

Fundamental mechanisms of tumor immune evasion: A summary for the clinician

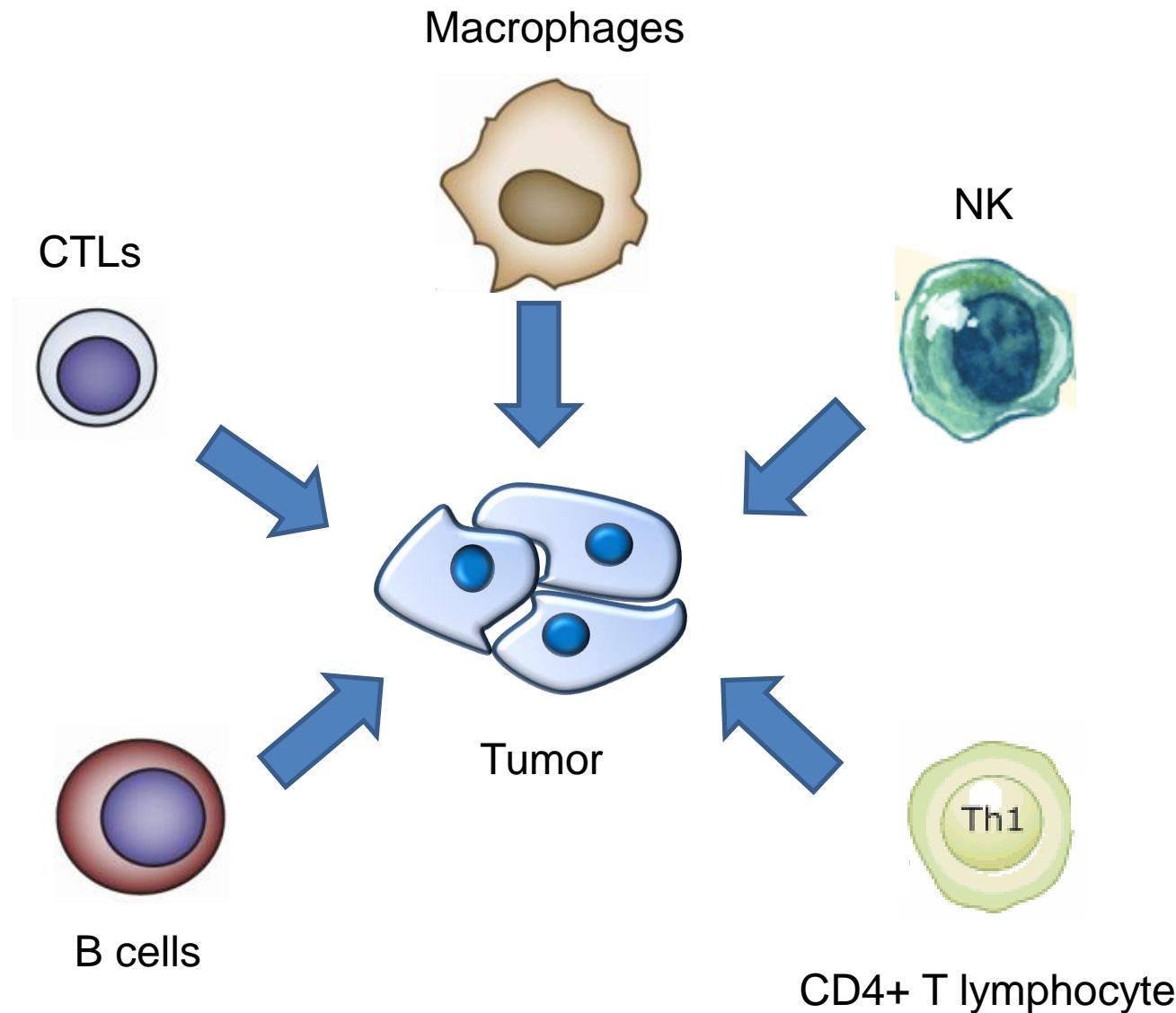
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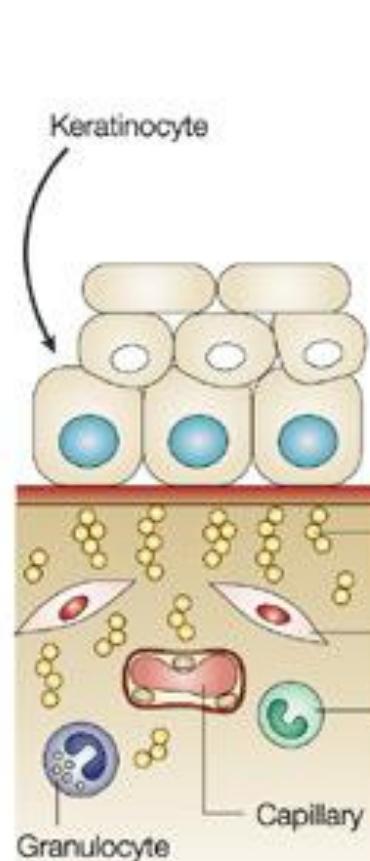
Successful antitumor immune response



