with the negative effect on Aqp3 being transient) while Aqp1 and Aqp11 are negatively regulated by E2. Superovulation increased Aqp1, Aqp3, Aqp5 and Aqp8 expression on D4 and triggered dramatic spatial changes in AQP expression in both D1 and D4 uteri. These aberrant changes in expression following superovulation likely reduce implantation success and might be managed by targeting E2 or P4 levels and actions in the uterus during *in vitro* fertilization and embryo transfer (IVF/ET).