This is a repository copy of *Defining skin xenobiotic metabolism using a combined in vitro/in silico approach*.

White Rose Research Online URL for this paper:  
http://eprints.whiterose.ac.uk/142093/

Version: Accepted Version

**Proceedings Paper:**  
Webb, S., Sharma, P., Colley, H.E. orcid.org/0000-0003-0053-7468 et al. (5 more authors)  

https://doi.org/10.1089/aivt.2018.29013.abstracts

Final publication is available from Mary Ann Liebert, Inc., publishers  
http://doi.org/10.1089/aivt.2018.29013.abstracts

**Reuse**  
Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

**Takedown**  
If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.
Defining skin xenobiotic metabolism using a combined in vitro /in silico approach
S.D. Webb¹, P. Sharma², H. Colley³, R. Shipley⁴, A. Sneddon¹, J. Leedale⁵, S. Smith⁶, C. Murdoch³

¹Department of Applied Mathematics, Liverpool John Moores University, Byrom Street, Liverpool L3 3AF UK.
²Department of Molecular and Clinical Pharmacology, MRC Centre for Drug Safety Science, Institute of Translational Medicine, University of Liverpool, Sherrington Building, Liverpool, L69 3GE.
³School of Clinical Dentistry, University of Sheffield, Claremont Crescent, Sheffield, S10 2TA.
⁴Department of Mechanical Engineering, University College London, Gower Street, London, WC1E 6BT.
⁵Department of Mathematics, University of Liverpool, Liverpool, L69 7ZL.
⁶University of Bristol, Bristol, BS2 8HW.

Skin represents an important route of exposure and determining whether such incidental or intentional exposure poses a risk to human health requires consideration of temporal concentration, in addition to assessing the chemical’s intrinsic hazard. In order to elicit a toxic response in vivo the chemical must reach its site of action in sufficient concentration, as determined by its absorption, distribution, metabolism and elimination (ADME) profile. Whilst absorption and distribution into and through skin layers have been studied for decades, only more recently has skin metabolism become a subject of intense research, now recognised as playing a key role in both toxification and detoxification processes. EU directives on animal use for toxicity testing and the lack of human skin for research has prompted an increase in the use of tissue-engineered human skin models. These models are histologically similar to human skin and express metabolising enzymes making them ideal in vitro tools for toxicity testing. In this talk, I will discuss how the use of these models in combination with in silico tools may be used to resolve a significant challenge in predicting toxicity following dermal exposure. I will highlight how in vitro data can be used to drive novel multiscale mathematical models that predict the kinetics of xenobiotic metabolising enzymes, their transdermal distribution, spatiotemporal metabolite distributions and whole body systemic exposures for a wide range of chemical structures. The ability to predict metabolism in the skin would significantly aid risk assessment and shorten the length of time from discovery to patient benefit.