Immune cells in tumor stroma

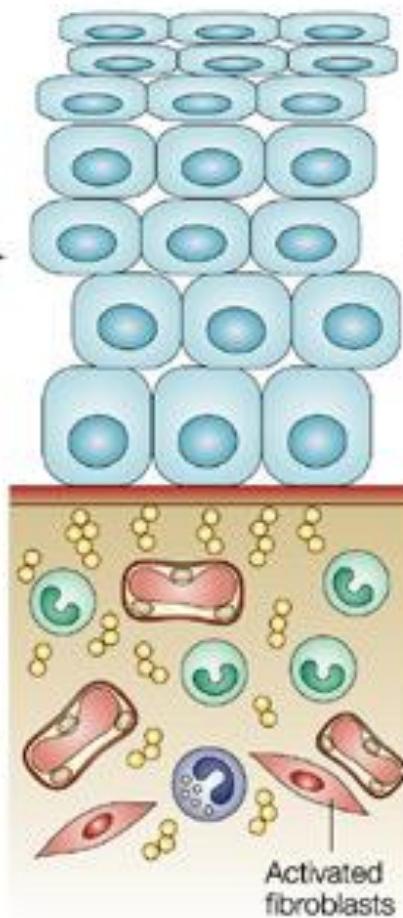
a Normal epithelium

Quiescent stroma



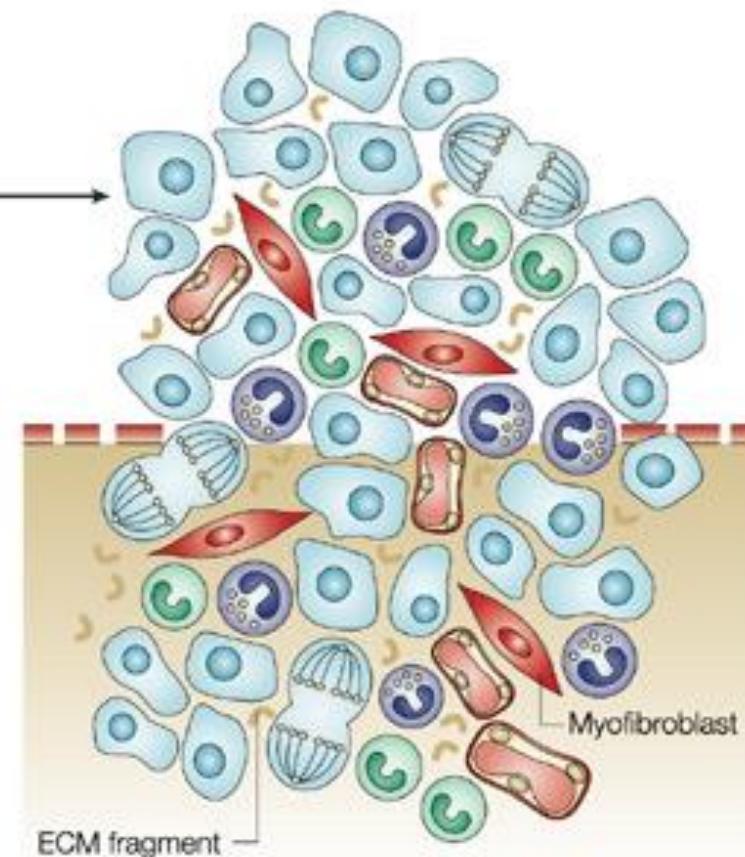
b Pre-malignant dysplasia

Activated stroma,
wound granulation tissue

