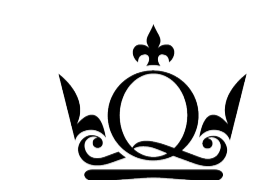# Using comprehensive transcriptome analysis to reveal the landscape of pathobiology in early rheumatoid arthritis

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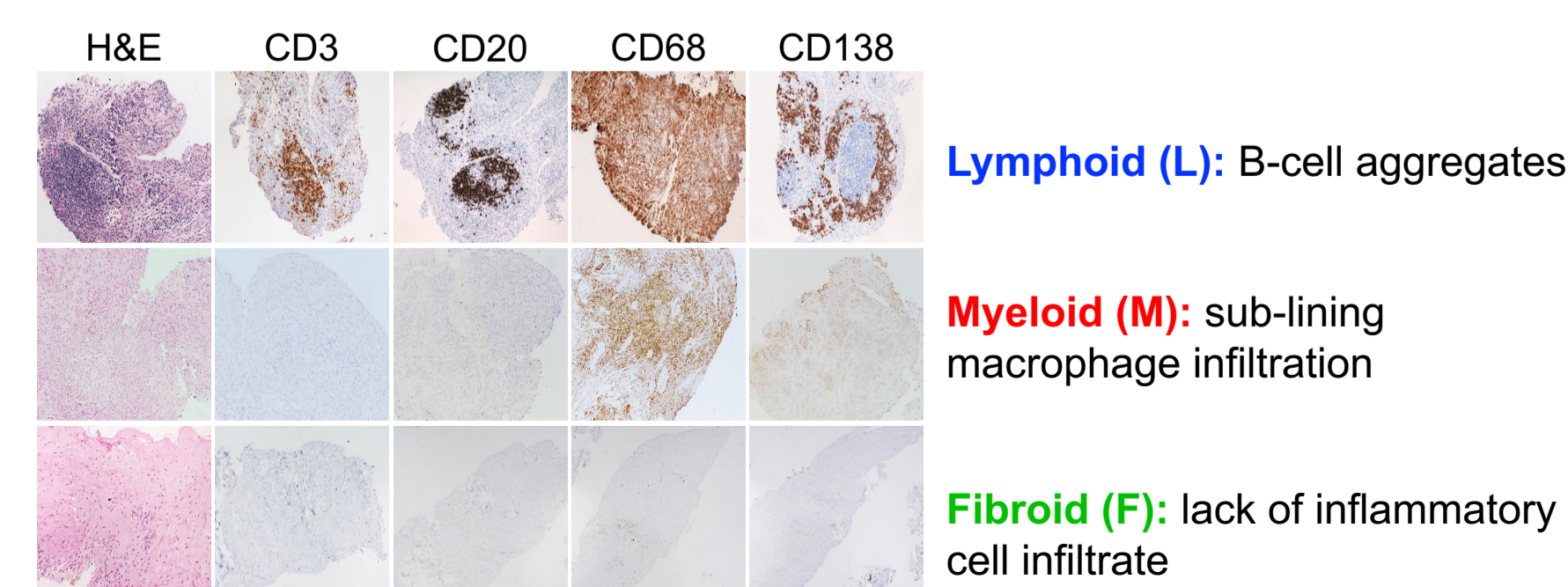EMR — Centre for Experimental Medicine & Rheumatology

1) Outcomes

- Comparison of gene expression in joints and blood identify markers that could predict disease course in rheumatoid arthritis (RA)

- An interactive web tool was deployed to allow the public to access and explore data easily

- A new R package, volcano3D, was developed for novel visualisations

2) Key Aims

- RA is a chronic autoimmune disease which affects the joints resulting in progressive pain, stiffness and swelling.

- Due to the limited response to treatment and heterogeneous nature of the condition, there is a drive to identify patient subgroups with distinct mechanisms of disease.

