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A new *ex vivo* method for studying transport and metabolism of azoles in human term placentas

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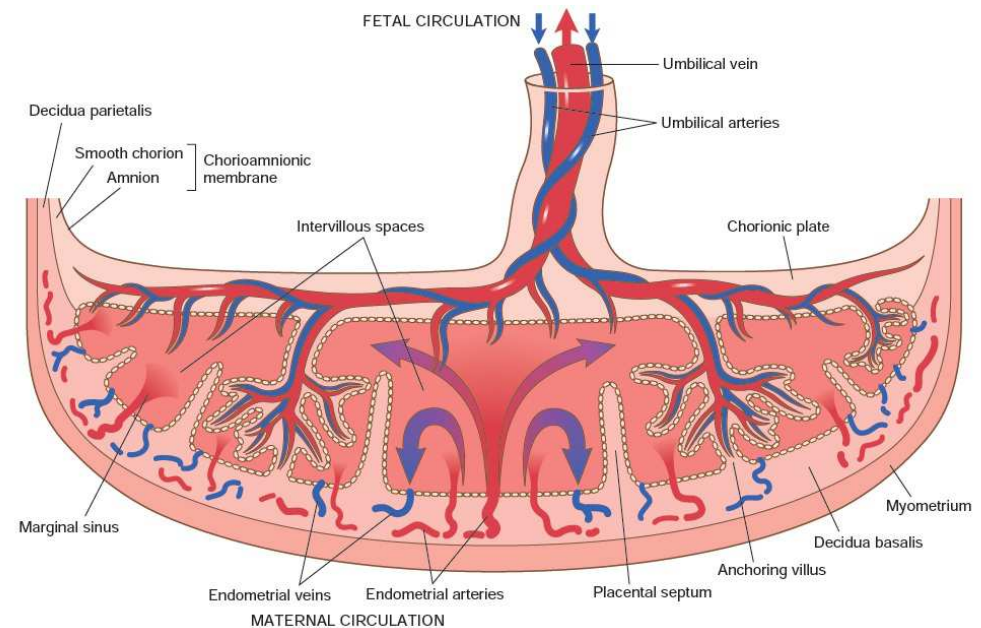


Introduction

The human placenta is a unique organ with limited anatomical resemblance to placentas of commonly used laboratory animals

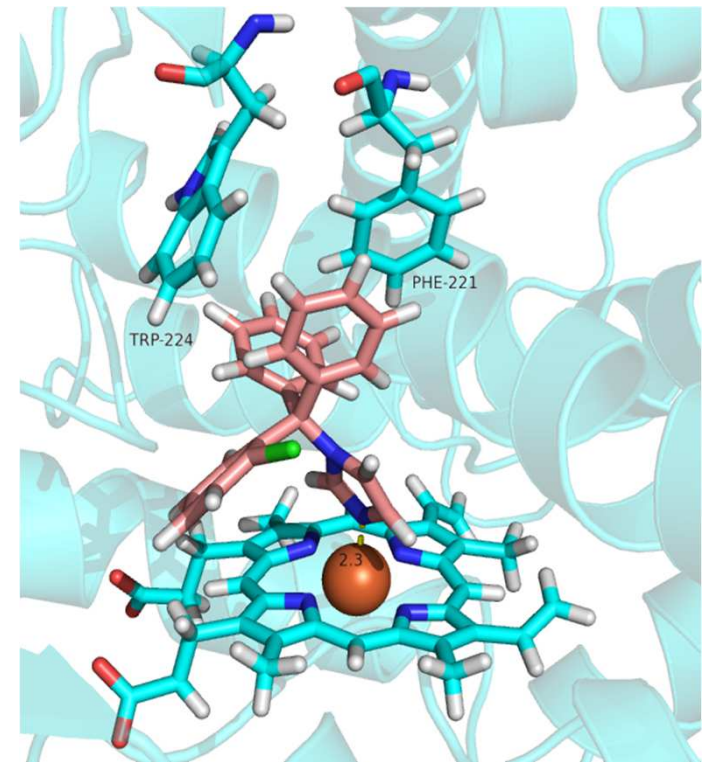
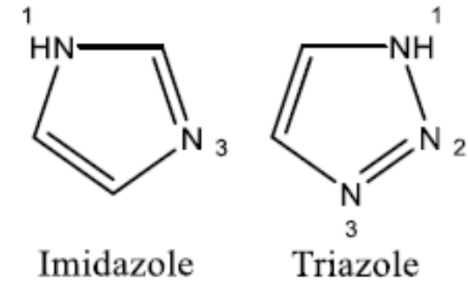
difficult to extrapolate results from animals to humans

