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Personalized medicine for breast cancer treatment

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One of the hallmarks of cancer is genetic instability. Many chemotherapeutic strategies make use of DNA damaging agent, that preferentially target dividing cells. Recently, DNA repair defects have been identified in many different types of tumors, suggesting that the effectiveness of such treatments may be modulated by the precise genetic make-up of the tumor; defects in specific DNA repair pathways can be used as the Achilles' Heel of the tumor. An important new concept is synthetic lethality, the observation that combinations of mutations can be lethal, while both single mutations are viable. In selected tumors, the specific DNA repair defect can be targeted in such a way that the tumor cells can be killed without causing severe side effect on normal tissues. The combination of PARP inhibitors and homologous recombination deficient hereditary breast and ovarian cancer is on its way to the clinic and more combinations are currently in the preclinical phase. Novel patient selection tools will be required to ensure proper treatment for the individual patient. Therefore, we developed ex vivo culture conditions for tumor tissue slices that allow toxicity testing of various possible treatments. We showed that both short term assays and toxicity testing for 3 to 4 days can be carried out. We are currently setting up validation assays to investigate whether the differences in ex vivo sensitivity correlate with tumor sensitivity in the patient. As a proof of concept we identified several tumors with inactivated BRCA1 or BRCA2 genes in this way, which would make them prime candidates for PARP inhibitor treatment. These approaches may change cancer medicine in a fundamental way, from a one-size-fits-all concept to an individualized treatment strategy based on the molecular make-up of the tumor for each patient.

Biography

Dik C van Gent did his PhD at the Netherlands Cancer Institute (NKI) and Postdoctoral studies at the National Institutes of Health (USA). He is now Associate Professor at the Department of Genetics of the Erasmus MC Rotterdam, the largest university medical center in The Netherlands. He is also Director of the MSc programme 'Molecular Medicine', which aims to bridge the gap between medicine and molecular life sciences. He has published more than 60 papers in reputed journals, including Cell, Science and Nature and serves as an Editorial Board Member of 'DNA Repair' and 'Genome Integrity'.

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