Using Skyline to Quantify Drug Metabolizing Enzymes and Transporters in Sandwich-Cultured Human Hepatocytes Exposed to Pregnancy Related Hormones

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Impact of pregnancy on the expression of drug metabolism enzymes and transporters

- Pregnancy alters the pharmacokinetic profiles of several clinically relevant drugs.

Parient *et al*. PLoS Med. 2016; 13(11): e1002160.

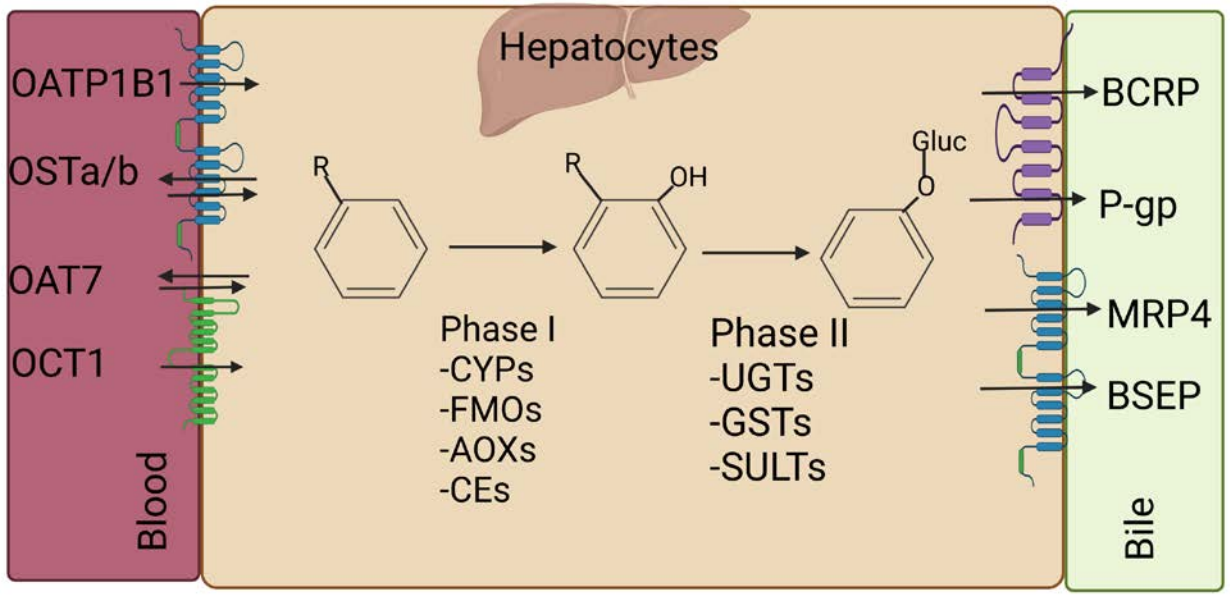
Aims:

1. Develop an *In Vitro* model of drug metabolism and transport in pregnancy

2. Quantify the impact of pregnancy conditions on the expression of over 70 drug metabolizing enzymes and transporters in this model.

- Human liver hepatocyte culture is considered a gold standard model in drug metabolism and transport studies.

Methods Mol Biol 2005;290:207-29



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- Conventional antibody-based methods of protein quantitation are inefficient, expensive, and laborious to perform a comprehensive quantitative proteomics analysis

Molecules. 2020 Jun; 25(11): 2718.

Targeted quantitative proteomic analysis of drug metabolizing enzymes and transporters by nano LC-MS/MS in the sandwich cultured human hepatocyte model

