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Disrupting the transcriptional machinery to combat triple-negative breast cancer

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Stellingen

Behorende bij het proefschrift

“Disrupting the transcriptional machinery to combat triple-negative breast cancer”

1. The insensitivity of triple-negative breast cancer cells to inhibition of molecularly altered kinases underscores the need for a more holistic therapeutic approach targeting multiple factors (*this thesis*).
2. Inhibiting transcription-associated CDKs efficiently eliminates and reprograms triple-negative breast cancer cells, offering a promising avenue for therapy (*this thesis*).
3. The selective disruption of gene expression programs by inhibition of transcription-associated CDKs suggest the presence of specialized mechanisms of gene regulation (*this thesis*).
4. Despite clinical setbacks targeting ABC-transporters, their early discovery and strong impact on drug efficacy underscores the need for renewed exploration of therapeutic strategies targeting, circumventing or exploiting them (*based on this thesis and Borst, P., FEBS letters, 2020*).
5. The complexity of cancer drug resistance presents a major challenge for cancer therapy and prompts for an approach focused on tackling the key determinants of resistance (*based on Vasan N., et al, Nature, 2019*).
6. Recognizing major off-target interactions of drugs, including interactions with transporters and enzymes, is pivotal for fully understanding their mechanistic and therapeutic impact (*based on Klaeger, S. et al, Science, 2017*).
7. Early consideration of therapeutic indexes in drug and target discovery is essential for identifying candidates capable of selectively eradicating cancer cells with minimal adverse effects (*based on Muller, P. et al, Nature reviews Drug discovery, 2012*).
8. The comprehensive and unbiased insights from high-throughput screening and -omics approaches are essential starting points for drug discovery and mechanistic research (*this thesis*).
9. Improving the overall impact of scientific research necessitates consideration of its broader environmental, societal, personal and future implications.
10. Given our history of uncontrolled growth, invasion of the environment, changed diet and other hallmarks of cancer, it is now time to show that humanity is more than a cancer to the Earth's ecosystem (*Hallmarks of cancer based on Hanahan D. and Weinberg R.A., Cell, 2011*).
11. Embracing doubt, failure, and engaging in self-critique and self-awareness throughout a PhD journey are indispensable elements facilitating personal growth and enhancement of research.

Vera van der Noord
Leiden, 25 April 2024