Towards predictive cardiovascular safety : a systems pharmacology approach

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Propositions

to the doctoral thesis

Towards predictive cardiovascular safety - a systems pharmacology approach

1. An adequate experimental design is pivotal to characterize a biological system using a systems pharmacology modeling approach.
   This thesis

2. A quantitative understanding of the functioning of a biological system leads to a better understanding of the mechanism of action of novel compounds.
   This thesis

3. The influence of cardiovascular drugs on cardiac output and total peripheral resistance is much larger than the influence on blood pressure. Therefore, measuring mean arterial pressure only exposes the tip of the iceberg.
   This thesis

4. After characterization of the cardiovascular system using cardiac output measurements, measuring heart rate and blood pressure suffices to elucidate the mechanism of action of novel compounds.
   This thesis

5. The possibility to extrapolate cardiovascular effects from rats to humans using a system specific CVS model needs further investigation.
   This thesis

6. Preclinical research may contribute to answer clinical research questions.

7. Animals are predictive for humans. The question is how to scale.

8. When published PK or PKPD models are available, animal experiments should not be repeated to obtain the same results.

9. Improving modeling techniques is only useful when it serves to improve the answer to a question, i.e. when it serves to meet the objectives.

10. Efforts invested in mechanism-based, mechanist or systems pharmacology models are returned only when these models can be used to support the development of multiple compounds.

11. Who struggles in details does not oversee the whole.

12. You can’t change others, but you can change yourself.

13. Aim for success, not perfection. Never give up your right to be wrong, because then you will lose the ability to learn new things and move forward with your life.
    Dr. David M. Burns

14. Perfection is not attainable, but if we chase perfection we can catch excellence.
    Vince Lombardi

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