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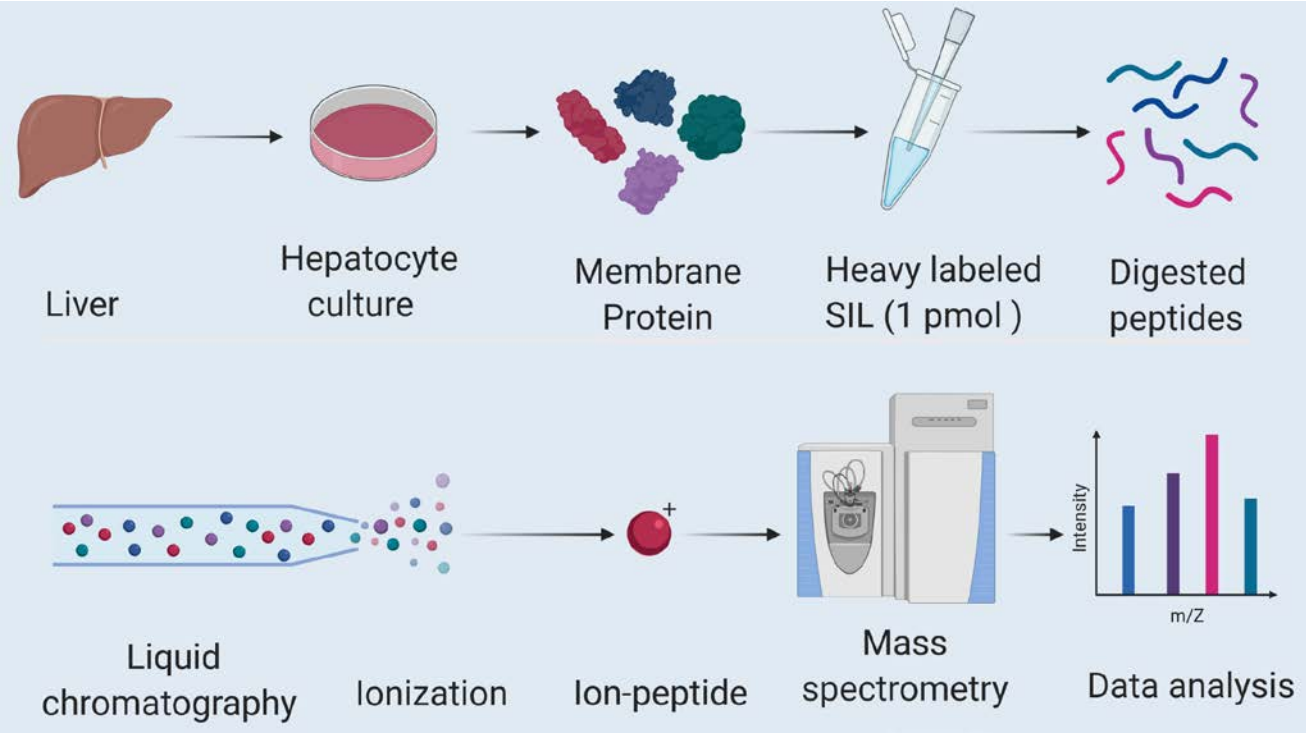
J Pharmacol Toxicol Methods. 2019;98:106590



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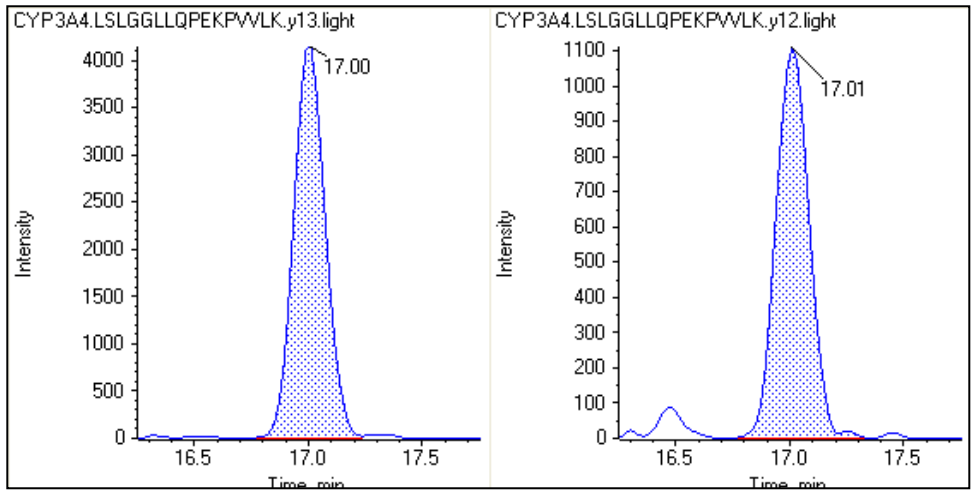
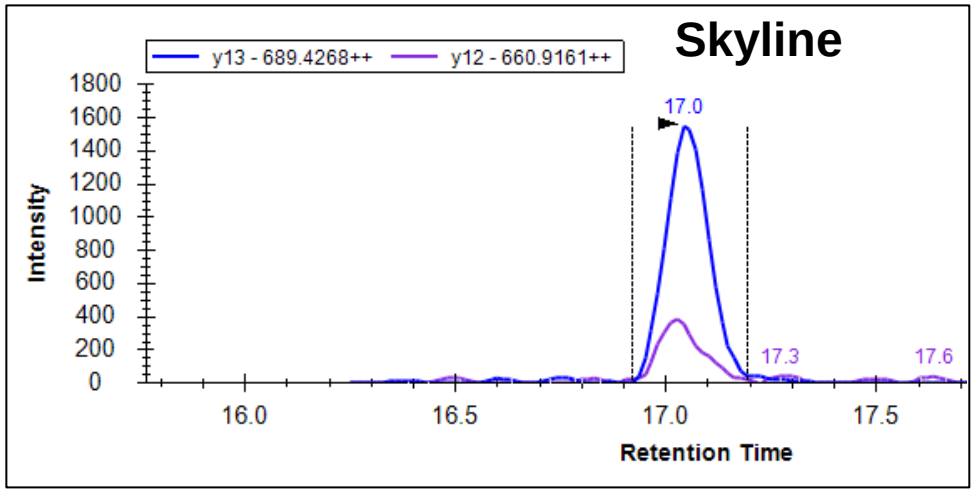


