IO17 | Large Scale Bioinformatics for Immuno-Oncology

Tumor-infiltrating immune cells

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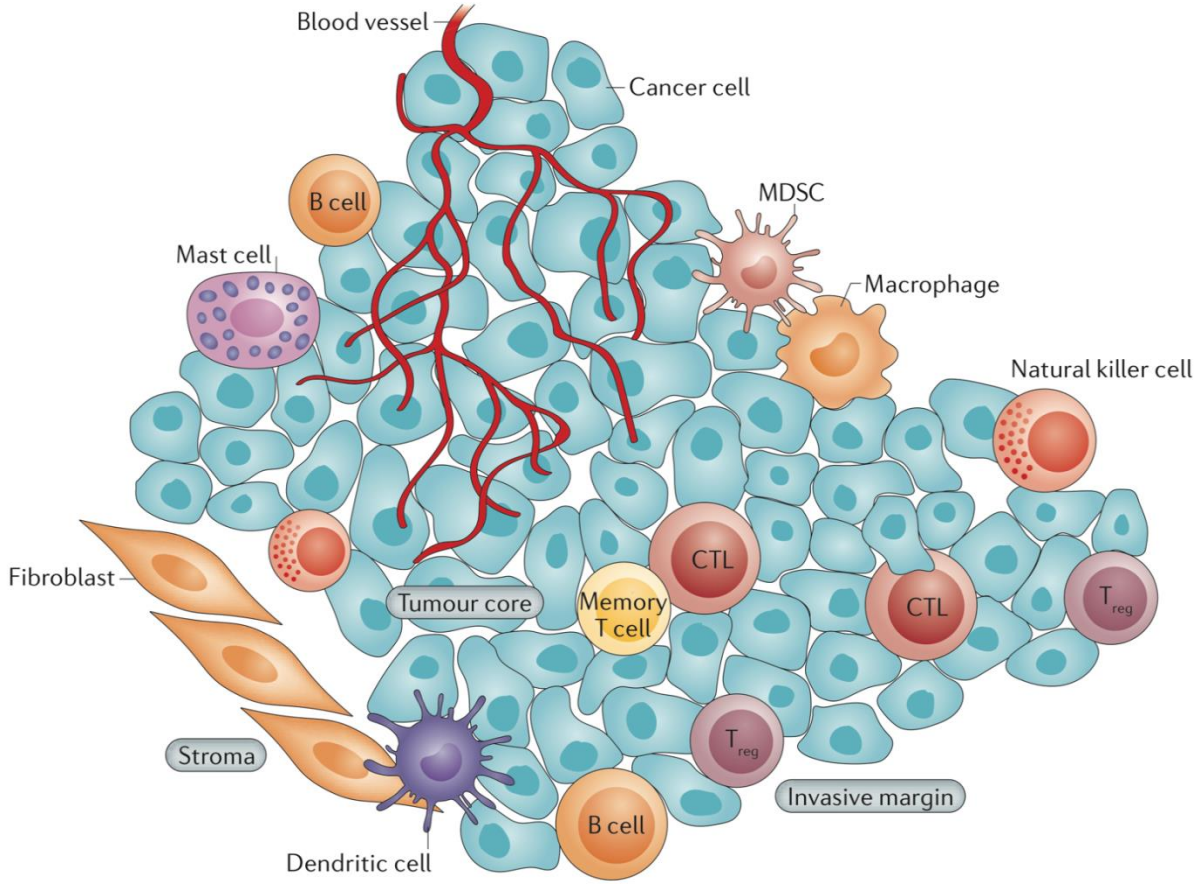
The immune contexture of human tumors