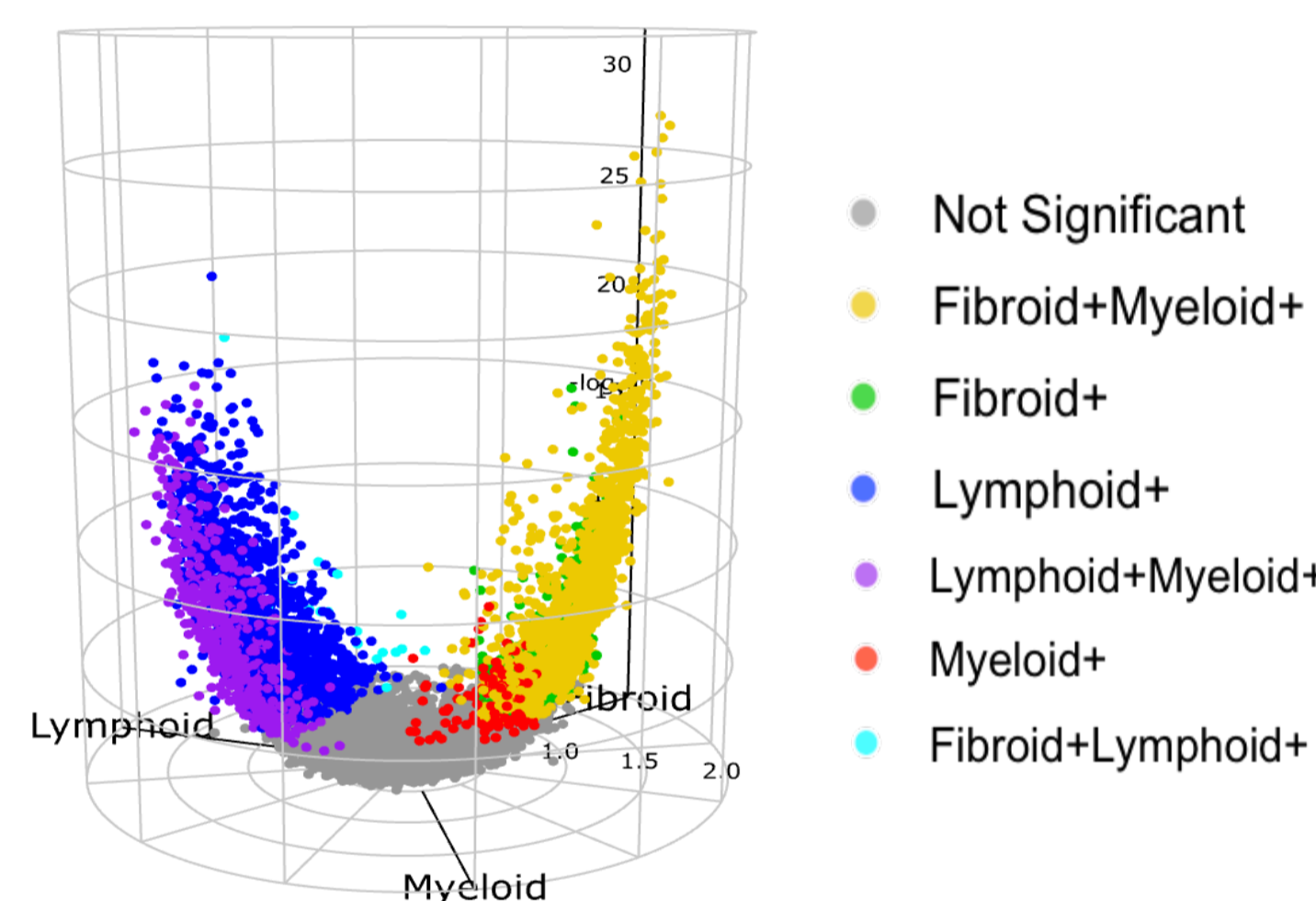## 3) Rheumatoid arthritis is separated into three distinct pathotypes

- Blood and synovial biopsies were taken from patients with early RA who were naïve to treatment.

- Synovial histology identified three distinct disease groups:

H&E   CD3   CD20   CD68   CD138

Lymphoid (L): B-cell aggregates

Myeloid (M): sub-lining macrophage infiltration

Fibroid (F): lack of inflammatory cell infiltrate

Immunohistochemistry to identify B cells, T cells, plasma cells and macrophages in RA synovium.

4) Novel visualisation of three-way differential gene expression highlight drivers of disease

- Relative gene expression between pathotypes was projected into polar coordinates

- Genes colour-coded according to upregulation (p < 0.05)

- Not Significant
- Fibroid+Myeloid+
- Fibroid+
- Lymphoid+
- Lymphoid+Myeloid+
- Myeloid+
- Fibroid+Lymphoid+

Three-dimensional volcano plot showing the differential expression between pathotypes in early rheumatoid arthritis.