- Limited license (SCIEX)

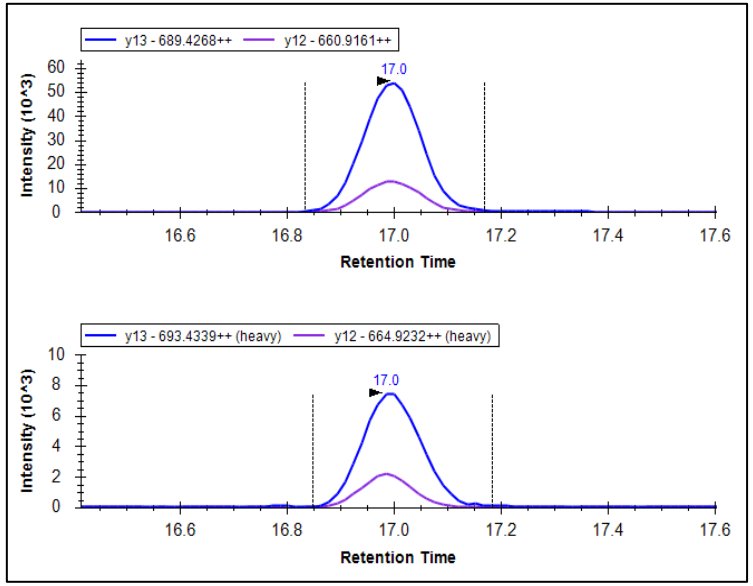
Skyline

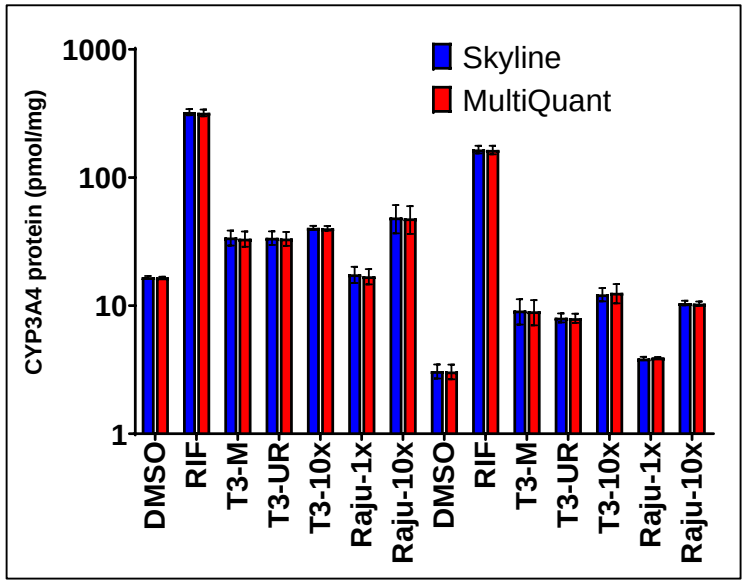


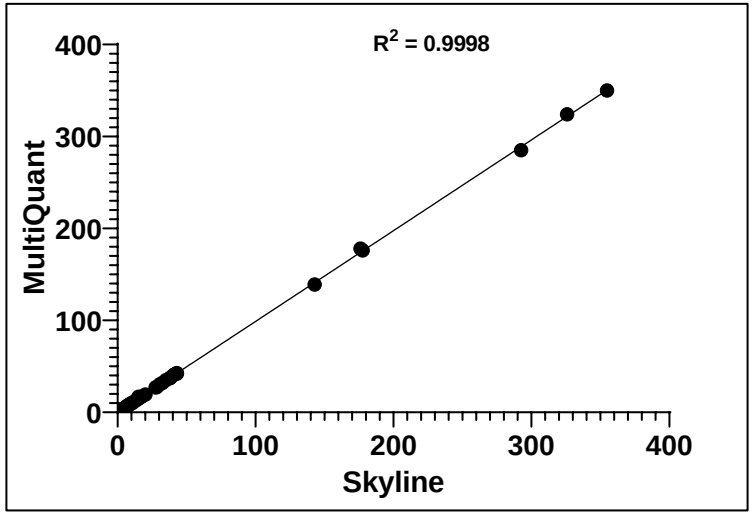
- Open access

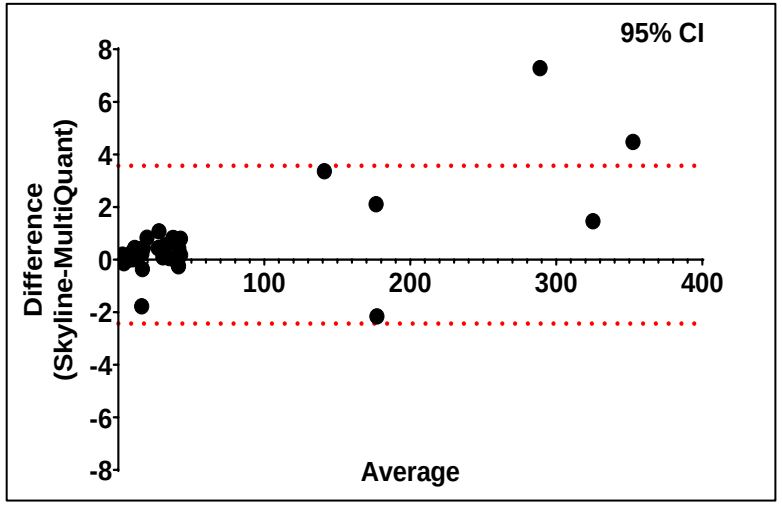