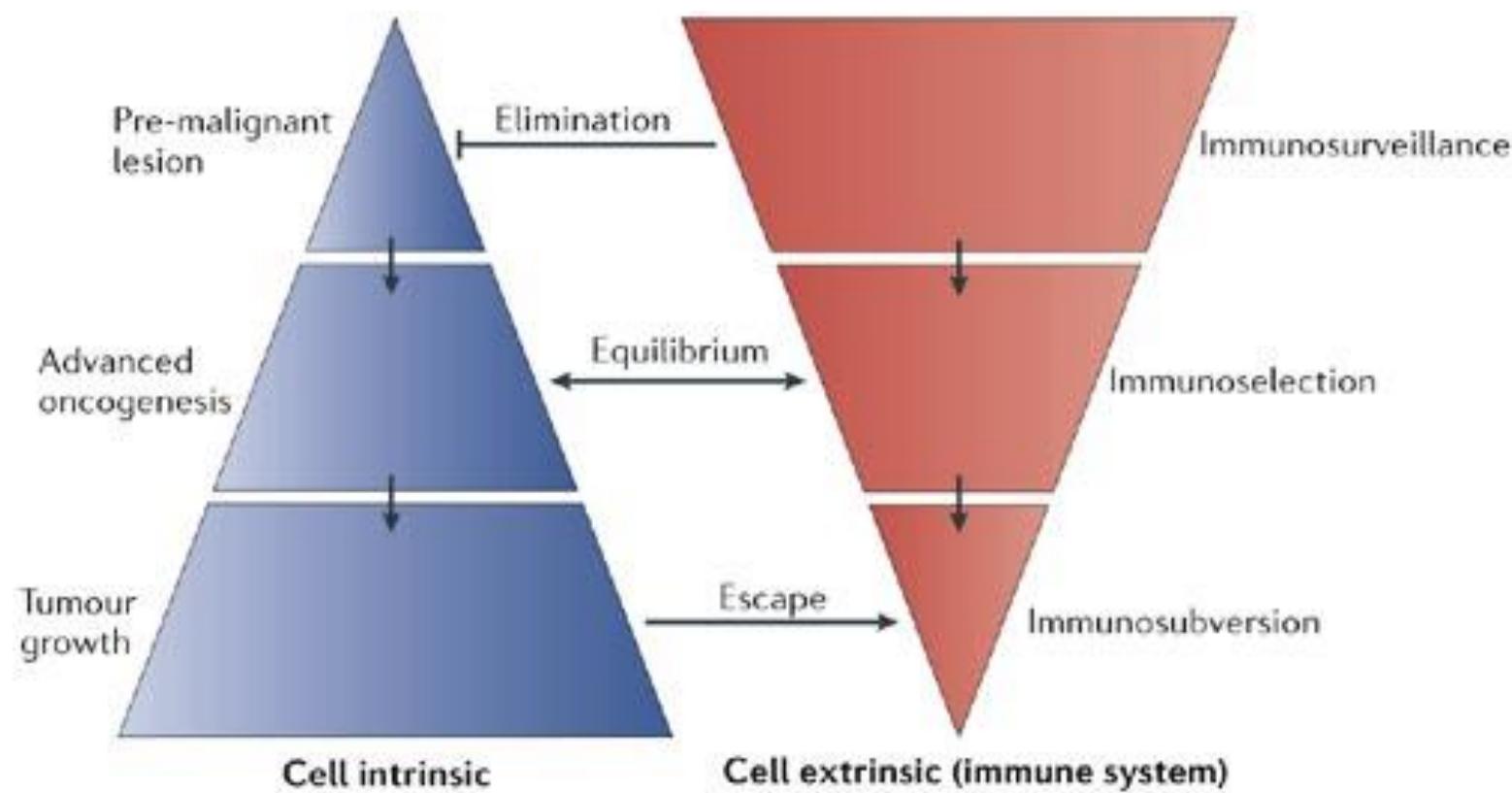


c Carcinoma

Reactive tumour stroma

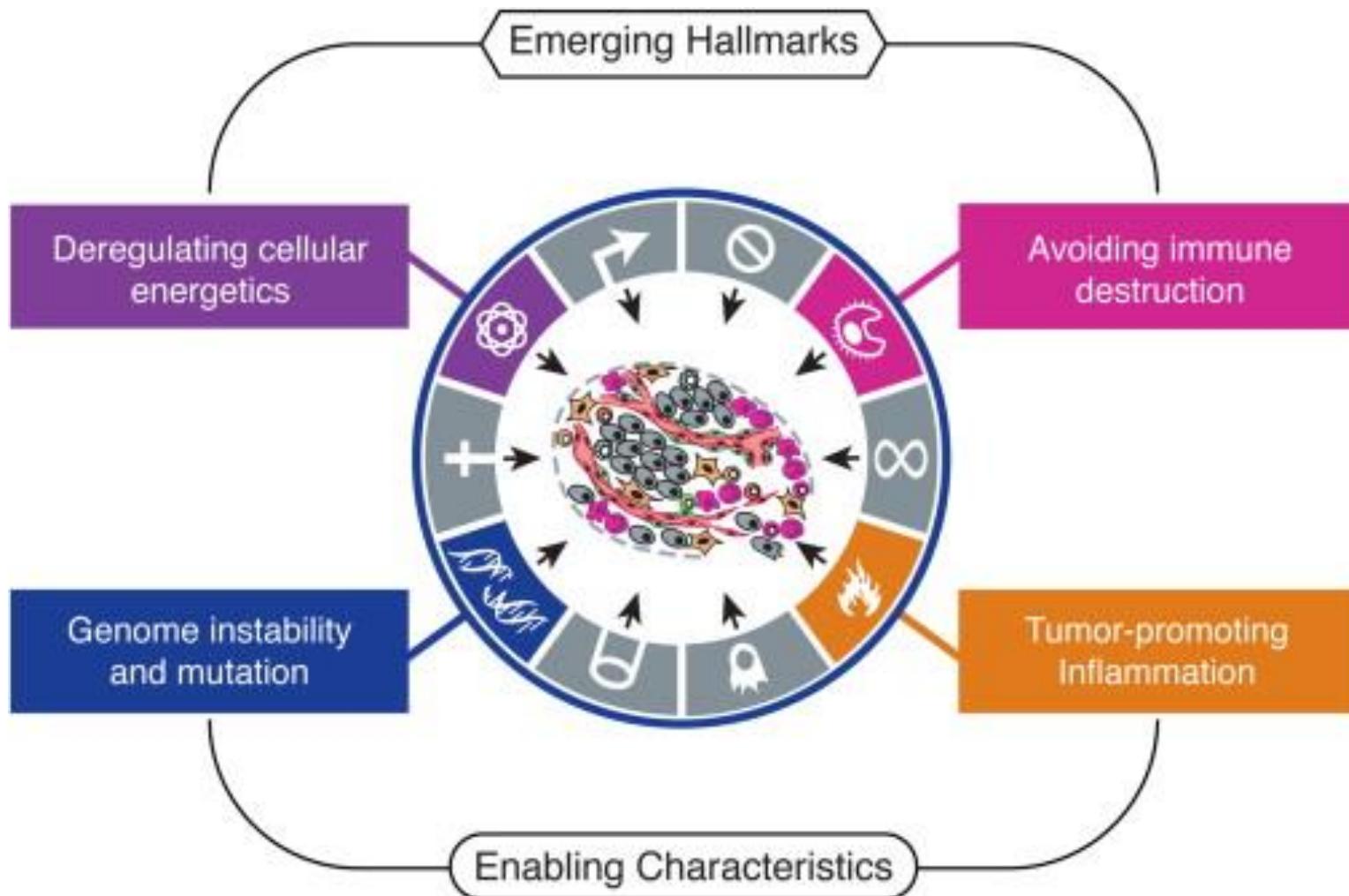


Cancer immunosurveillance and immunoediting



Zitvogel *et al.* Nat Rev Immunol. 2006 Oct;6(10):715-27.

