

# FOCUS ON RESEARCH

## THE ROLE OF THE HEMEOXYGENASE/CARBON MONOXIDE SYSTEM IN TROPHOBLAST INVASION AND IN PROTECTION FROM OXIDATIVE STRESS DURING PREGNANCY

### Researchers

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### Aim

This study aimed to further understand the role of an enzyme known as hemeoxygenase (HO) which is found both in the placenta and in the cells which help to establish blood flow to the placenta and baby during pregnancy (known as invasive trophoblast cells). The HO enzyme produces the gas carbon monoxide (CO) which dilates placental blood vessels and may also have antioxidant properties. The aim of this study was to understand the role of oxygen in regulating the HO enzyme and to learn whether the enzyme may help the specialised invasive trophoblast cells invade the uterus and establish the blood circulation between mother and baby.

### Project Outline/Methodology

- To use a cell culture system designed to mimic the invasion of trophoblast cells in the body and then attempt to interfere with the HO enzyme to determine its role in invasion of the uterus.
- To use a "real life" model of oxygen deprivation, namely women living at high altitude to determine if living in a low oxygen environment affects the HO enzyme. We had previously shown that the pregnancy condition pre-eclampsia (associated with low oxygen in the placenta) is associated with less HO protein in cells which line the inside of placental blood vessels (endothelial cells).
- To establish a model of blood flow in the pregnancy condition pre-eclampsia (blood flow is abnormal and results in a type of "oxidative stress") and then find out how this affects HO.
- To try and increase the amount of HO protein in placental cells using a variety of chemicals.

### Key Results

The major findings were as follows:

- Antibodies and chemicals which interfere with HO function were found to inhibit the invasion of trophoblast cells.
- The amount of the HO enzyme in endothelial cells (which keep blood vessels wide open in the

placenta) was found to be reduced in pregnant women at high altitude

- The various types of oxidative stress applied to the placental cells did not appear to affect the amount of HO protein
- The substance "hemin" was able to increase the amount of HO protein in placental trophoblast cells.

### Conclusions

This work provides evidence that the HO/CO system may be involved in development of the fetal-placental circulation by helping trophoblast cells invade the uterus. It also suggests that the reduction in HO protein in pre-eclampsia may be related to a defect in the oxygen environment, as a similar abnormality was seen in high altitude pregnancy.

### What does this study add to the field?

Our understanding of what controls trophoblast invasion is minimal and this study is the first to show that the HO system may be involved. This study also expands our knowledge of what goes wrong in pre-eclampsia and how it is affected by changes in oxygen and HO.

### Implications for Practice or Policy

At the moment this research does not affect practice directly.

### Where to next?

There are many areas to explore. These include understanding what causes the reduction of the HO protein on blood vessel endothelial cells and if this can be restored using agents such as hemin to induce HO protein. This could one day be a possible target for increasing blood flow in the placenta in problem pregnancies such as pre-eclampsia.

### Further details from:

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