Regulation of LH/CGR receptor signalling in human endometrium

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**Introduction**

The interaction that takes place between an implanting embryo and the endometrium is essential for successful implantation. However, this process in humans is relatively inefficient and the frequency of subfertility is high, affecting one in six couples in developed countries. As well as a high frequency of subfertility, embryo wastage and pregnancy loss in humans is also prevalent, with an estimated 30% of embryos lost prior to implantation and a further 30% before 6 weeks gestation (Salter et al., 2010). The glycoprotein hormone human chorionic gonadotrophin (hCG) is one of the earliest signals secreted by the embryo, and may facilitate implantation. It is well known that hCG is an essential signal for successful implantation. However, this process in humans is relatively inefficient and the frequency of subfertility is high, affecting one in six couples in developed countries. The interaction that takes place between an implanting embryo and the endometrium is essential for successful implantation. However, this process in humans is relatively inefficient and the frequency of subfertility is high, affecting one in six couples in developed countries.

**Background**

**Human Endometrial Stromal Cells (HESCs) and hCG responses**

![Image](https://example.com/image1.png)

**Aims**

1. Identify the trafficking mechanism for the LH/CR in HESCs, and investigate potential interacting proteins that may mediate this during decidualisation.
2. Define and characterise the LH/CR signalling pathways that are activated in differentiated and undifferentiated HESCs both constitutively and in response to hCG.

**Results: LH/CR Trafficking**

1. Trafficking of the LH/CR receptor alters between undifferentiated and decidualised HESCs and this is receptor specific

![Image](https://example.com/image2.png)

2. Truncation of the C-terminal tail of the LH/CR does not affect receptor trafficking

![Image](https://example.com/image3.png)

**LH/CR Signalling**

1. HESCs display changes in receptor trafficking following decidualisation that is specific to the LH/CR receptor

![Image](https://example.com/image4.png)

2. A truncated LH/CR receptor unable to bind trafficking proteins such as GIPC changes the endocytic compartmentalisation of the receptor

3. Knockdown of APPL1 and GIPC may direct the LH/CR to larger, EE-like compartments

4. The MAPK signalling pathway is activated in HESCs

5. HCG couples to the Gαi pathway in HESCs to decrease levels of cAMP but the signalling profile changes when the receptor is over-expressed

6. Splice variants of the receptor are expressed in control and decidualised HESCs and may explain why this receptor activates the non-classical Gαi pathway in these cells

**Conclusions**

1. HESCs display changes in receptor trafficking following decidualisation that is specific to the LH/CR receptor
2. A truncated LH/CR receptor unable to bind trafficking proteins such as GIPC changes the endocytic compartmentalisation of the receptor
3. Knockdown of APPL1 and GIPC may direct the LH/CR to larger, EE-like compartments
4. The MAPK signalling pathway is activated in HESCs
5. HCG couples to the Gαi pathway in HESCs to decrease levels of cAMP but the signalling profile changes when the receptor is over-expressed
6. Splice variants of the receptor are expressed in control and decidualised HESCs and may explain why this receptor activates the non-classical Gαi pathway in these cells

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**References**

Dickinson et al., 2009


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**Imperial College Healthcare NHS Trust**

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**Imperial College London**