An emerging hallmark of cancer



Fundamental immune escape mechanisms

A) Tumor variants invisible to the immune system

1) Alteration of the antigen-processing machinery

2) Tumor variants with reduced sensitivity to immune effectors

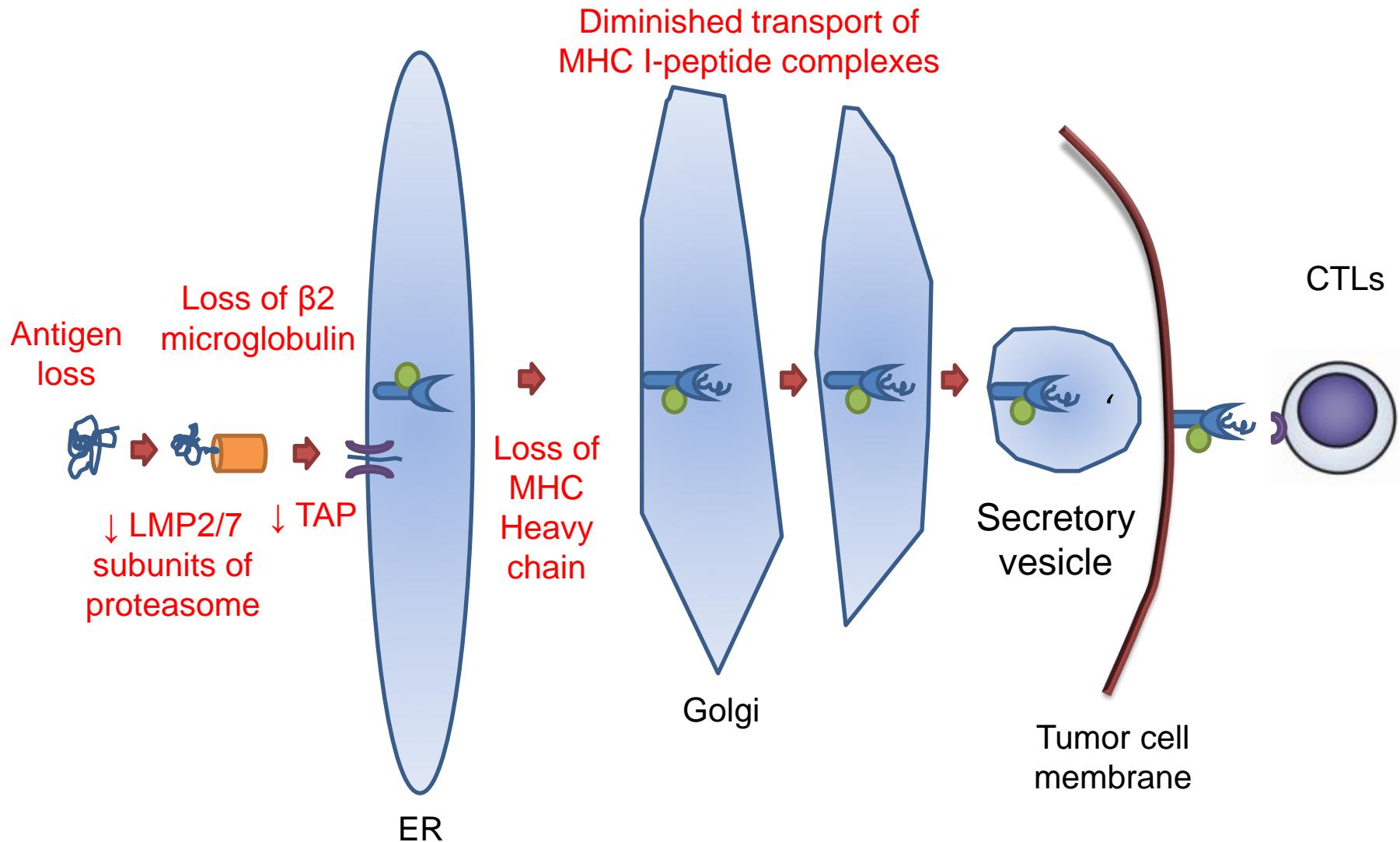
B) Tumor variants that suppress the antitumor immune response

3) Infiltration of suppressor myeloid cells

4) Infiltration of T regulatory cells

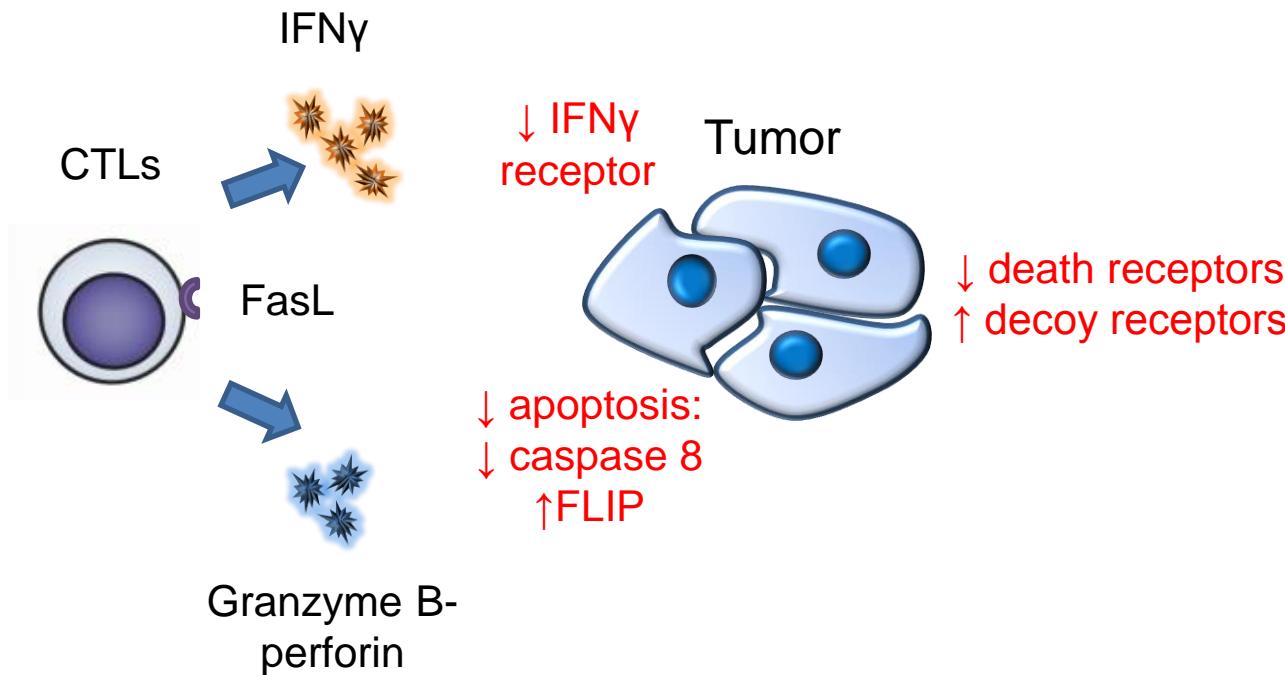
5) Production of immunosuppressive factors

