Whole transcriptome profiling of liquid biopsies from tumor xenografted mouse models enables specific monitoring of tumor-derived extracellular RNA

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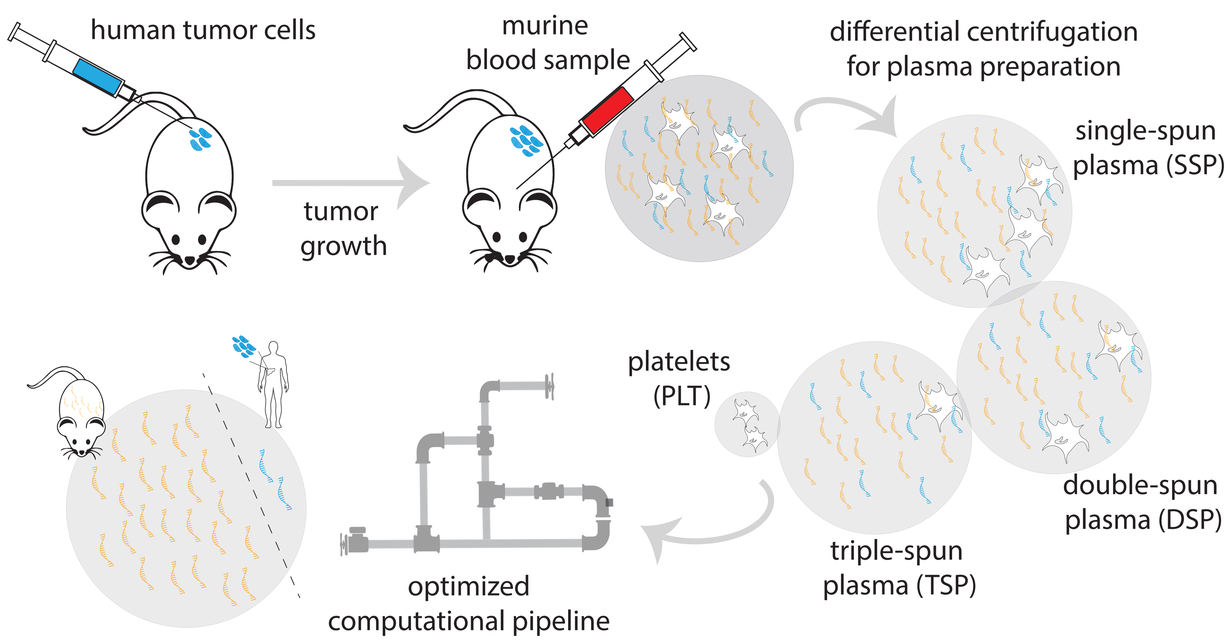
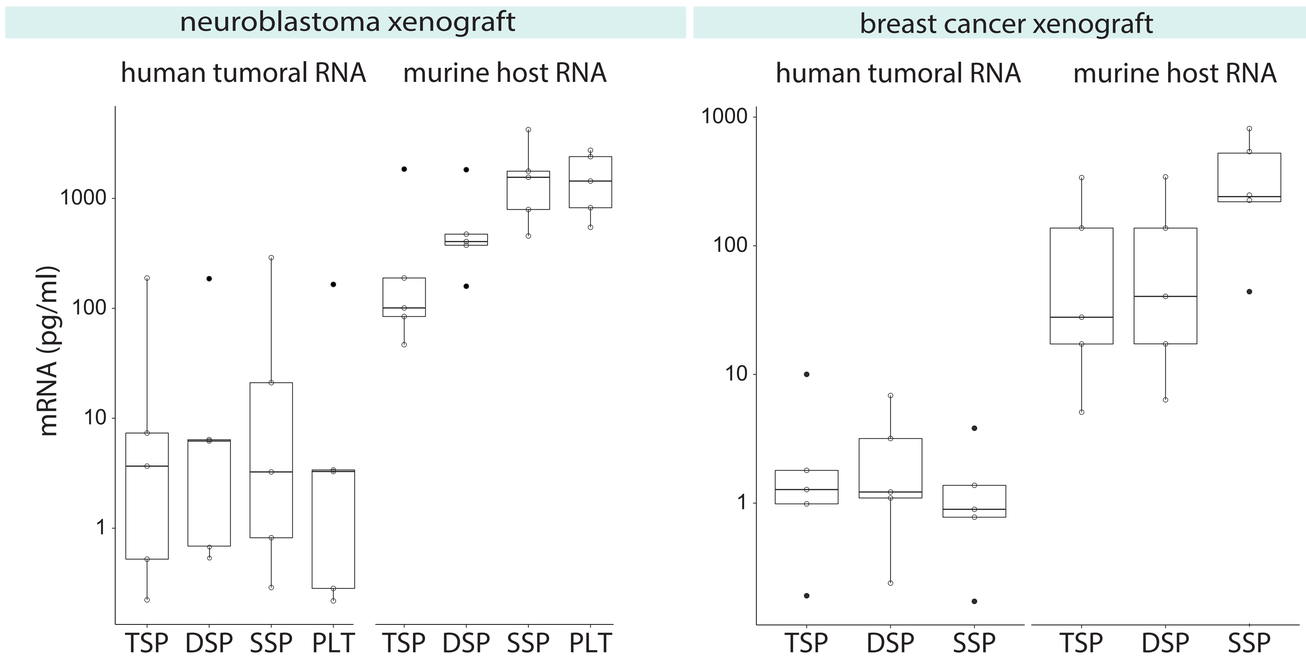
introduction

