Title: A One-Two Punch Model for Cancer Therapy - Exploiting Powerful Sequential Combinations by Functional Genetics

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Profile

Dr. Bernards is a professor of molecular carcinogenesis at the Netherlands Cancer Institute. His laboratory uses functional genomic approaches to find vulnerabilities of cancers that can be exploited therapeutically. His laboratory identified the combination of a BRAF inhibitor and an EGFR inhibitor as effective for the treatment of BRAF mutant colon cancer. He also developed the first clinically used gene expression test for early breast cancer prognosis: MammaPrint. Amongst his honors are the Pezcoller Foundation award, the Ernst Bertner Award for Cancer Research from the M.D. Anderson Cancer Center and the ESMO Lifetime Achievement Award. He is also a member of the Royal Netherlands Academy of Sciences and of the AACR Academy.

Cancer remains difficult to treat, even with the new generation of targeted cancer drugs. By far the most formidable obstacle is the rapid emergence of therapy resistance.
Indeed, many of the new cancer drugs elicit powerful initial responses, leading to dramatic effects on progression free survival, but far less long-term benefit is seen in terms of overall survival. Combination therapies can help fight therapy resistance, but with an arsenal of over 1000 cancer drugs in clinical development, the number of possible combinations seems nearly endless. In his laboratory they employ functional genetic screens to find powerful combinations of cancer drugs by exploiting the concept of "synthetic lethality". Using RNA interference-based genetic screens with collections of shRNAs that target drugable gene families, they search for genes whose inactivation is particularly synergistic with clinically-relevant cancer drugs. Such screens can identify drug combinations that are far more powerful than the sum of the two single agents. They aim to understand the molecular rationale for the observed synergy between two cancer drugs. Once they have insight into the molecular mechanism, they aim to bring such rationally-designed combinations to the cancer clinic as soon as possible through collaboration with clinicians in our comprehensive cancer center.

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