Unraveling Immunogenomic Diversity in Single-Cell Data

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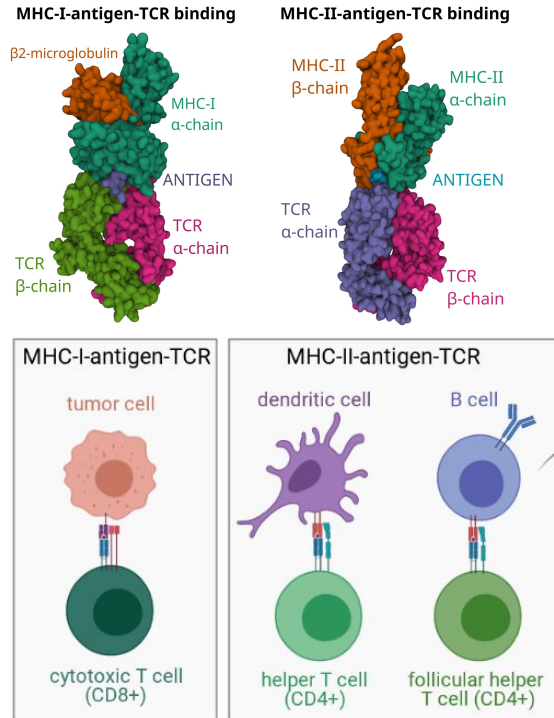
Grand Rapids
25 July 2024

Demo material

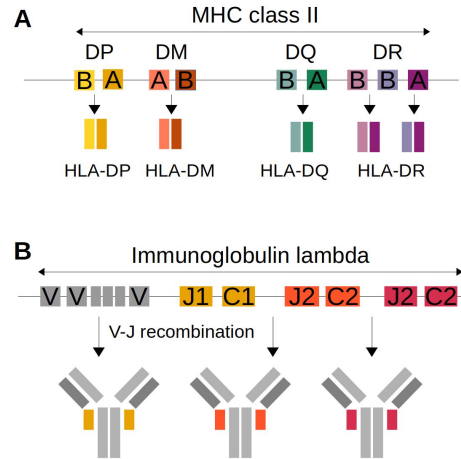https://github.com/ahmadalajami/scIGDWorkflowDemoBioC2024

Structural diversity of receptors

- Receptors that coordinate antigen specificity in immune responses

Genetic mechanisms of structural diversity

Polygeny:
Multiple similar genes
encode same function

Gene group	Number of **similar genes** (incl. pseudogenes)
IGHG	5
HLA-DRB	8
…	…

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Hyperpolymorphism:
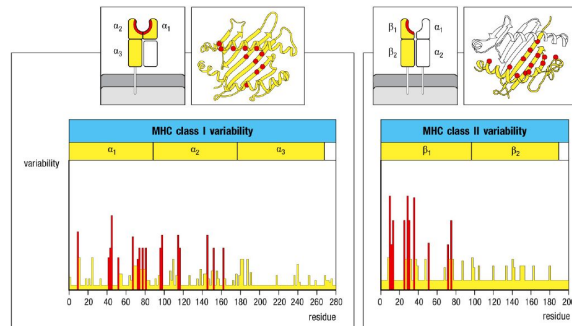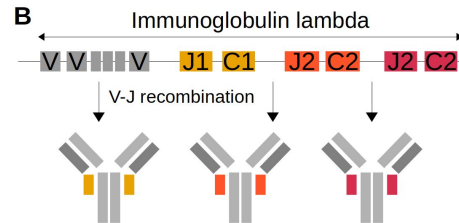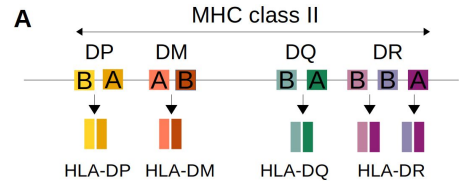Multiple alleles
for one gene

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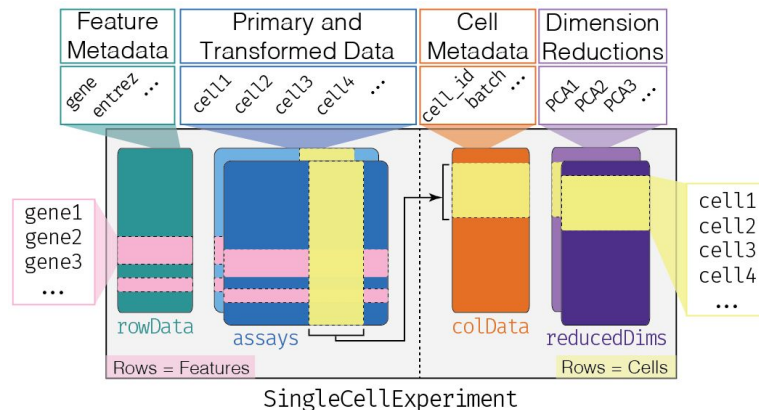| Gene group	Number of **alleles** (incl. pseudogenes)
IGHG	71
HLA-DRB	~4200
…	…

