A single-cell, spatial multiomics atlas and cellular interactome of all major skin cancer types

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Introduction

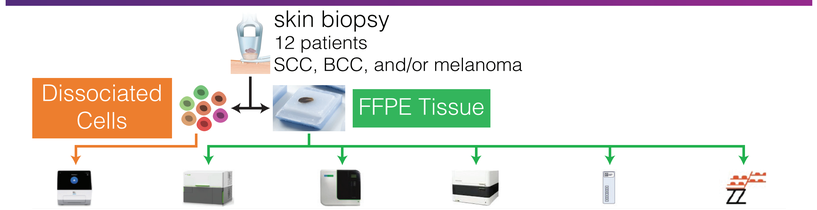
2 in 3 Australians will be diagnosed with **skin cancer** by age 70*

* Australian Institute of Health & Welfare, 2016
# Guy 2014, PMID: 25442229

- Three major forms of skin cancer:
  - Squamous cell carcinoma (SCC)
  - Basal cell carcinoma (BCC)
  - Melanoma

  USD 5 bn/yr #
  USD 3 bn/yr #
- Spatial mapping of cell types, their environment and interactions enhances understanding of causes and may improve diagnosis
- We here take a multi-omics approach to build a cell atlas and interactome of cell types and their activities in native tissue across three skin cancer types

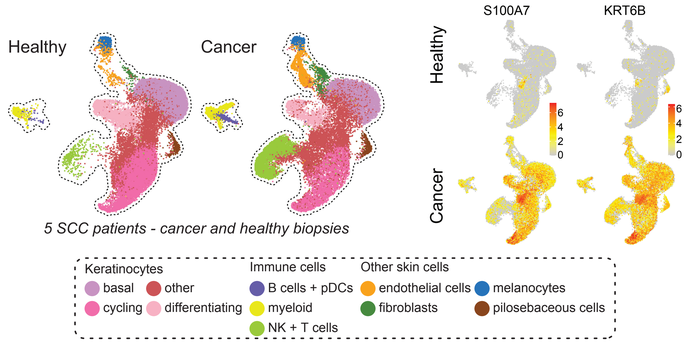
Methods



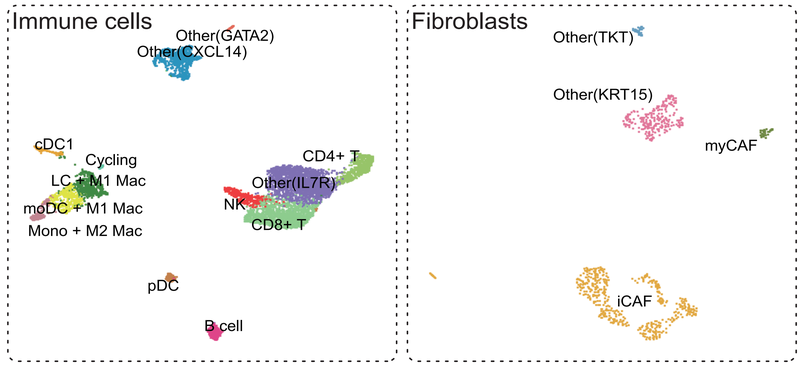
scRNASeq	CosMx®™	Polaris	GeoMx®	Visium	RNAscope
RNA	RNA	Protein	RNA, Protein	RNA	RNA
Single cell	Single cell	Single cell	ROI	1-9 cells	Single cell
✗	✓	✓	✓	✓	✓
✗	✓	✓	✓	✓	✓
~20,000	960	7	1825 (RNA) 48 (protein)	~20,000	5

Single-cell SCC atlas

Our scRNASeq atlas of 30 cell types shows changes in cell type and expression across healthy and cancer samples in SCC

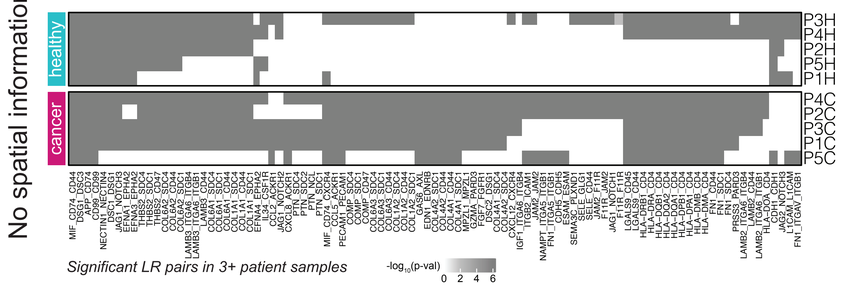


Immune, fibroblast and endothelial clusters can be divided into subtyes



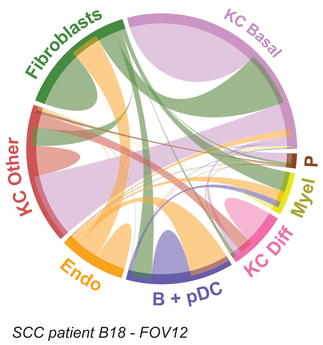
Cellular Interactome

scRNASeq-inferred LR pairs are more prevalent in cancer samples

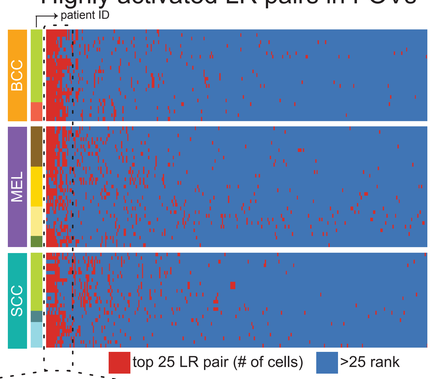


With spatial information (CosMx)