The *ex vivo* human placental perfusion model is an experimental model used to investigate placental transport and metabolism of xenobiotics



Introduction

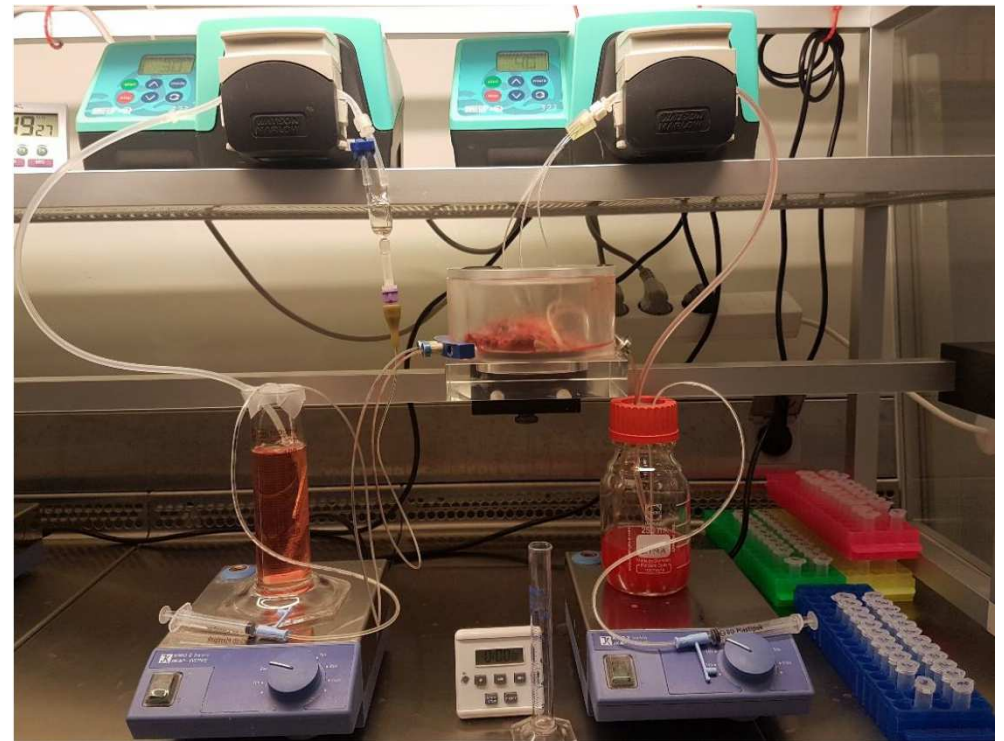
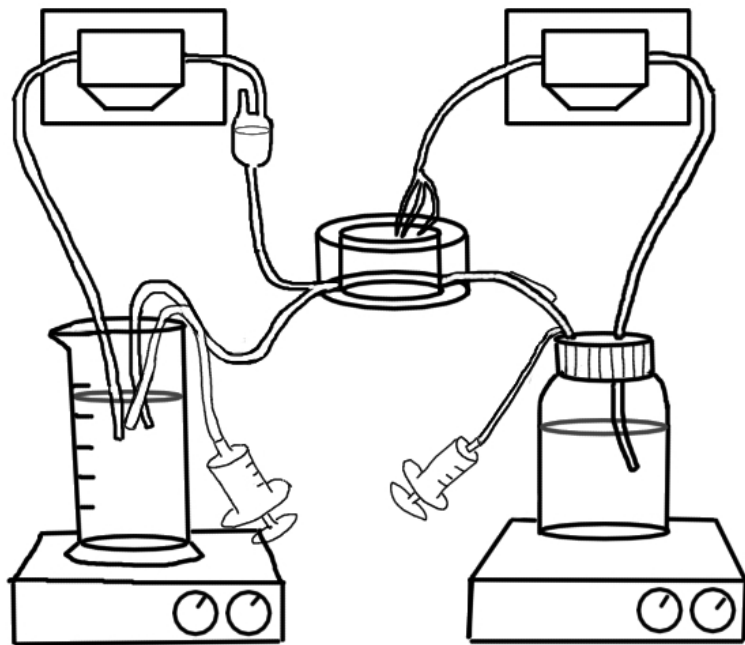
- Increased risk of vulvovaginal fungal infection during pregnancy
 - Hormone levels
- Azole antifungals are first-line of treatment
 - Inhibits fungal 14α -lanosterol demethylase (CYP51)
 - BUT also inhibit human CYP enzymes
- Proven to disrupt the endocrine system *in vitro* and *in vivo*



