An interview with Roderick L. Beijersbergen, Associate Professor and Head of The Netherlands Cancer Institute's NKI Robotics and Screening Centre

Dr. Roderick Beijersbergen's work evolves around the development and application of large-scale functional genomic technologies in the field of cancer. He pioneered large scale shRNA screens in mammalian cells by generating the first genome wide shRNA collection. Furthermore, he developed the pooled shRNA screening technology that is now widely applied by many research groups as screening tool.

His work has led to the identification of biomarkers that predict treatment response, the understanding of the mechanisms of action of novel drugs and the identification of novel mechanisms of intrinsic and acquired resistance to pathway targeted therapeutics.

SMi are delighted to have Dr Beijersbergen present at its 8th annual conference on Advances in Cell Based Assays conference, taking place on 10th - 11th November 2015 in Central London.

The address entitled: L**ARGE SCALE FUNCTIONAL GENOMIC SCREENS: MODELS MATTER**, will identifying key cellular pathways driving treatment responses in 3D culture. Employing gene-editing and screening technologies to advance mechanistic understanding; and the development of relevant screening models for clinical needs, will also be discussed.

In the run up to the show, we caught up with him to discuss his work and upcoming presentation.

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1. About you. What is your role and what perspective do you bring to the conference?

At the Netherlands Cancer Institute, I lead a research group and I am head of the NKI Robotics and Screening Center. The focus of our work is the development and implementation of large-scale functional genomic screening technologies with the goal to identify more effective treatments for different types of cancer, including melanoma, colorectal- and breast-cancer. A strong focus of our work is the understanding of the limited duration of the response of cancers to molecularly targeted therapeutics. By using unbiased functional genomic screens we gain insight in potential mechanisms of resistance and identify targets that can enhance the response to these therapeutics. This approach has led to the discovery of several combinations treatments that are currently investigated in the clinic. We believe that the clinical benefit for molecular targeted therapeutics can be greatly improved by selection more effective combination therapies in combination with the selection of patients based on genetic alterations.

2. What will attendees take away from your talk?

An important aspect for the success of unbiased large-scale functional genomic screening to identify novel targets of treatment combinations is the development of the appropriate screening model that reflects a clinical question in combination with an efficient screening technology. Recent developments in both areas hold promise for the near future and examples exist that illustrate the power of these approaches.

3. Are there any sessions you are particularly looking forward to and why?

I am looking forward to the presentations that discuss the implementation of high content imaging in combination with the use of 3D models. The ability to grow patient derived organoid cultures has received a lot of attention and also generated the expectation that these models are more reflective of the patients' tumor but at the same time these models are challenging for the selection of phenotypic markers for screening.

4. In terms of off-target and on-target screening, how challenging is it in getting on-target screening results?

Indeed, the use of RNAi technologies has been met with high frequencies of off-target effects and therefore limited confidence in the selected hits. The implementation of more strict selection criteria, other analysis methods and rigorous validation have increased the confidence on the selected hits. However, this remains an issue with RNAi. The recent developments on genome editing technologies, including the CRISPR/CAS9 appear to be more robust and produce less noise allowing for higher screen quality and less false-positives. Improved understanding of the different methods and the screening models will further improve the quality, relevance and potential clinical implementation of screen results.

5. What new developments do you envision for 2016?

A major advance in the application of functional genomic screening has been the development of the pooled screening technology. This has been greatly facilitated with the capabilities of next generation sequencing. Ongoing developments that allow for the monitoring of gene expression in single (sorted) cells can also be combined with the pooled screening technology. This will open up a whole new area of screen phenotypes not restricted to cellular phenotypes but also on (multi) gene-expression, protein expression and even dynamic read-outs of the activity of cellular processes. For this we need the integration of different technologies currently under development. The understanding of the capabilities and limitations at this moment can be used in the further development of these new screening techniques.

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