

Pre-clinical animal models: useful asset or a waste of resources?

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Time and time again I hear “preclinical *in vivo* models are not predictive of clinical results” and they are blamed for the failure of research programs. Having spent 3 decades working with these models, it does tend to grind. To be fair, the statement isn't incorrect, its more that “we” should be realistic of what the rodent models can really tell us. In my view the *in vivo* systems are very useful for PK/PD modelling i.e. looking for target engagement and then a related function, and linking that to exposure/dose. It's when it comes to modelling diseases that the models can fail: the lung structure, the cells, the physiology, the immunology, the mediators etc are different in rodents compare to man. Add to that is we, as yet, do not know what triggers the majority of human respiratory diseases, and, indeed they are likely to multifactorial – *precision medicine* is the rallying cry for the majority of on-going projects.

I would like to share with you some data we published a few years ago (ref below) in which we looked at the role of an ion channel expressed on airway sensory nerves, TRPV1, in chronic cough. The preclinical data was very supportive of progressing to clinical assessment but when the human study read out, the data were very disappointing. I will show you how we are currently trying to address how we can improve the predictivity of the *in vivo* systems and hope that going forward they can be used in the development of anti-tussive therapies.