5) Comparisons between tissues reveal discordance and differential axes of expression.
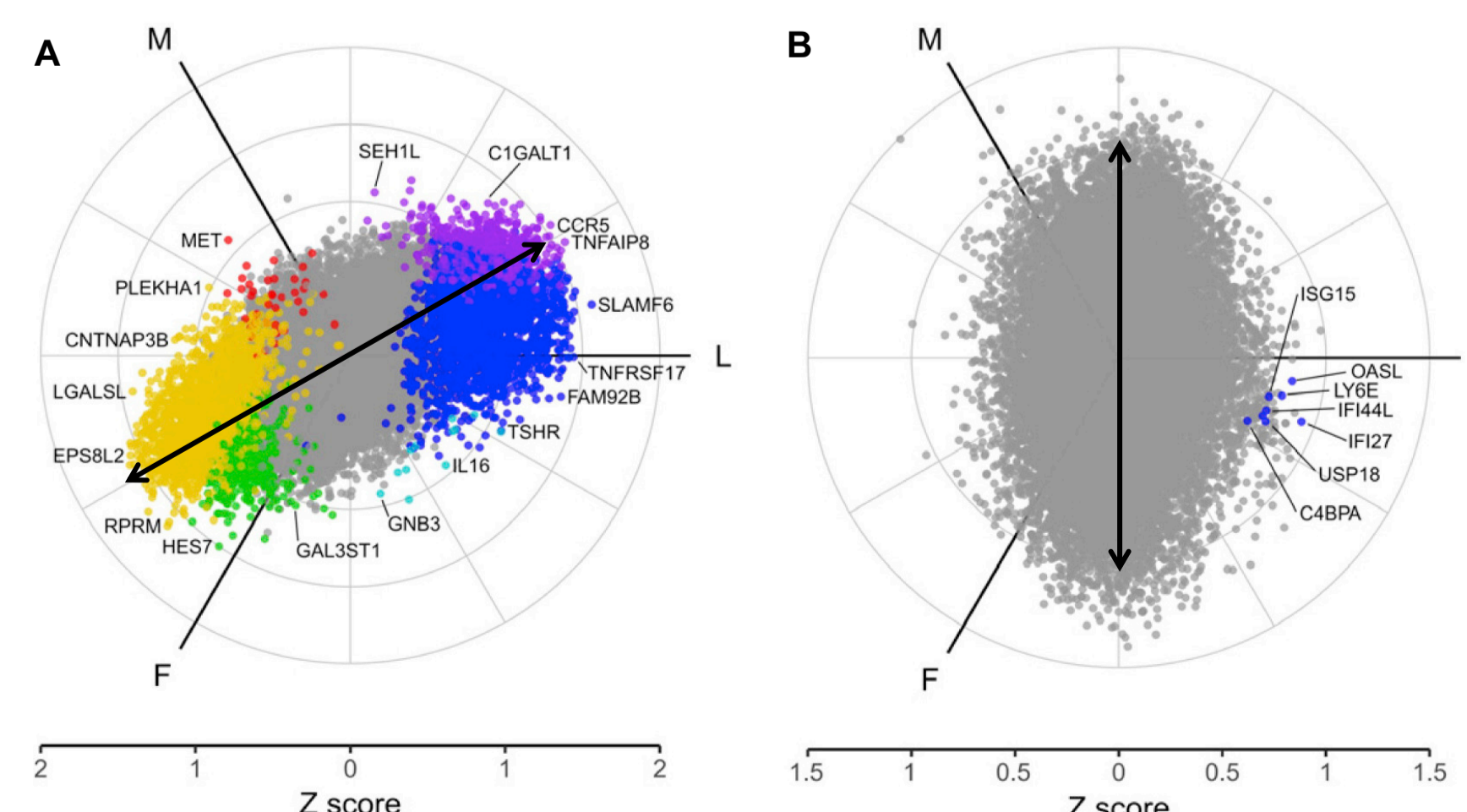
Synovium (A) shows higher heterogeneity than blood (B) and different axes of expression.