Source: IMGT and IPD-IMGT/HLA

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Typical transcriptomic analysis workflow

1. For each sequencing read:
   a. identify cellular barcode
   b. identify unique molecular identifier (UMI)
   c. map read to reference genome
2. Count unique transcripts per gene and barcode using UMI
3. Generate feature count matrix (genes x cells)
4. Downstream analysis
   a. dimension reduction
   b. clustering
   c. differential gene expression
   d. …

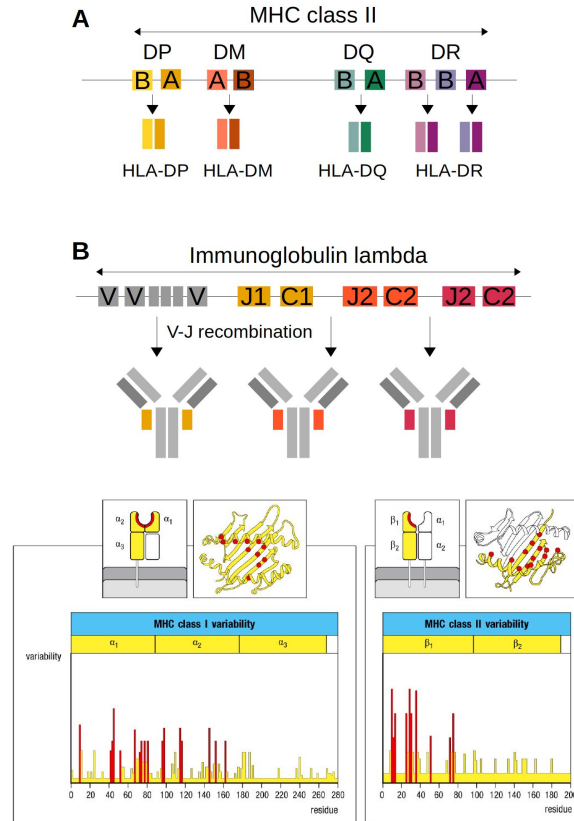SingleCellExperiment

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SingleCellExperiment

Allelic diversity and polygeny pose a bioinformatic challenge

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Hyperpolymorphism:
Multiple alleles
for one gene
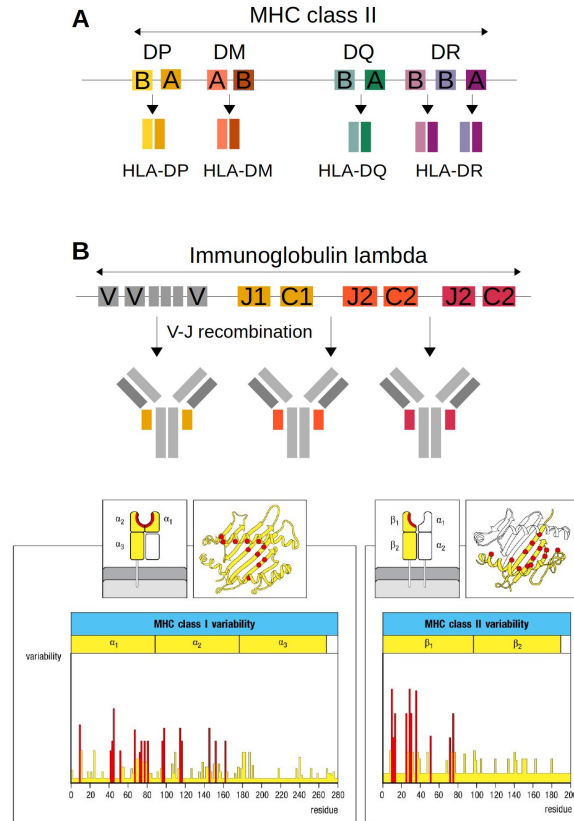

