Progesterone's effect on gamete transport in the fallopian tube

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin vid Göteborgs universitet kommer att offentligt försvaras i hörsal Ivan Östholm Medicinare gatan 13, Göteborg, onsdagen den 3 december 2014, kl 9:00

av

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Avhandlingen baseras på följande delarbeten

I. ***Rapid effects of progesterone on ciliary beat frequency in the mouse fallopian tube.***

Bylander A, Nutu M, Wellander R, Goksor M, Billig H, Larsson DGJ.
Reprod Biol Endocrinol 2010, 8:48

II. ***The classical progesterone receptor mediates the rapid reduction of fallopian tube ciliary beat frequency by progesterone.***

Bylander A, Lind K, Goksor M, Billig H, Larsson DGJ.
Reprod Biol Endocrinol 2013, 11:33.

III. ***Progesterone-mediated effects on gene expression and egg transport in the mouse fallopian tube.***

Bylander A, Gunnarsson L, Shao R, Billig H, Larsson DGJ.
Submitted manuscript

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ABSTRACT
The fallopian tube plays an important role for successful female reproduction as it transport gametes to the fertilization site, nourish the developing embryo and transport it to the uterus at the suitable time for implantation. The overall aim of this thesis was to investigate the role of progesterone in control of gamete transport.

Ciliary cells are important for the transport of gametes and embryos through the fallopian tube. In paper **I** we developed a method to measure ciliary movement in the mouse fallopian tube. By using a high speed camera connected to a microscope we were able to document rapid effects of progesterone on the ciliary beat frequency *in vitro*. In ciliary cells from mice fallopian tube treated with progesterone at concentrations of 20 μM and a more physiological relevant concentration of 100nM, we found a rapid reduction in ciliary beat frequency with 10 % and 15 % respectively, within 30 minutes after addition of progesterone.

In paper **II** we investigated the possible involvement of the classical progesterone receptor in mediating the rapid effect of progesterone. The ciliary beat frequency was significantly reduced within 10-30 minutes by low concentrations of progesterone (10-100 nM) and by another more specific agonist. Co-exposure to an antagonist completely blocked the effect of progesterone. In mice lacking a functional progesterone receptor we found no effect of progesterone. This strongly indicates that progesterone reduces ciliary beat frequency by acting on the classical progesterone receptor. The rapid onset of the effects suggests that a non-genomic mechanism is involved.

In paper **III** we used microarray to investigated possible changes in gene expression in mice fallopian tube after *in vitro* exposure to progesterone for 20 minutes or 2 hours. We could not detect any change in gene expression with microarray after 20 minutes exposure to progesterone, which is coherent with the hypothesis that the rapid reduction in ciliary beat frequency is not dependent on transcription. In fallopian tubes exposed to progesterone for 2 hours 11 genes were differently expressed compared to controls. This change was confirmed by quantitative PCR at 2h and 8h. The most interesting gene regulated by progesterone was endothelin-1, a signal peptide known to induce muscle contraction in the fallopian tube. In this paper we also studied the role of the progesterone receptor in the transport of the oocyte-cumulus complex. Gonadotropin-treated mice were given a single injection of one of the progesterone receptor antagonist Org 31710 or CDB2194 or vehicle 6 hours before ovulation. In mice treated with both antagonists the oocyte-cumulus complex travelled faster through the fallopian tube than in mice only given vehicle.

In conclusion, we found that progesterone rapidly reduces the ciliary beat frequency in ciliary cells from mice fallopian tube and that this reduction is mediated through the classical progesterone receptor, probably via a non-transcriptional mechanism. We show that progesterone regulates endothelin-1, a peptide known to induce muscle contractions in the fallopian tube. This suggests that endothelin-1 is as a mediator of the previously shown effects of progesterone on tubal contractility. We confirm earlier studies by demonstrating that progesterone and the progesterone receptor are important for a normal tubal transport. Taken together, this thesis contributes to a deeper understanding of the role of progesterone and the progesterone receptor in the regulation of gamete and embryo transport along the fallopian tube.

Keywords: Fallopian tube, progesterone, ciliary beat frequency, gamete transport
ISBN: 978-91-628-9178-7