Electrospray Mass Spectrometry coupled to a Gut-on-a-Chip

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In vitro models of the intestine are widely used to evaluate the absorption potential of foods, drugs and toxins. Currently, the most used *in vitro* model is the transwell. Transwells are porous membrane inserts on which cells can be cultured to study permeability. They are easy to use and can be handled in high numbers. However, the transwell has its limitations, cells are grown in a static environment not representing the dynamic nature of the intestine. Furthermore, sampling is performed offline with large time intervals making it difficult to capture metabolites. Development in the organ-on-a-chip technology has led to more advanced *in vitro* cell culture systems mimicking the *in vivo* microenvironment. The so called gut-on-a-chip is a miniaturized *in vitro* system that resembles the intestine. Cell culture medium is flowing through the gut-on-a-chip creating a dynamic environment and inducing shear forces on the cells just like the *in vivo* situation. In our work a co-culture of Caco-2 and HT29-MTX cells were grown on a porous membrane that was placed in a flow through transwell device. An electrospray quadrupole time-of-flight mass spectrometry (ESI-Q-TOF-MS) was connected to the gut-on-chip via a series of switching valves (fig.1), which allowed for measurements of the apical and basolateral side of the flow through transwell. Prior to detection two nano trap C8 column were integrated in the series of switching valves for sample pre-treatment. Total analysis time including sample pre-treatment and MS measurement was just 15 min. The coupling was validated by measuring the permeability of verapamil and ergotamine. This research resulted in a fast and continuous online measuring system of the permeability in the gut-on-a-chip.

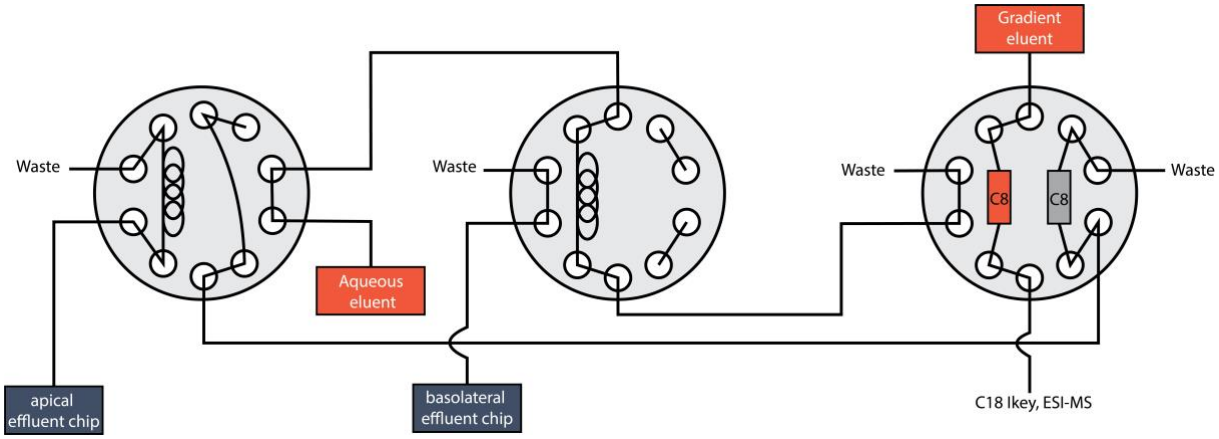

Figure 1: Coupling of the flow through transwell to ESI-MS

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