6) An interactive web interface allows data exploration

- A web interface was constructed using R Shiny and Plotly to allow interactive exploration of:

  - 3D volcano plots
  - Gene transcript levels, histological pathotype, and clinical parameters
  - Blood transcript modules.
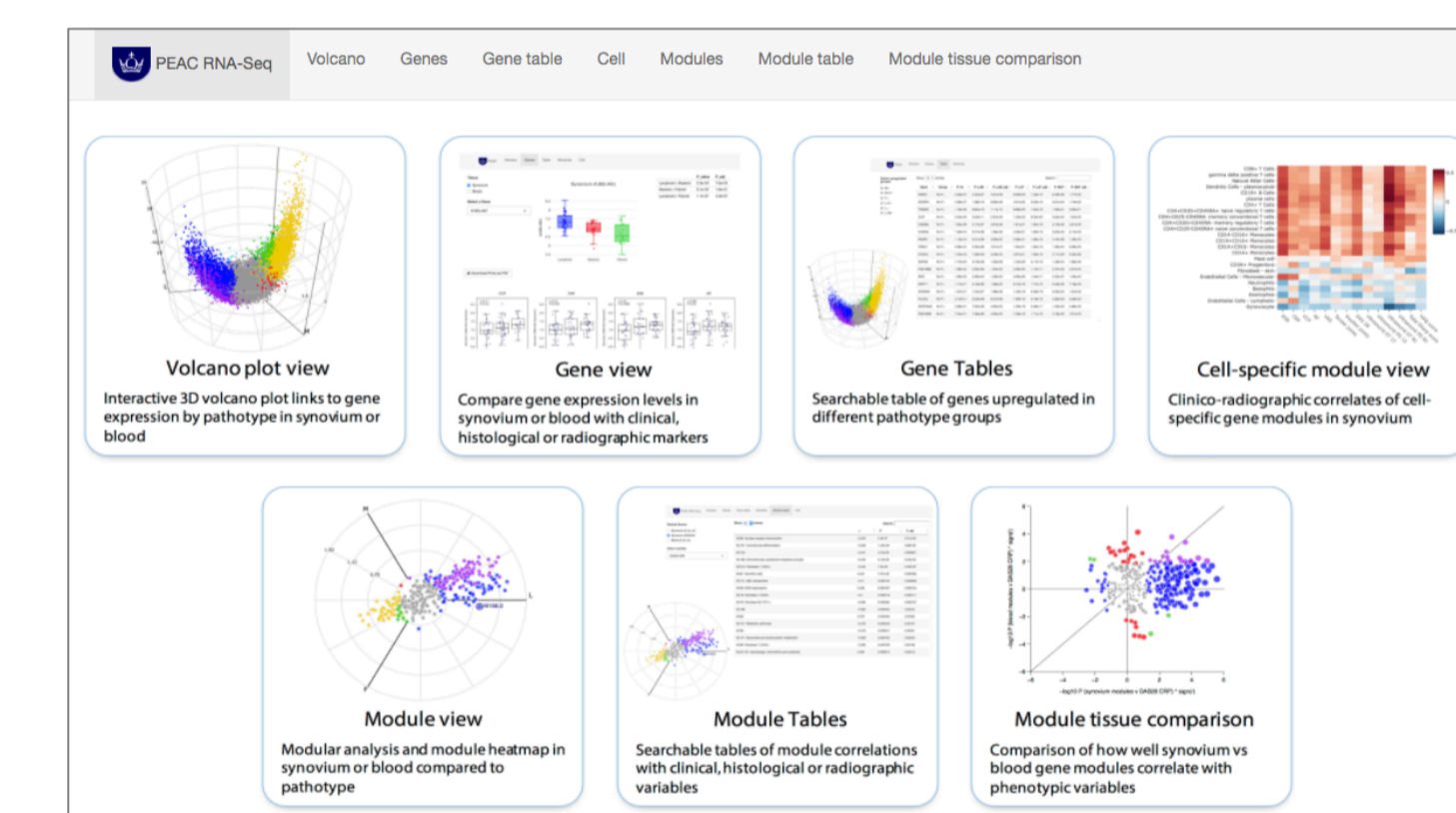
web interface available at https://peac.hpc.qmul.ac.uk/

7) volcano3D: R package for three-way visualisation

- An open source R package was developed for similar interactive visualisations

- Now available on CRAN and Gihub

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