Pan-cancer evaluation of the association between immune cell infiltration and Necroptosis activity

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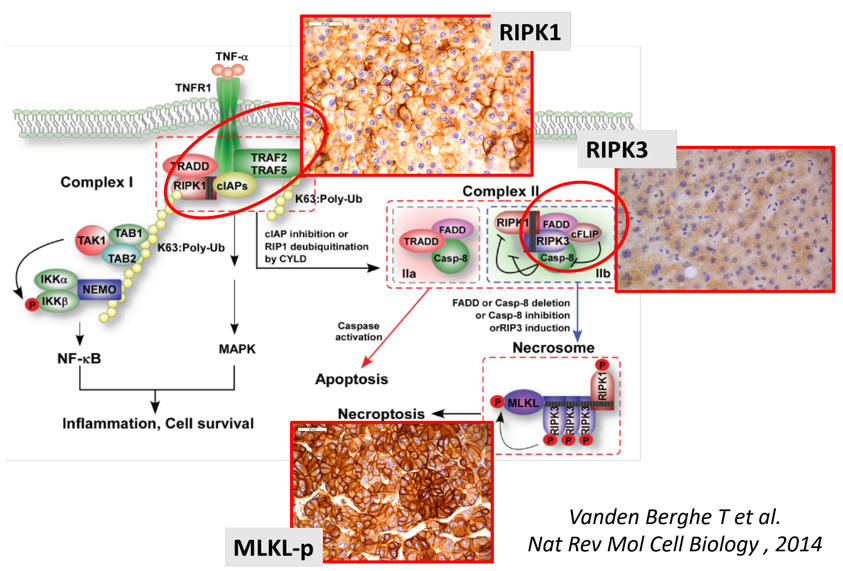
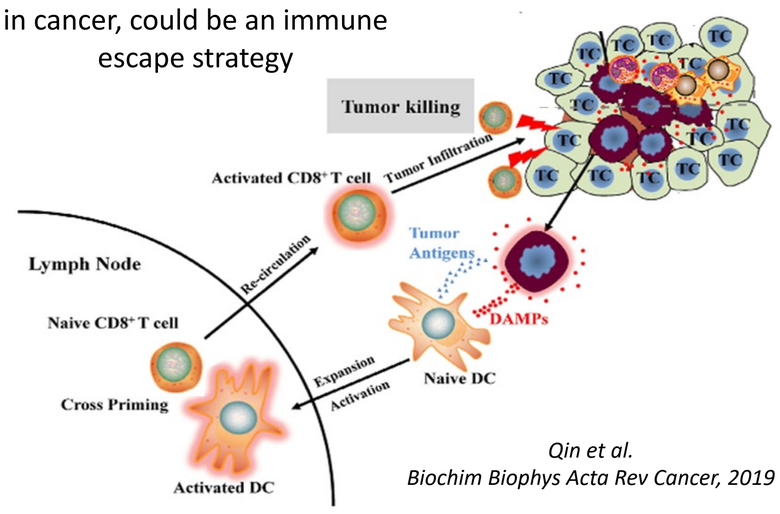
BACKGROUND

- **Necroptosis** (NPC) is a form of programmed cell death that culminates with the rupture of the cell membrane followed by the releasing of cellular elements[1].
- Evidence showed that tumors with high expression of NCP-related genes are associated with high cytotoxic CD8+ T-cell infiltrates, mediated by signaling from Dendritic (DC) and CD4+ T-cells[2].