- There's a high need for less toxic treatments in children: shift towards targeted therapies is occuring.
- We aim to explore effectiveness of targeted therapies by analyzing the tumoral exRNA content in liquid biopsies from cancer patients, included in basket trials.
- As it is challenging to distinguish tumoral from host responses in plasma from patients, we optimized an experimental and computational workflow for preclinical tumoral exRNA analyses.
- The preclinical data will be instrumental for the interpretation of transcriptional responses in cancer patients' blood plasma.

experimental overview

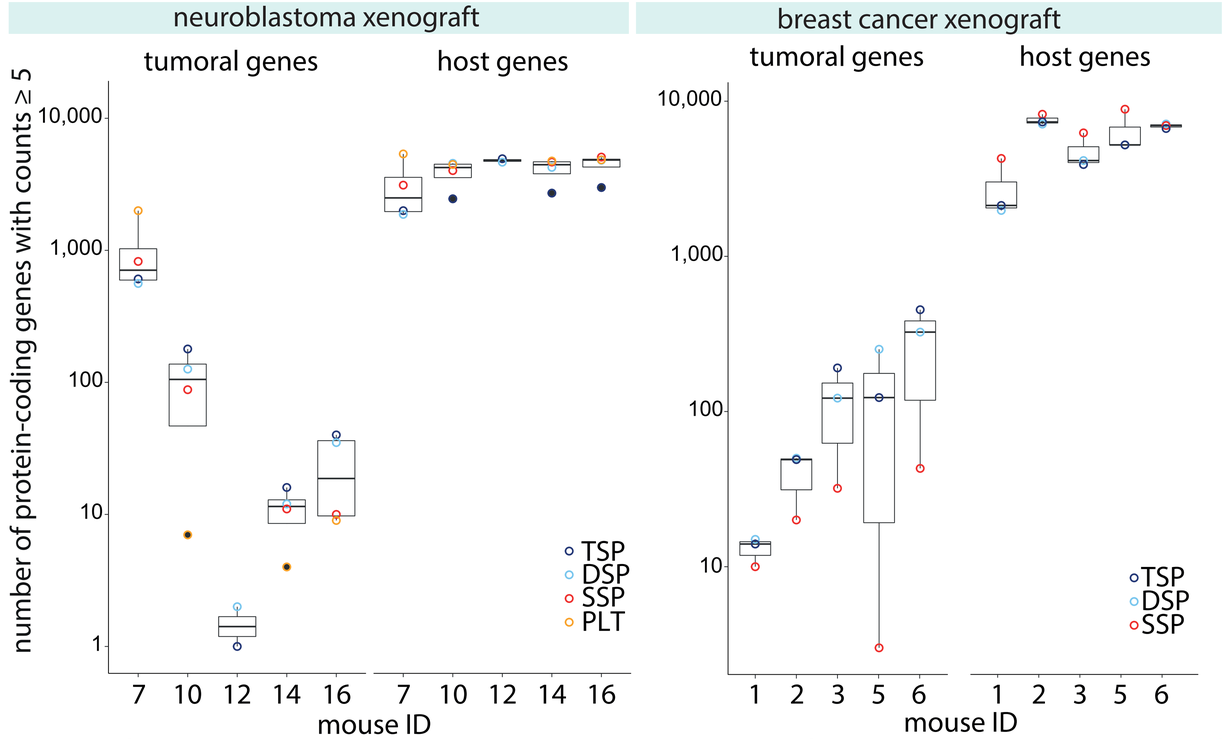


the tumoral RNA concentration is not determined by the platelet level in plasma



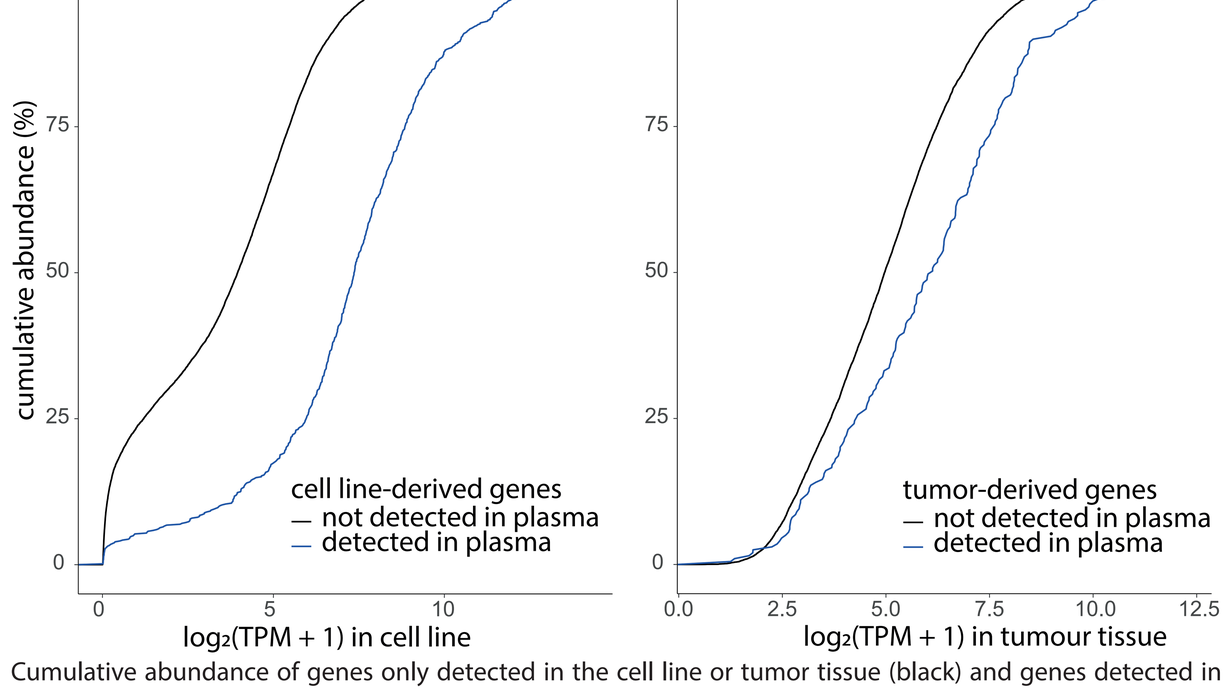
The tumoral exRNA concentration is relatively constant across the different liquid biopsies, in contrast to the host exRNA concentration. TSP: triple spun plasma; DSP: double spun plasma; SSP: single spun plasma; PLT: platelets.

the circulating tumor transcriptome is highly variable across xenografted mice



Number of host and tumor protein-coding genes varies across xenografted mice. Shown are the numbers of robustly detected protein-coding genes (i.e. ≥ 5 counts) in the individual mice. The different colours represent the different liquid biopsies. TSP: triple spun plasma; DSP: double spun plasma; SSP: single spun plasma; PLT: platelets.

the gene detectability in plasma is correlated with the expression in the originating tumor tissue or cell line



Cumulative abundance of genes only detected in the cell line or tumor tissue (black) and genes detected in both the cell line or tumor tissue and plasma (blue). (two-sample Kolmogorov-Smirnov test, $p < 2.2e\text{-}16$)

future perspectives

step 1: optimization xenograft model for tumoral exRNA analyses by exploring factors influencing the shedding of RNA in circulation
step 2: exRNA treatment response analyses in xenografts' blood plasma
step 3: integration of results for the interpretation of transcriptional responses in cancer patients' blood plasma

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