Bioinformatic challenge

Cross-mapping: uniquely
mapping to the wrong gene

Allelic diversity and polygeny pose a bioinformatic challenge

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Hyperpolymorphism:
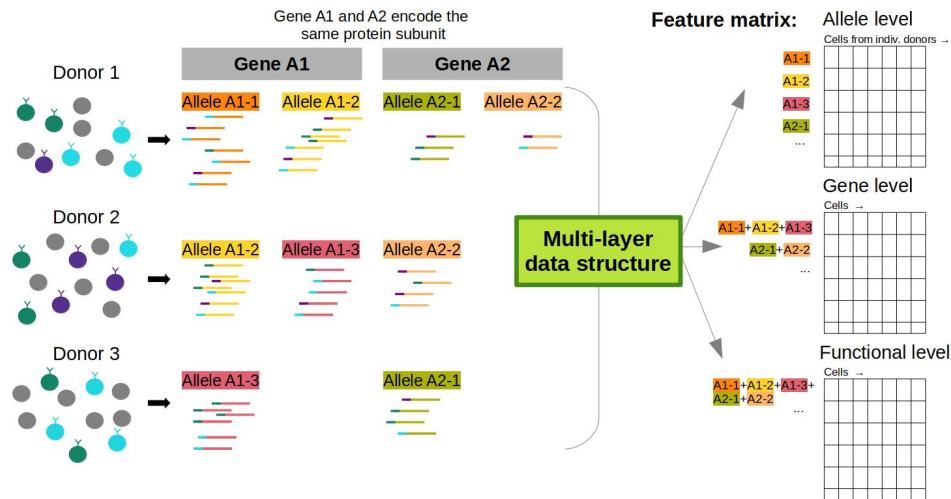Multiple alleles
for one gene

Figure 6.21 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Aim

To perform quantification of allele-specific expression for immunogenomic analysis

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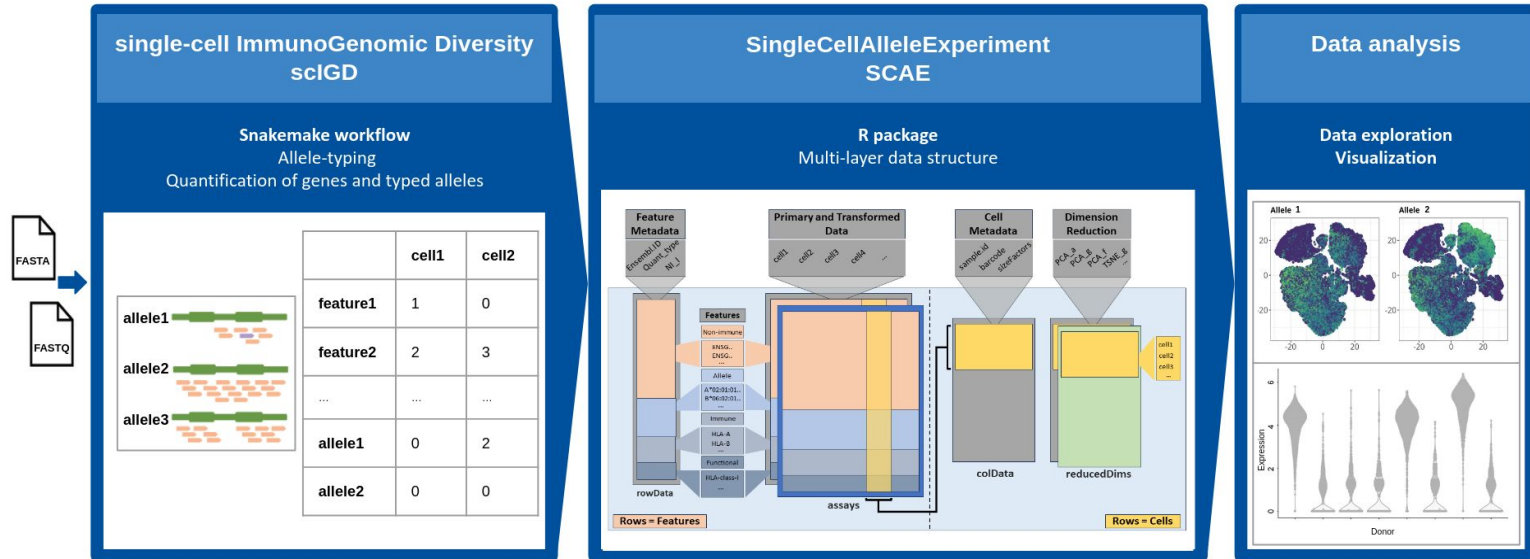# Implementation of allele and functional information
What we want

- Building a multi-layer data structure for immune gene representation in single-cell data

Workflow
How to get there

● Example datasets present in *scaeData* – R/ExperimentHub data package

Acknowledgements

scIGD

scaeData

SingleCellAlleleExperiment