



Physiomics: Predicting Optimal Therapeutic Strategies for the Pharmaceutical Industry

David Fell & Christophe Chassagnole

Physiomics

<http://www.physiomics-plc.com/>

Physiomics was established in 2001 to develop computer models of cellular systems that could be used to aid rational target selection for drug development. As it proved difficult to be involved in such early-stage decisions, our focus changed to providing insight into results obtained from lead compounds. For example, we used a cell cycle model to investigate the interaction between specificity and cytotoxicity of CDK2 inhibitors. With this came a shift from modelling the time course of responses to drug administration in a typical cell to predicting the effects on a cell population as they would appear in typical experimental tools such as FACS analysis of cell cycle phases.

Our next challenge was to move along the drug development pipeline from cell-based assays to animal studies. We focussed on xenograft studies for anti-cancer therapies. This involved combining our cell population modelling with PK/PD simulation of drug concentrations at the tumour site to predict growth or regression of the tumour. Our 'Virtual Tumour' platform then gives us predictive capability for exploring the outcome of different dosing regimens, and even more importantly, of combination therapies of a drug candidate with existing standard therapies. As a result, we can now model different combinations and regimens to establish the most efficacious way to use the new drug candidate, and this predictive capability has been experimentally validated in a blind trial. Hence we have the means to reduce animal usage in xenograft trials by reducing the possibilities that need to be tested. We are currently extending this approach from xenografts to clinical trial simulation in 'Virtual Tumour Clinical', with validation in metastatic melanoma. In conclusion, our progress illustrates the scope for modelling and Systems Biology approaches to support drug development, but also shows that modelling and prediction are not synonymous, and the latter requires different types of models from those used to increase our understanding of biological mechanisms.