Establishing Skyline as an Alternative for Proteomics data analysis

CYP3A4









Opportunities for improvements – Retention time annotation on LC/MS chromatogram

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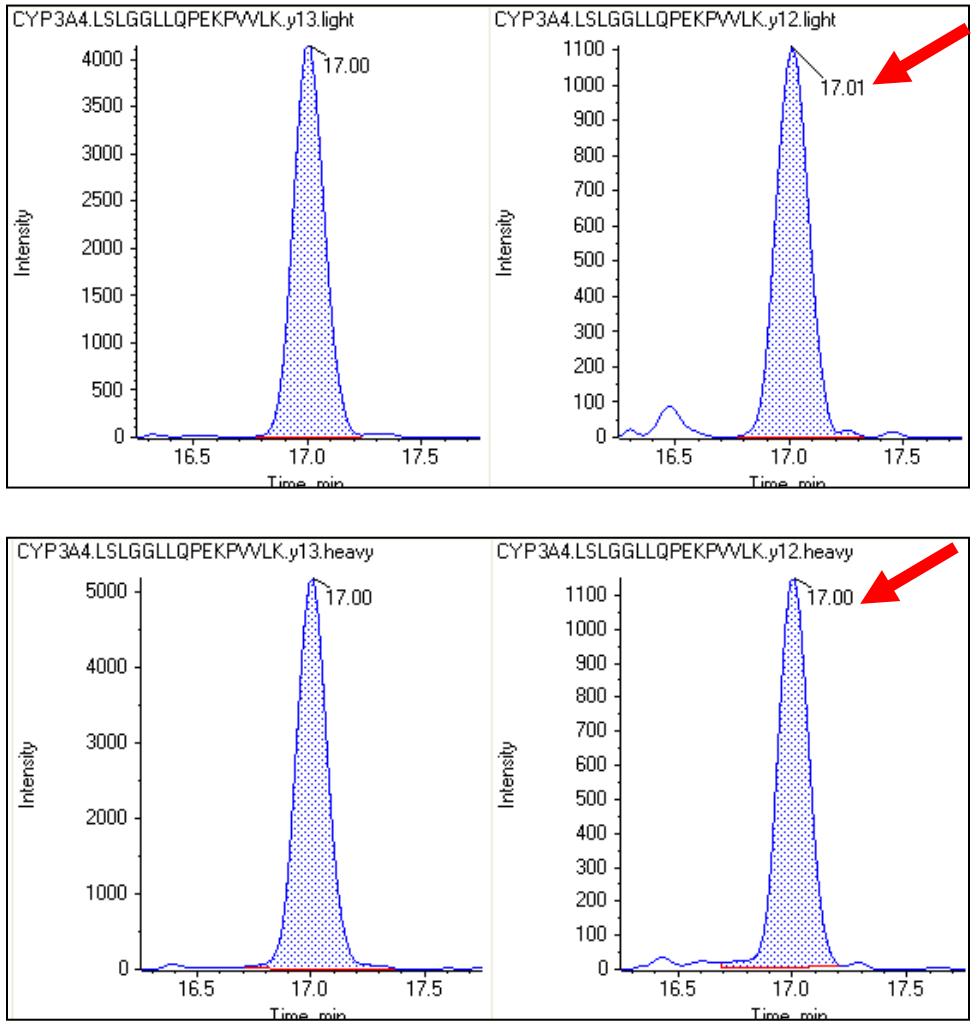