Alteration of the antigen-processing machinery



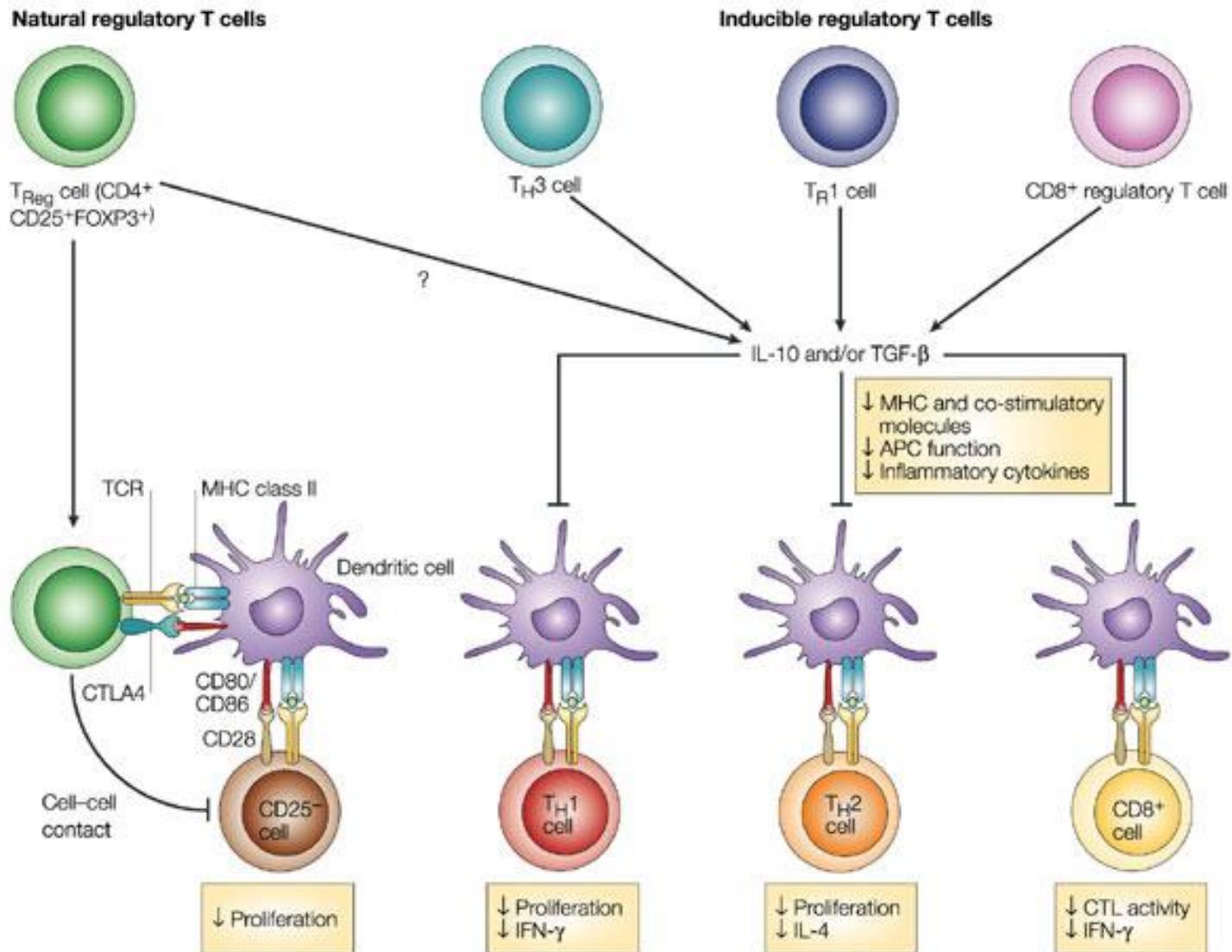
Adapted from Drake *et al.* Adv Immunol. 2006;90:51-81.