Vanden Berghe T et al.
Nat Rev Mol Cell Biology , 2014

Downregulation of Necroptosis in cancer, could be an immune escape strategy

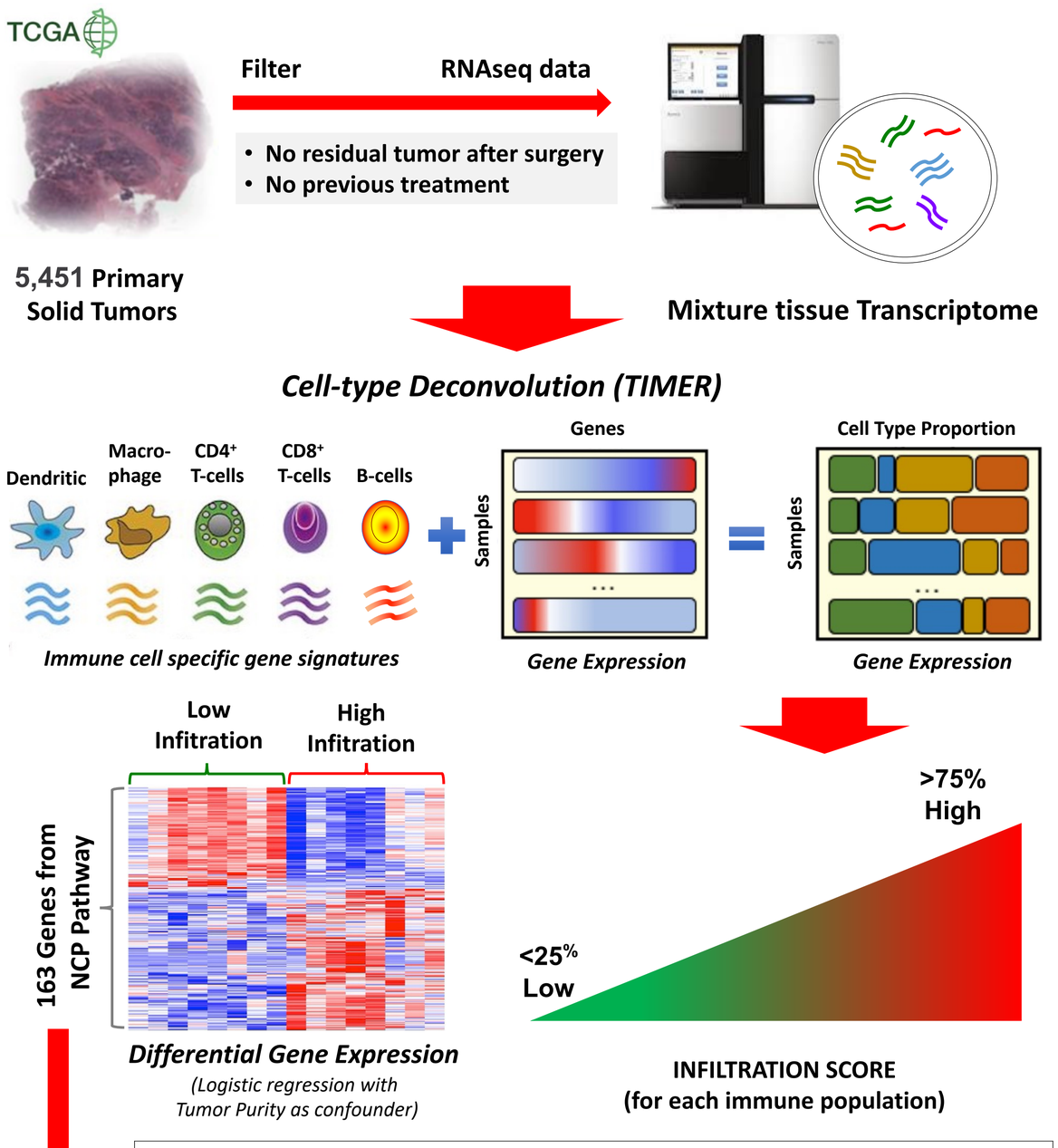


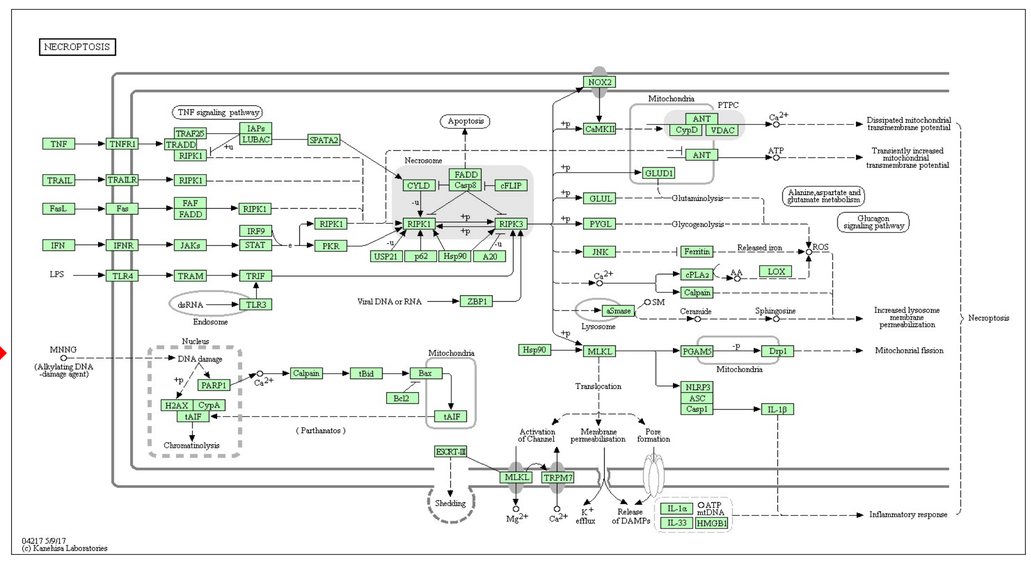
Qin et al.
Biochim Biophys Acta Rev Cancer, 2019