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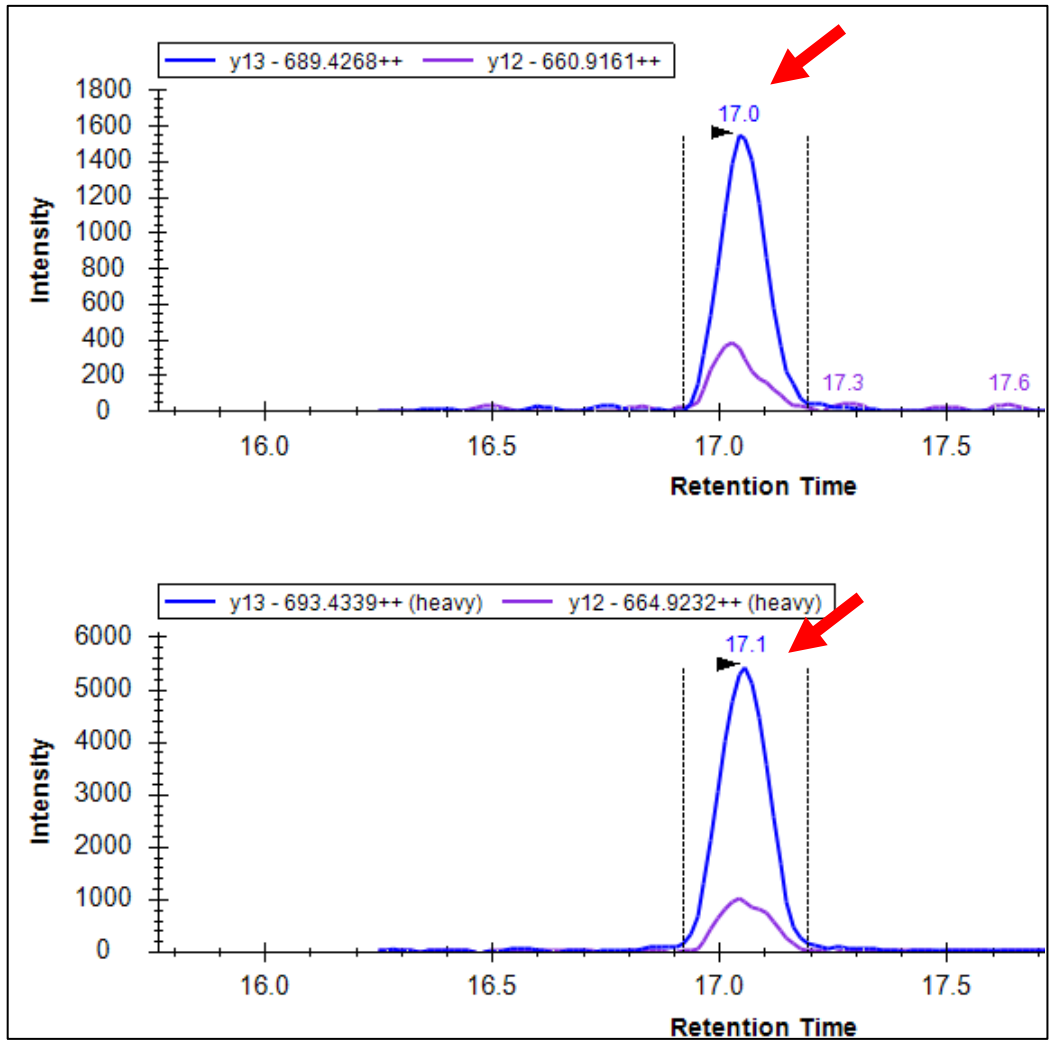

Peak acceptance criteria:
RT = ± 0.02 min difference between heavy labeled standard and the analyte

Summary

- Skyline may be used to analyze proteomics data for drug metabolizing enzymes and transporters in human primary hepatocyte cultures.

- Improvements on the retention time annotation on the LC/MS chromatogram may greatly increase user friendliness and workflow efficiency.

Thank You.

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