- Various immune cell types
- Pro- or anti-tumorigenic roles

E.g. regulatory CD4+ T (T_{reg}) cell → immunosuppressive



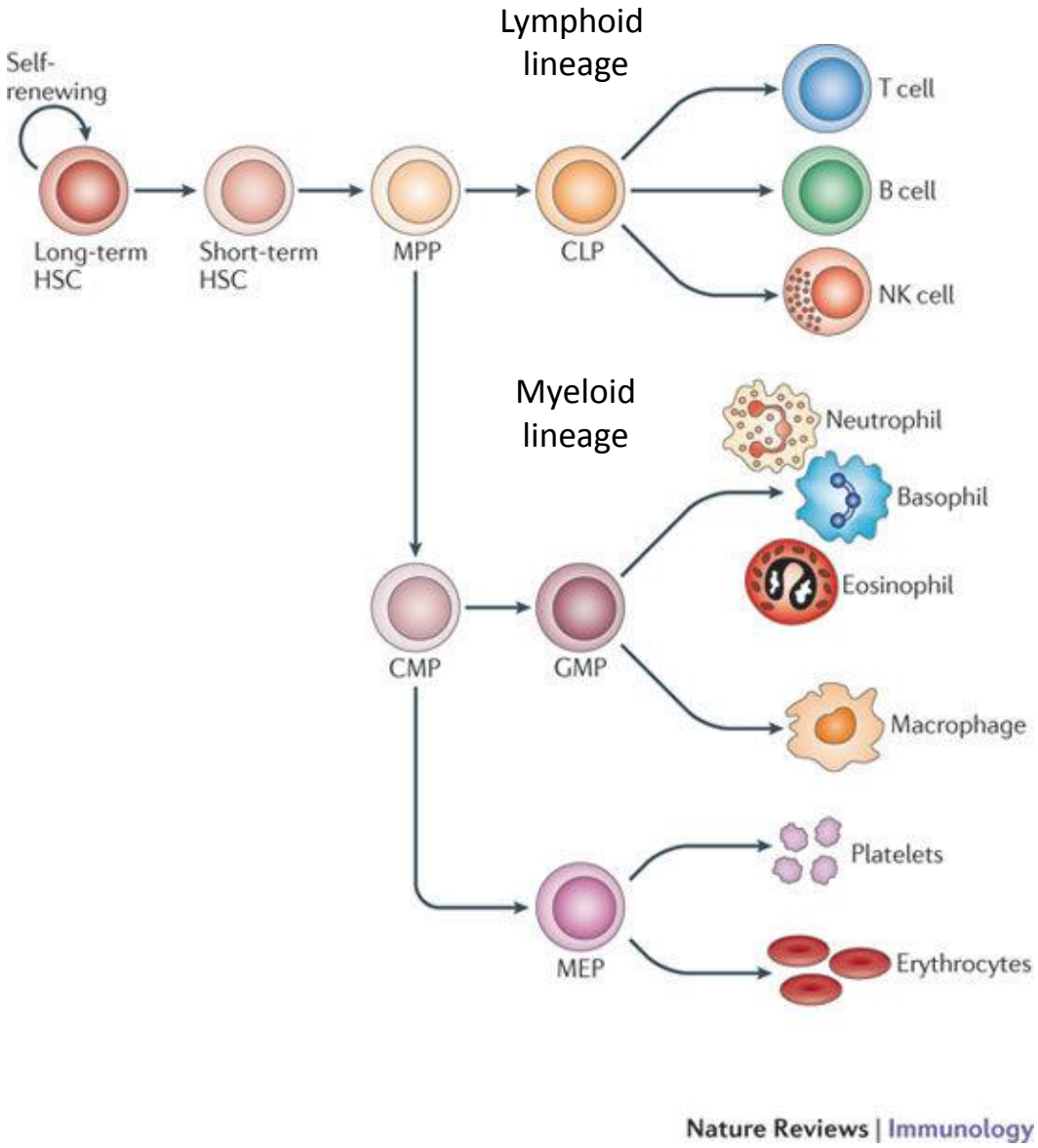
Immune cells influence tumor progression and response to therapy

→ identify biomarkers (monitoring and predict response) for immunotherapy

→ develop combination therapies

H Hackl*, P Charoentong*, F Finotello* et al., Nature Reviews Genetics, 2016

The (simplified) hematopoietic tree



Long-term haematopoietic stem cells (HSCs) give rise to all the cells of the immune system and other blood cells

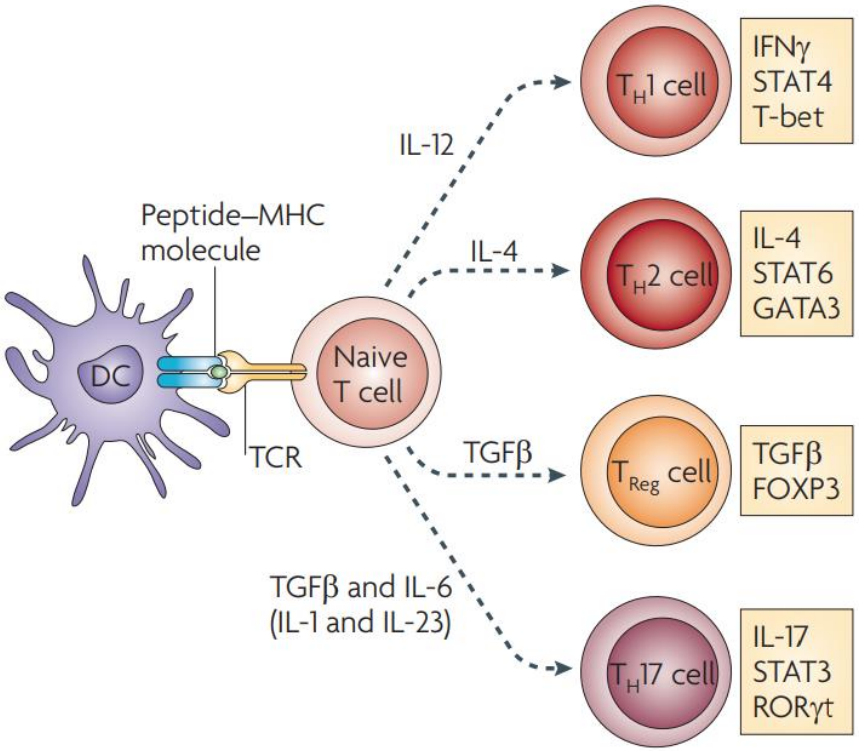
+ immune cell types not represented here (e.g. dendritic and mast cells)