Clotrimazole inhibiting aromatase (CYP19A1)

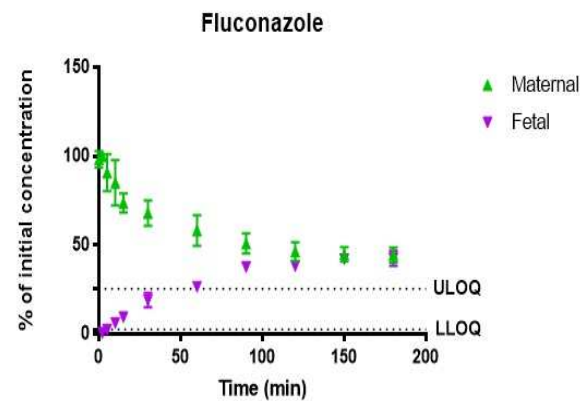
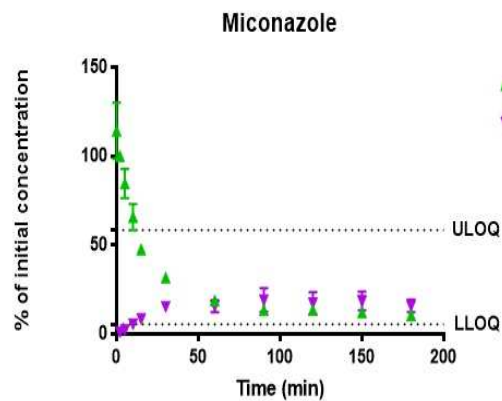
Method

- Obtain placentas from women giving birth by elective caesarean section
- Reestablish maternal and fetal circulation

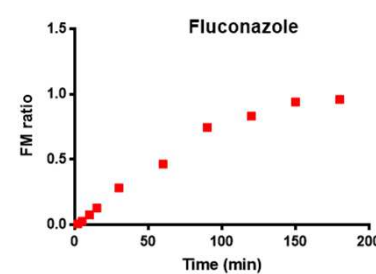
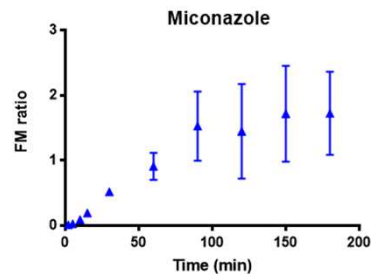
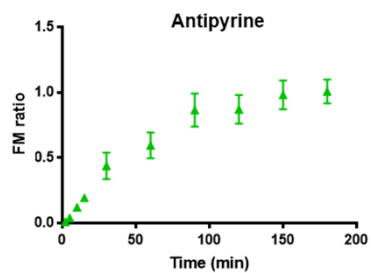


