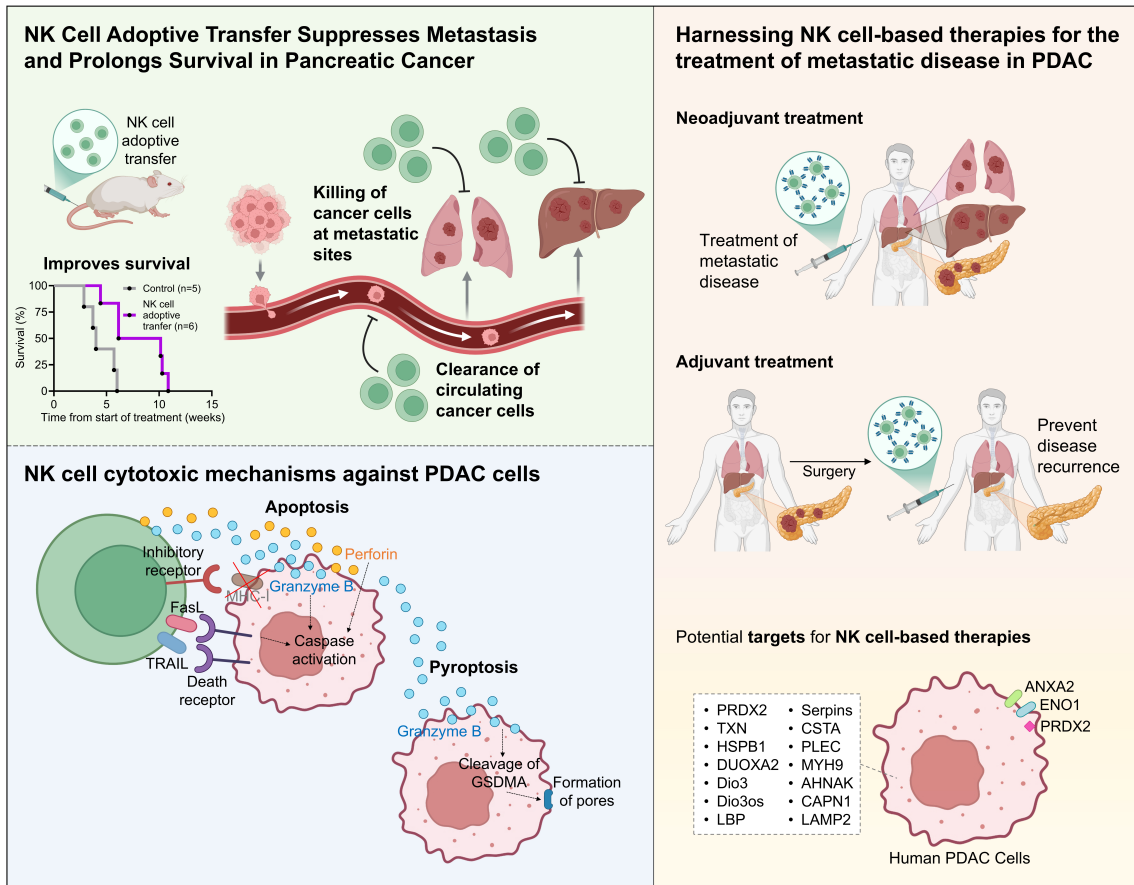


Graphical Abstract



Schematic of the potential of NK cell-based therapies for the treatment of PDAC. Our work demonstrates that NK cells control metastases development in PDAC through clearing of circulating tumor cells and induction of apoptosis of cancer cells present in secondary organs. We show that NK cells kill PDAC cells through both apoptosis and pyroptosis. In addition, NK cell adoptive transfer highlights the potential of NK cell-based therapies for the treatment of metastatic disease (neoadjuvant approach) and prevention of metastasis relapse (adjuvant approach). Furthermore, we identify some molecules upregulated by cancer cells as an adaptive response to NK cells attack, which are prospective therapeutic targets to improve the efficiency of NK cell-based therapies and the development of targeted CAR-NK cell therapies.