+ sub-types (e.g. CD4+ and CD8+ T cells)

+ different functional orientations or polarizations

KY King and MA Goodell, Nature reviews Immunology, 2011

Polarization of CD4+ T cells

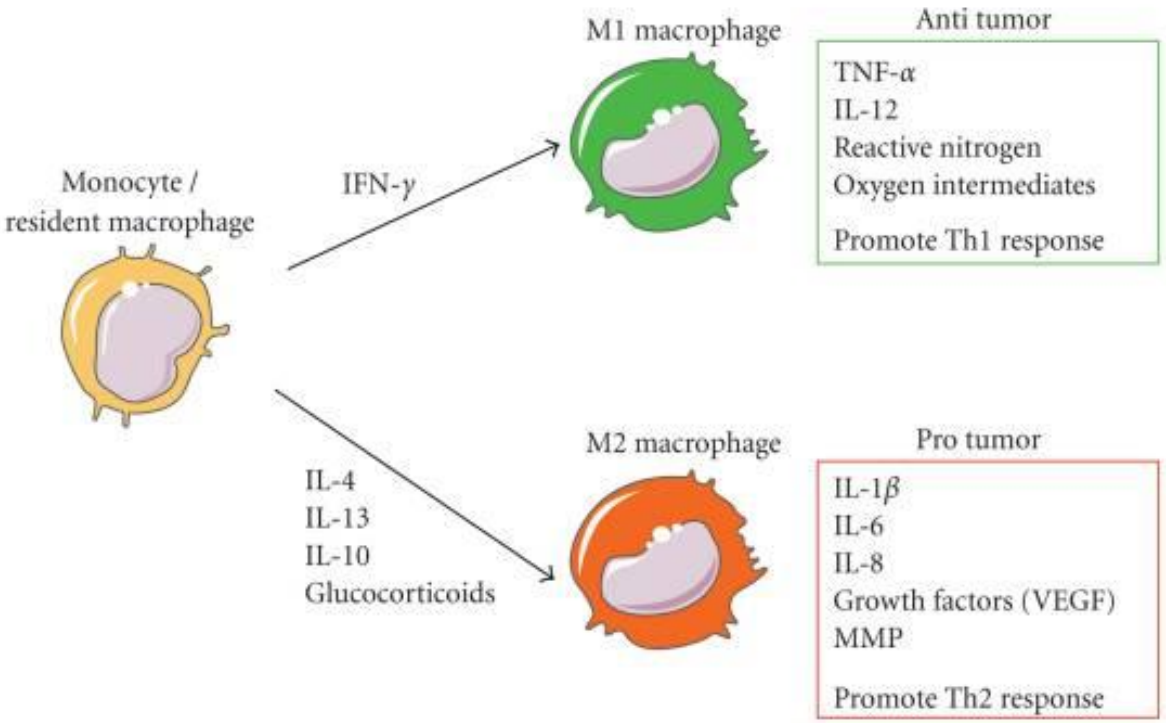


Activation of naïve **CD4+ T cells** by dendritic cells → polarization (depending on the local cytokines and transcription factors)

- T_H1: immunity to intracellular microbes, help to activate macrophages, cytotoxic cells, and B cells, inhibit T_H2 development, anti-tumor role
- T_H2: immunity to extracell pathogens, stimulate B cells, inhibit T_H1 development, pro-tumor role
- T_{reg}: pherpheal tolerance, immunoinhibitory, suppress effector T cells, pro-tumor role
- T_H17: pro-inflammatory, recruit neutrophils and macrophages to infected tissues

Z Weiping and NP Restifo, Nature Reviews Immunology, 2010

Polarization of macrophages



Classically activated macrophages (M1)

Alternatively activated macrophages (M2)

MC Schmid and JA Varner, Journal of oncology, 2010