Acquired resistance in pancreatic cancer: characterization and exploration of actionable targets of a multifactorial disease

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Stellingen

Behorende bij het proefschrift

Acquired resistance in pancreatic cancer: characterization and exploration of actionable targets of a multifactorial disease

1. PDAC is a multifactorial disease, and as such, treatment strategies should be designed to target it from multiple angles, using integrated approaches. (this thesis and Wang J. *J Hematol Oncol*. 2024)
2. ABCB1-mediated drug efflux represents a major cause for paclitaxel resistance in PDAC. (Chapter 2 of this thesis)
3. Since decreased activity of dCK is associated with gemcitabine resistance in multiple PDAC models, exploring strategies to restore dCK activity in combination with gemcitabine or identifying dCK-independent chemotherapies, may point the way to better treatment of PDAC patients. (Chapter 4 of this thesis)
4. Acquired resistance mechanisms can arise in different ways and affect different cancer-related pathways; therefore, generalization is possible only when multiple models are studied. (this thesis)
5. While cell intrinsic molecular mechanisms of resistance may be resolved, the mechanical interplay with the surrounding extracellular matrix can modulate resistance and should be considered in design of therapeutic strategies. (*this thesis*)
6. The tumor microenvironment plays a dual role in the response to therapy. Gaining a deeper understanding on its interplay with tumor cells is paramount to design effective therapies. (based on Kung, HC, *Nat Rev Clin Oncol*. 2025)
7. One size does not fit all. Considering the heterogeneity of resistance mechanisms, using broad panels of biomarkers for characterizing patients and screening of drugs on ex vivo models can lead to more successful therapeutic solutions. (based on N. Dusetti *Cancer Treat Rev*. 2025)
8. PDAC is one of the most lethal cancers and research efforts should be focused on multiple stages, namely: early diagnosis, personalized treatments, and strategies to overcome chemoresistance. (based on Stoop, TF et al. *The Lancet*. 2025)
9. Despite the advances in understanding PDAC biology, most phase III clinical trials fail. This highlights the need for trial designs that more closely resemble the successful pre-clinical conditions. (based on Halbrook et al., *Cell 2023*)
10. Growth stems from failure and both are integral parts of nearly every PhD journey. The real challenge is learning to navigate obstacles and find new paths forward.
11. Those who believe that since nature involves a struggle for survival, human society should work the same way are misguided. Many species survive through cooperation, sharing and empathy, and those are values upon which our societies should be built on. (Adapted from Frans de Waal, *The Age of Empathy: Nature's Lessons for a Kinder Society*)

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