Tailoring the tools to study prostate cancer metastasis

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Stellingen behorend bij het proefschrift getiteld

"Tailoring the tools to study prostate cancer metastasis"

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1. Multiple models of advanced prostate cancer (PCa) could be targeted by the dual mTORC1/2 inhibitor Rapalink-1 and revealed an alteration of PCa subpopulation homeostasis. *(this thesis)*

2. Tumor engraftment is consistently higher for PDXs from advanced compared to primary PCa, underrepresenting early-stage cases. The PNPCa is the only reported case of an early metastasis, retaining androgen sensitivity and with high microsatellite instability, that has been modeled *in vivo*. *(this thesis)*

3. The developed patient-derived organoid (PDO)-based drug assay can be performed routinely, uses limited amounts of tissue, and has an average duration of two weeks from initial organoid formation until readout, making it compatible with clinical decision-making. *(this thesis)*

4. In order to implement a near-patient assay, the preservation of high molecular correlation between tissue and organoids is preferred over the opportunity to perform prolonged serial organoids propagation. *(this thesis)*

5. In terms of the ability to analyze metadata related to research studies, it is important to have a data-driven approach also while reviewing scientific literature. *(this thesis)*

6. There is a yet unmet need to understand which individual patients are at risk of developing lethal forms of PCa, to prevent under- or over-treatment of patients with more aggressive or more benign PCa, respectively.

7. Big data can support a precision medicine approach to PCa, especially when sophisticated, AI-driven tools are developed.

8. The intrinsic heterogeneity of PCa, its complex interactions with the supporting stroma and with the endocrine system are hampering the development of curative approaches. Determining the relative contribution of plasticity and clonality in PCa progression could assist to identify the most effective therapeutic strategies.

9. The mTOR signaling pathway plays a fundamental role in the progression to advanced PCa. Yet, mTOR-targeting therapies are proving less effective than expected.

10. In the present age, a lonely originality is favored over reliable, collaborative functionality. However, *much of the joy of science is the joy of solid work done by skilled workmen. Many of us are happy to spend our lives in collaborative efforts where to be reliable is more important than to be original.* (Freeman Dyson, 1923-2020, in "Disturbing the universe")

11. The conscious mind of the researcher is a fundamental tool, realizing a process of understanding that, although logic, is essentially creative. This creative structure can be reported using Rudolf Steiner (1861-1925) words: "*Cause and effect must be sought in the world, but before we can discover it in the world we ourselves must first produce causality as a thought-form.*"

12. The attitude of an inspired researcher encompasses a certain degree of braveness towards the unknown. To quote Marie Skłodowska Curie (1867-1934), "*nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less*".