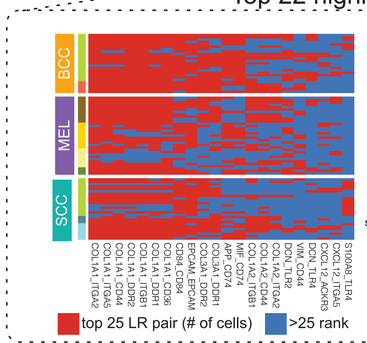
Cellular crosstalk



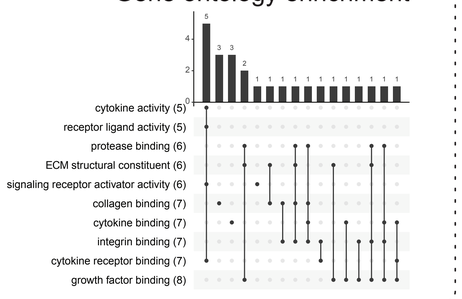
Highly activated LR pairs in FOVs



Top 22 highly-activated LR pairs

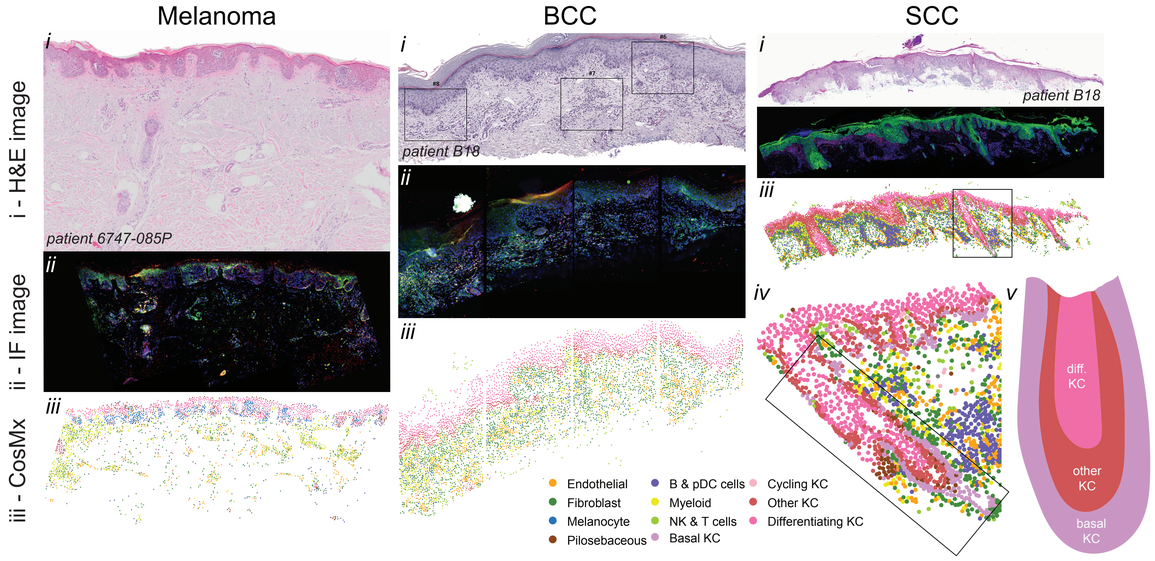


Gene ontology enrichment

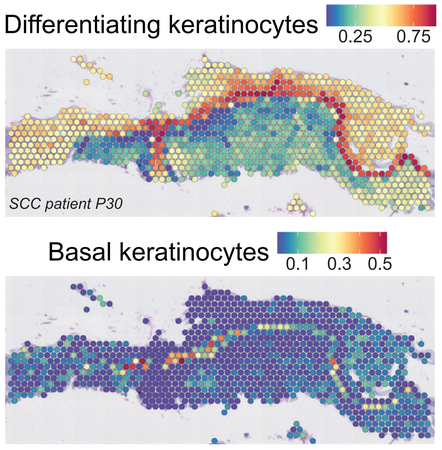


Spatial atlas of melanoma, BCC and SCC

Cell type mapping in CosMx data reveals distinctive cellular layers



Spot deconvolution in Visium data shows corresponding tissue layers in outer keratinocyte layers



Conclusions

- We generated a single-cell atlas of 28 SCC celltypes, which we validated spatially using complementary technologies
- Spatial transcriptomics data highlights cell type organisation in distinct functional tissue layers
- scRNASeq reveals cancer-specific cell crosstalk
- Spatial data indicates cancer-, patient- & region-level differences in cell-cell interaction

Acknowledgements

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