Tumor variants with reduced sensitivity to immune effectors

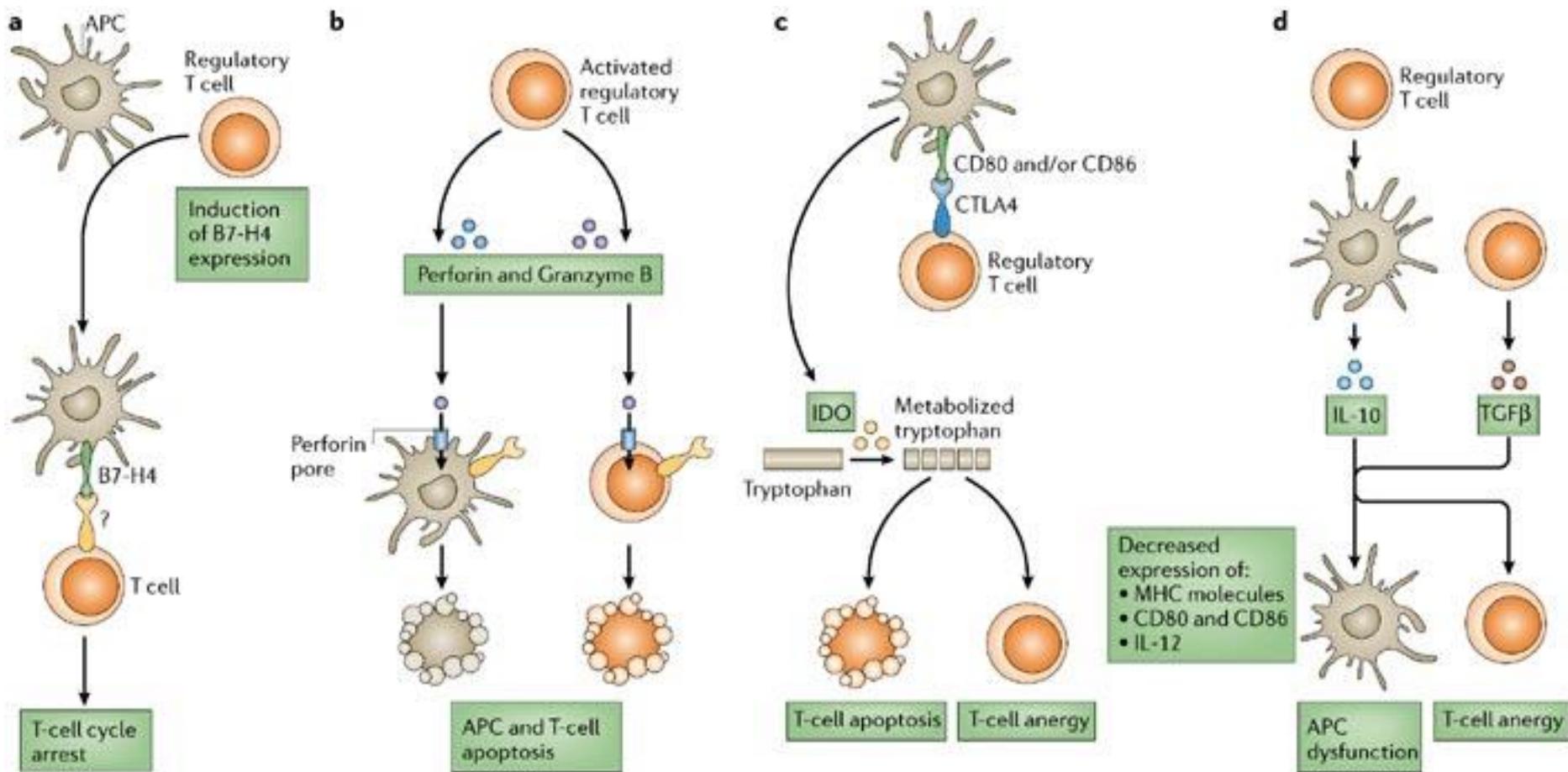


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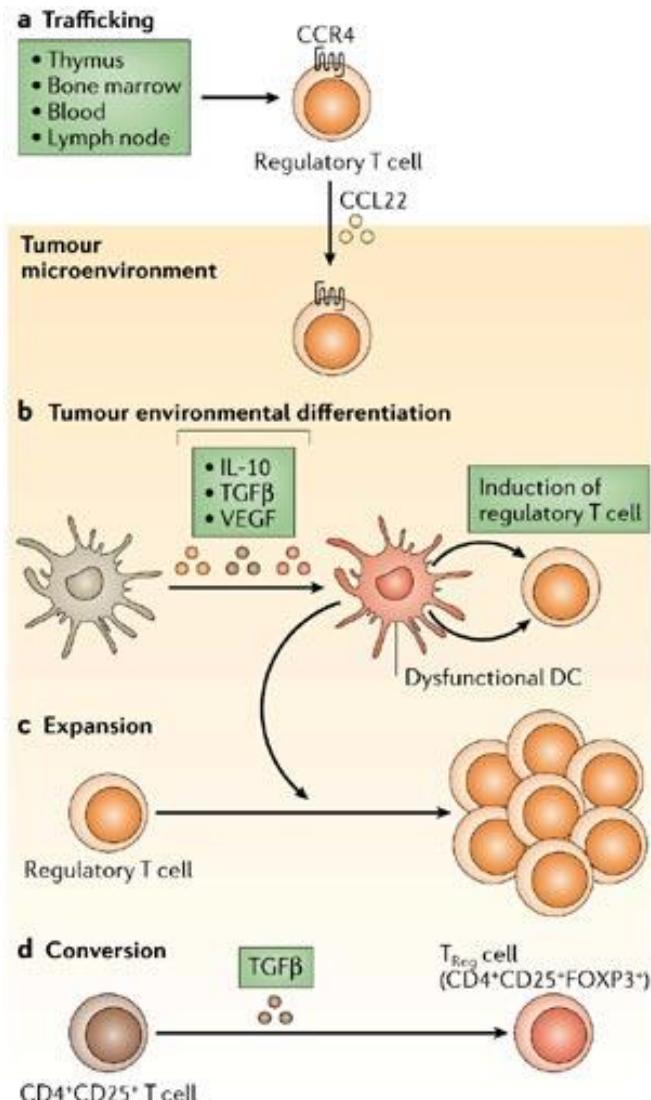
Infiltration of T regulatory cells



