Columbia University Kim Lab

August 16, 2021

**Transcriptomic feature of Ang2 (ANGPT2) contribution to T-cell exclusion in melanoma**

**Suggestion from Dr. Ben Izar**

1. Determine the major cell type expressing angpt2

2. Develop a single cell signature associated with angpt2 high vs low

3. Correlate the entire signature with bulk TCGA data to infer the associated T cell infiltration

**Project 1 Analysis of human scRNA-seq data (published)**

**1)** Develop a single cell signature associated with angpt2 high vs. low from melanoma human scRNA-seq data

(n=31 including untreated, post-immunotherapy resistant, and post-immunotherapy responder)**1**.

\* Code and expected results/output can be found here: <https://github.com/livnatje/ImmuneResistance>

**2)** Correlate the entire signature with bulk TCGA data (TCGA-SKCM, metastasis vs primary in Sample Type) to infer the association with T-cell tumor infiltration

**Project 2 Analysis of TCGA-SKCM data set**

**1)** Stratify Ang2 high and low (e.g. >90th (high) vs. <50th (low) expression)2 using TCGA-SKCM data (Metastasis samples and Primary tumor samples, respectively)

**2)** Compare T-cell exclusion signatures**1** in Ang2 high and Ang2 low groups from the TCGA-SKCM data.

![Chart, scatter chart

Description automatically generated]()

**![Chart, diagram, schematic, box and whisker chart

Description automatically generated]()**

Reference:

1 Jerby-Arnon, L., Shah, P., Cuoco, M. S., Rodman, C., Su, M. J., Melms, J. C., Leeson, R., Kanodia, A., Mei, S., Lin, J. R., Wang, S., Rabasha, B., Liu, D., Zhang, G., Margolais, C., Ashenberg, O., Ott, P. A., Buchbinder, E. I., Haq, R., Hodi, F. S., Boland, G. M., Sullivan, R. J., Frederick, D. T., Miao, B., Moll, T., Flaherty, K. T., Herlyn, M., Jenkins, R. W., Thummalapalli, R., Kowalczyk, M. S., Canadas, I., Schilling, B., Cartwright, A. N. R., Luoma, A. M., Malu, S., Hwu, P., Bernatchez, C., Forget, M. A., Barbie, D. A., Shalek, A. K., Tirosh, I., Sorger, P. K., Wucherpfennig, K., Van Allen, E. M., Schadendorf, D., Johnson, B. E., Rotem, A., Rozenblatt-Rosen, O., Garraway, L. A., Yoon, C. H., Izar, B. & Regev, A. A Cancer Cell Program Promotes T Cell Exclusion and Resistance to Checkpoint Blockade. *Cell* **175**, 984-997 e924, 2018, PMID:30388455. PMC6410377.

2 Gengenbacher, N., Singhal, M., Mogler, C., Hai, L., Milde, L., Pari, A. A. A., Besemfelder, E., Fricke, C., Baumann, D., Gehrs, S., Utikal, J., Felcht, M., Hu, J., Schlesner, M., Offringa, R., Chintharlapalli, S. R. & Augustin, H. G. Timed Ang2-Targeted Therapy Identifies the Angiopoietin-Tie Pathway as Key Regulator of Fatal Lymphogenous Metastasis. *Cancer Discov* **11**, 424-445, 2021, PMID:33106316.