Phenotypic screening with 3D cell-based assays

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STELLINGEN/PROPOSITIONS

behorend bij proefschrift/accompanying thesis

"Phenotypic screening with 3D cell-based assays"

1. Improving drug success rates will require shifting the balance between throughput and physiological relevance to find a 'sweet spot', which is dependent on available technology. *(this thesis)*

2. Phenotypic profiling of compound effects on 3D cell-based assays can be used to discriminate selective from non-selective inhibitors of receptor tyrosine kinases, to classify compounds according to their molecular targets and to identify drugable targets. *(this thesis)*

3. In addition to identifying on-target effects of compounds, phenotypic profiling can reveal phenotypic changes that are indicative of off-target effects. *(this thesis)*

4. Celastrol inhibits cystogenesis in *in vitro* and *in vivo* models for Polycystic Kidney Disease, through currently unknown mechanisms that do not appear to involve mTOR, STAT3 or CREB. *(this thesis)*

5. In order to study biological processes in the human body using cultured cells, cells need to be provided with a relevant physiological context to display physiologically relevant behaviour. *(Pampaloni F. et al., Nat Rev Mol Cell Biol. 2007 and Baker M. et al., J Cell Sci. 2012)*

6. Incorporation of laboratory automation equipment in 3D cell-based assays is necessary to both increase throughput and improve experimental quality. *(this thesis, Rimann M. et al., Curr Opin Biotech. 2012 and Rimann M. et al., J Lab Autom. 2014)*

7. Tumour cell morphology in 3D culture corresponds with invasive and metastatic potential, and this correlates with their gene expression profile. *(Kenny P.A. et al., Mol Oncol. 2007)*

8. Abnormal ECM deposition and ECM-integrin interactions contribute to cystogenesis and should therefore be considered as therapeutic targets for PKD. *(Subramanian B. et al., Biomaterials. 2012)*

9. Regardless of how well it is prepared, moving a lab does not bode well for sensitive equipment, or PhD students.

10. "A scientist is a device for turning coffee into theorems" *(modified from Alfréd Rényi)*. Hence, good coffee may contribute to good research.

11. "Alternative facts" lead neither to good science nor good politics.