Results

Ex vivo experiments with miconazole and fluconazole using antipyrine as positive control. Samples analysed using LCMS/MS

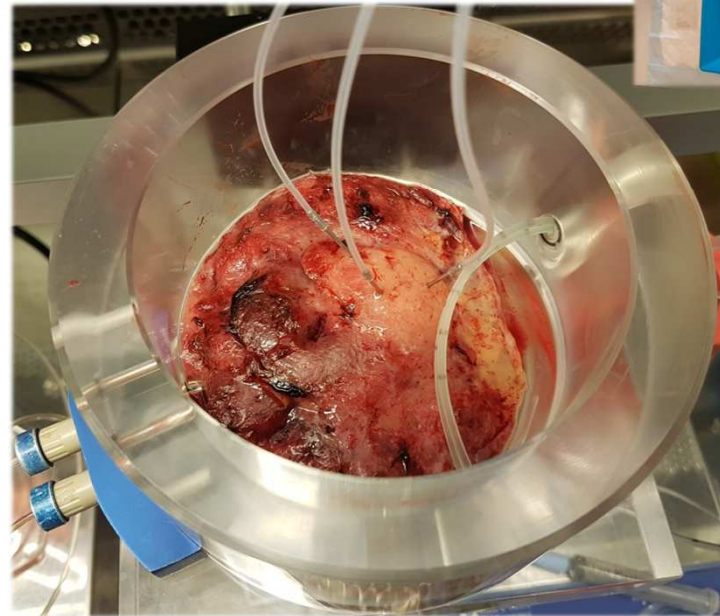


The LCMS/MS setup used to analyze the samples



Future perspectives

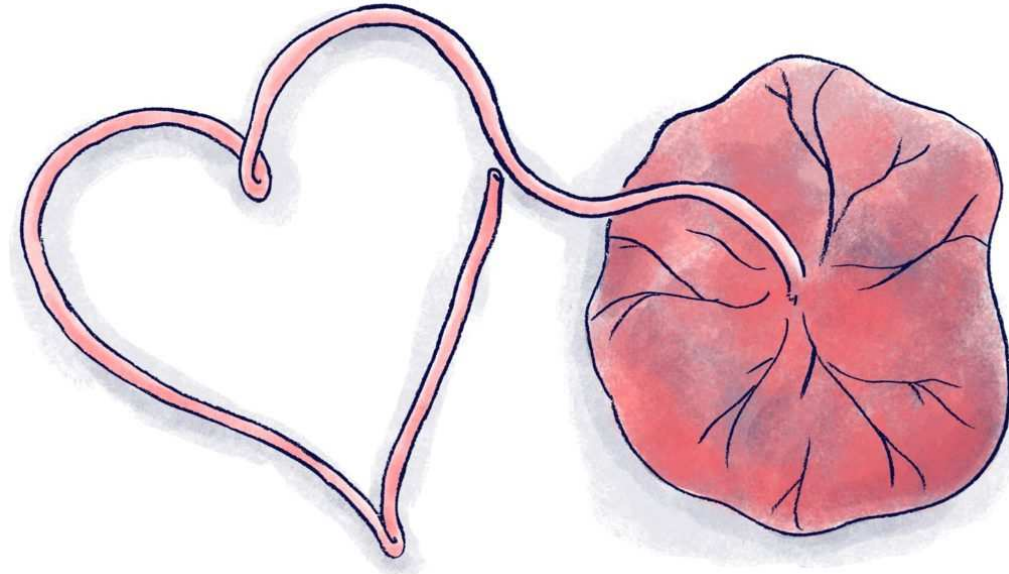
- More azoles will be added to the method
- Improve the LCMS-method
- Gene expression
- Steroid profiling



Conclusion

- The *ex vivo* method has proven to be a solid alternative to *in vivo* studies of animals
 - Once established, the setup is reliable and provide robust results
- Possibility to evaluate and/or change recommendations for treatment of fungal infections in pregnant women





Thank you for your time