Infiltration of T regulatory cells

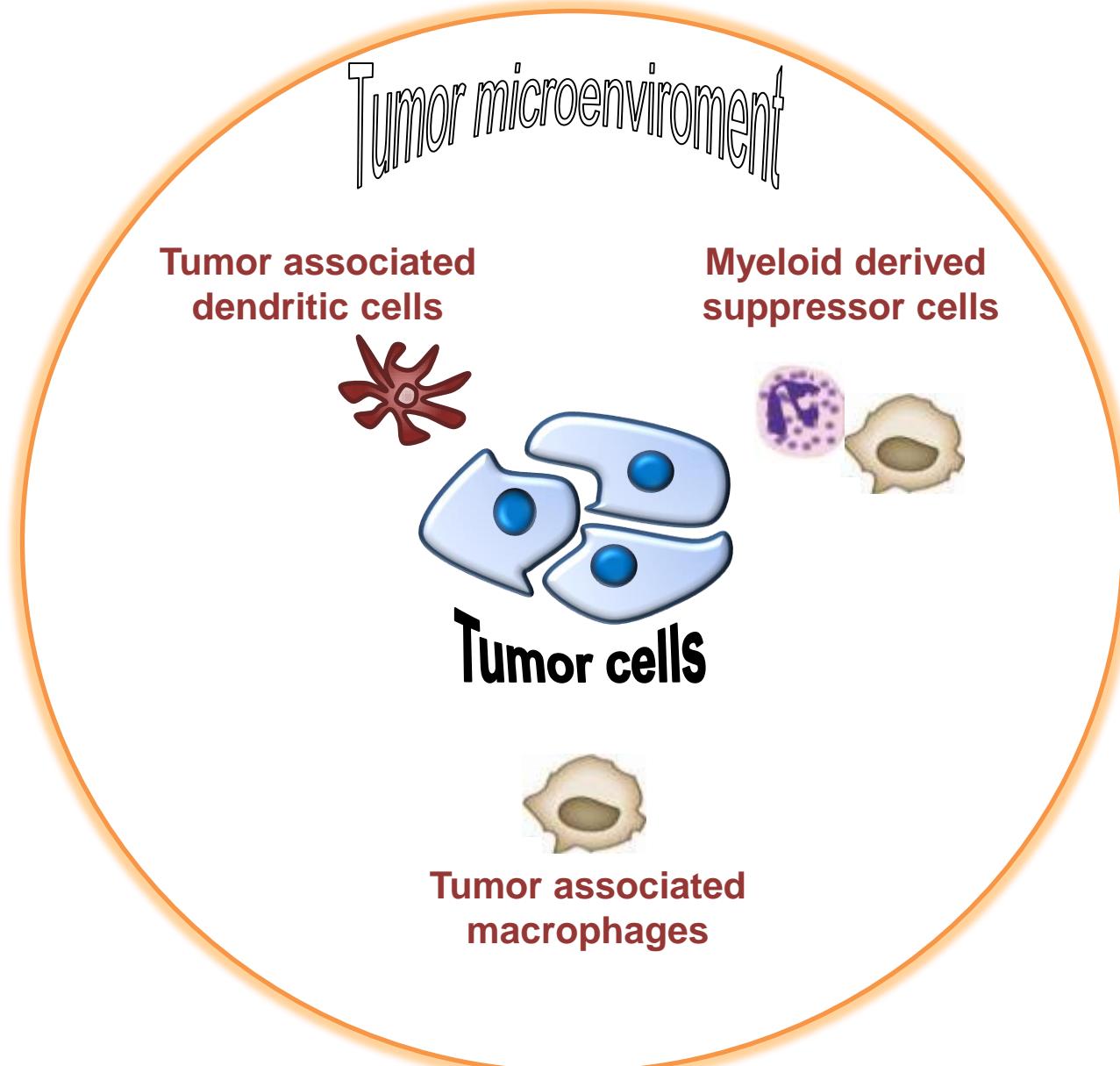


Infiltration of T regulatory cells

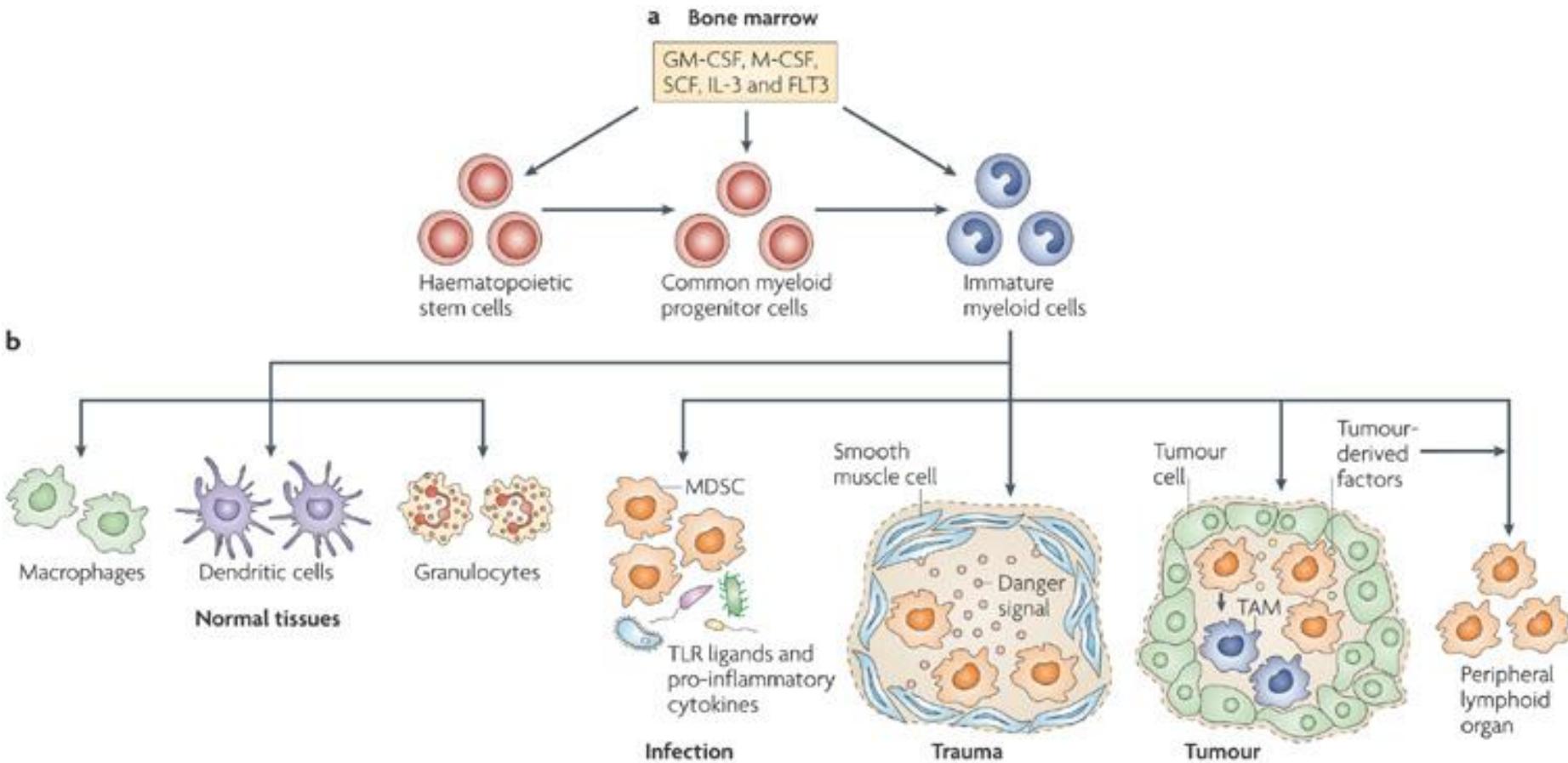