AIM

- Pan-cancer view of the relationship between NCP and immune infiltration and their prognostic relevance across 24 cancer types from The Cancer Genome Atlas.
- Evaluate whether there are some immune populations able to interact more with NCP in specific cancer types.

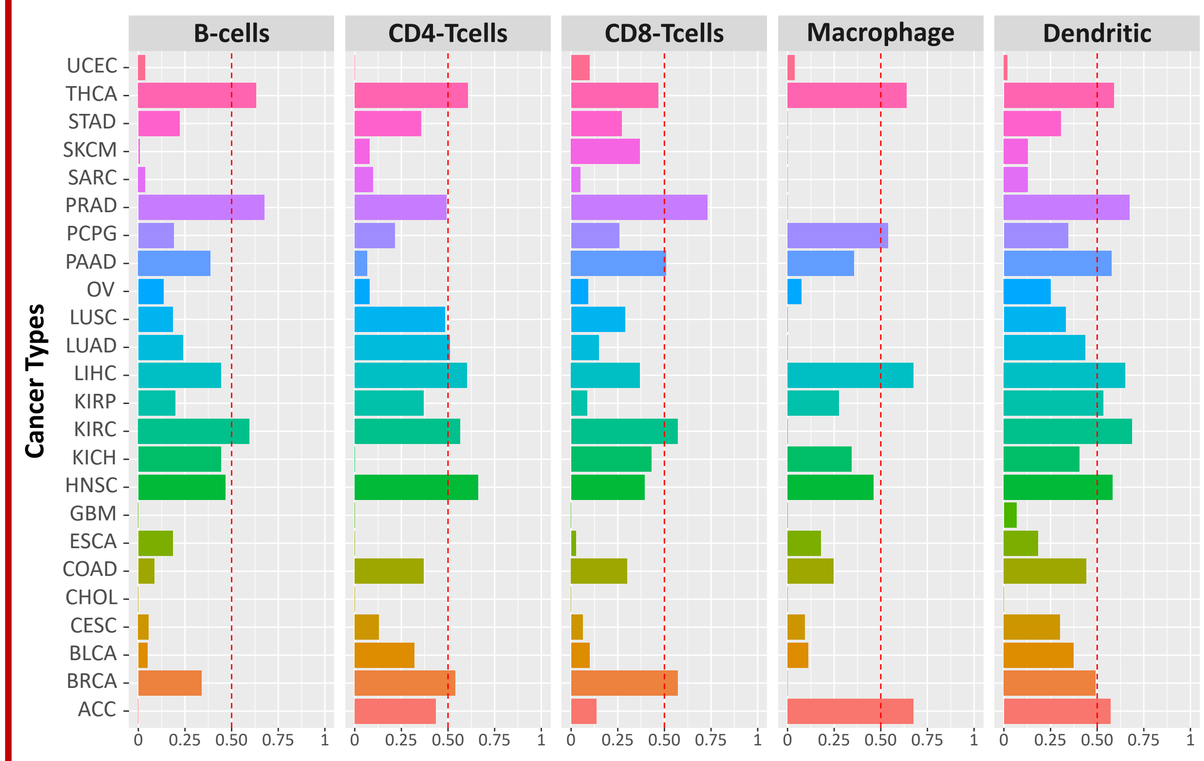
METHODS



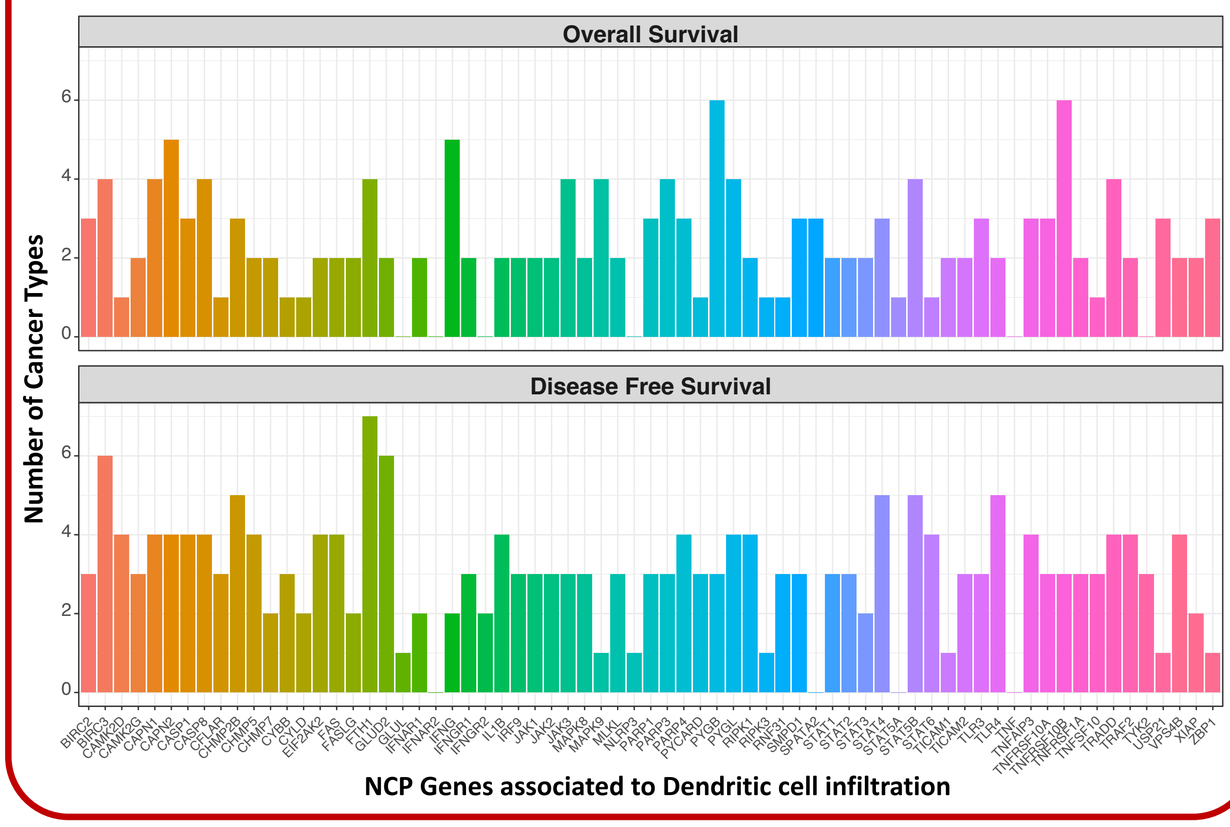


RESULTS

- Dendritic and CD4+ T-cells showed significant correlation with more than 50% of NCP genes across the largest number of cancer types: kidney renal clear cell carcinoma (KIRC), head and neck squamous cell (HNSC), liver hepatocellular (LIHC), thyroid carcinoma (THCA) for both; adrenocortical (ACC), kidney renal papillary cell carcinoma (KIRP), pancreatic adenocarcinoma (PAAD), prostate carcinoma (PRAD) for only DC; breast cancer (BRCA) and lung adenocarcinoma (LUAD) for only CD4+ T-cells.



- Dendritic cells also showed the highest number of NCP genes (69) correlated with their infiltration in more than half of the cancer types, including the main genes involved in NCP execution: RIPK1, RIPK3, MLKL and CFLAR. > 90% of these genes showed a prognostic relevance (p<5%) for overall (OS) and disease-free (DFS) survival in at least one cancer type, respectively. Most of them (>20 in both OS and DFS) were found prognostically significant in KIRC and KIRP.



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CONCLUSIONS

NCP has a relevant role in eliciting immune response against tumor through Dendritic cell-mediated immunity in specific cancer types. Genomic data were shown to be important in characterizing the interaction between the tumor and its microenvironment, which is crucial to develop immunotherapy approaches. Validation studies on specific cancer types will be considered in future studies.

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