HUMAN PRECISION-CUT INTESTINAL SLICES AS AN *EX VIVO* MODEL FOR INDUCTION OF THE ABCB1 TRANSPORTER

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Drug-drug interactions (DDIs) on the eflux and uptake transporters in the intestinal barrier can play crucial role in drug absorption. One of the main transporters involved in DDIs is ABCB1 which can have high impact on drug intestinal absorption. The drugs causing DDIs on this transporter can act as substrates, inhibitors and/or inductors. Therefore, the absorption of the compounds can be dramatically changed and can lead to inappropriate drug plasma levels which can cause side effects and/or failure of the pharmacotherapy. No high throughput *ex vivo* model for the induction studies exist. Nowadays there is no clinically relevant induction model for DDIs except *in vitro* cell lines, mostly of LS 174T or LS 180. For this purpose, we decided to evaluate and optimise human precision-cut intestinal slices (PCIS) to be suitable for long term induction studies. 3 types of media were evaluated: I) Williams' Medium E (WME) as a standard medium used for PCIS, II) two different organoid media (ORG and Vacy) with cooperation of University of Utrecht. Viability of the tissue was evaluated using ATP levels measurement. RT-PCR and immunohistochemical methods were used to study ABCB1 levels. Rhodamine123 accumulation assay was used as a functional control of ABCB1 expression. To induce ABCB1 was used well known inducer Rifampicin.
During evaluation we collected samples after 24,48,72h from all media with/without Rifampicin. In WME we saw increasing activity of the ABCB1 after 24h with Rifampicin, we also saw increasing the mRNA level of the ABCB1, which suggest the increasing level of the ABCB1 transporter. With increasing time we saw similar effect, but also with the increasing deviation. On the other hand, Vacy medium has the best effect on the ATP level, proliferation and the stability of the activity of ABCB1, but we saw no effect on the induction with added Rifampicin. In ORG medium activity of the ABCB1 is higher than in WME and also we don't see any effect of the Rifampicin on any level.
As a conclusion we can say, that human PCIS can be used as an *ex vivo* induction model of the ABCB1 in WME medium. The effect is observed on the activity and mRNA level. Vacy medium has a best properties for long time incubation, like a ATP level, proliferation factors.

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