Regarding "A process-based review of mouse models of pulmonary hypertension"

Editor:

We wish to respond to the review article by Mita Das et al. entitled "A process-based review of mouse models of pulmonary hypertension" (Pulmonary Circulation October-December 2012:2[4]). Genetically modified mouse models have provided curious data for researchers in cancer, obesity, heart disease, diabetes, arthritis, substance abuse, anxiety, aging, and Parkinson's disease; but how cost-effective or translational is this mouse research? Just one gene knockout kit will set you back US $ 38,000.[1] Crowley[2] and Contopoulos-Ioannidis et al.[3] have shown that successful translation to humans for this kind of basic research is exceedingly rare.[4]

According to the review article "Transgenic mouse models are a perfect tool for studying the processes involved in pulmonary vascular function and disease, and can be used effectively to test interventions designed against particular molecular pathways and processes involved in disease." Unfortunately, any attempt to extrapolate results between complex systems with different evolutionary trajectories (mice and humans are examples of complex systems, separated by 70 million years) will be limited to conserved processes whose trait or response being studied occurs at the same level of organization or in the same module.[5]

Pulmonary vascular function has both intrinsic and extrinsic multifactorial genetic components, which are not amenable to such reductionist study. Genes work in networks and in the context of complex systems, small changes at the gene level can have major consequences for the individual. Thus, it is irrelevant to focus on observed similarities in genetic makeup (including transgenes) between mice and humans, since the details of the differences are in the interactions between conserved genes, not in the genes themselves.[6]

We conclude that the use of animals as human models for drug and disease research ignores the very principles upon which modern personalized medicine is based. Therefore, human-based research should become the primary means for obtaining data about human diseases and response to drugs.[7]

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Quick Response Code:	Website: www.pulmonarycirculation.org
	DOI: 10.4103/2045-8932.114782