Zou W. *Nat Rev Immunol.* 2006 Apr;6(4):295-307.

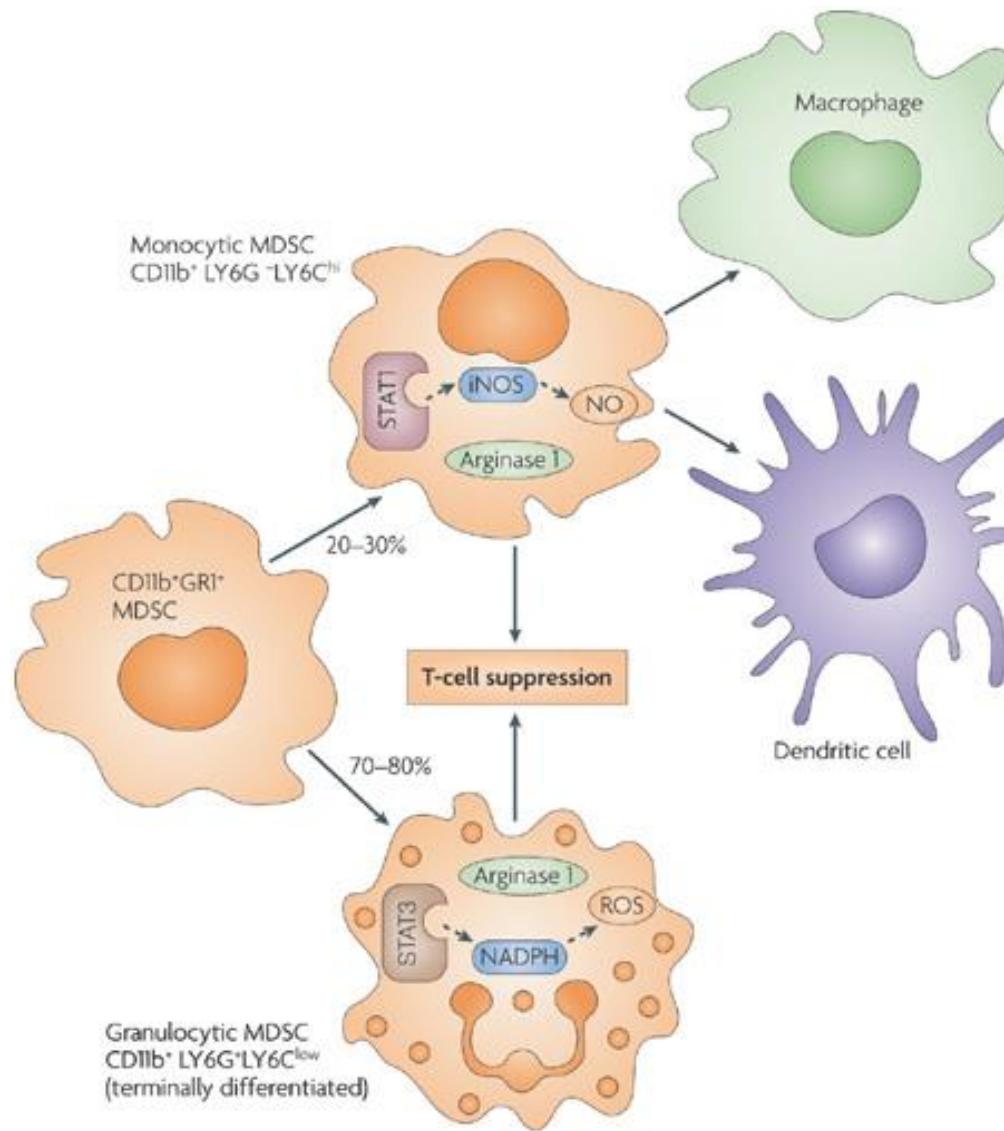
Infiltration of suppressor myeloid cells



Myeloid-derived suppressor cells

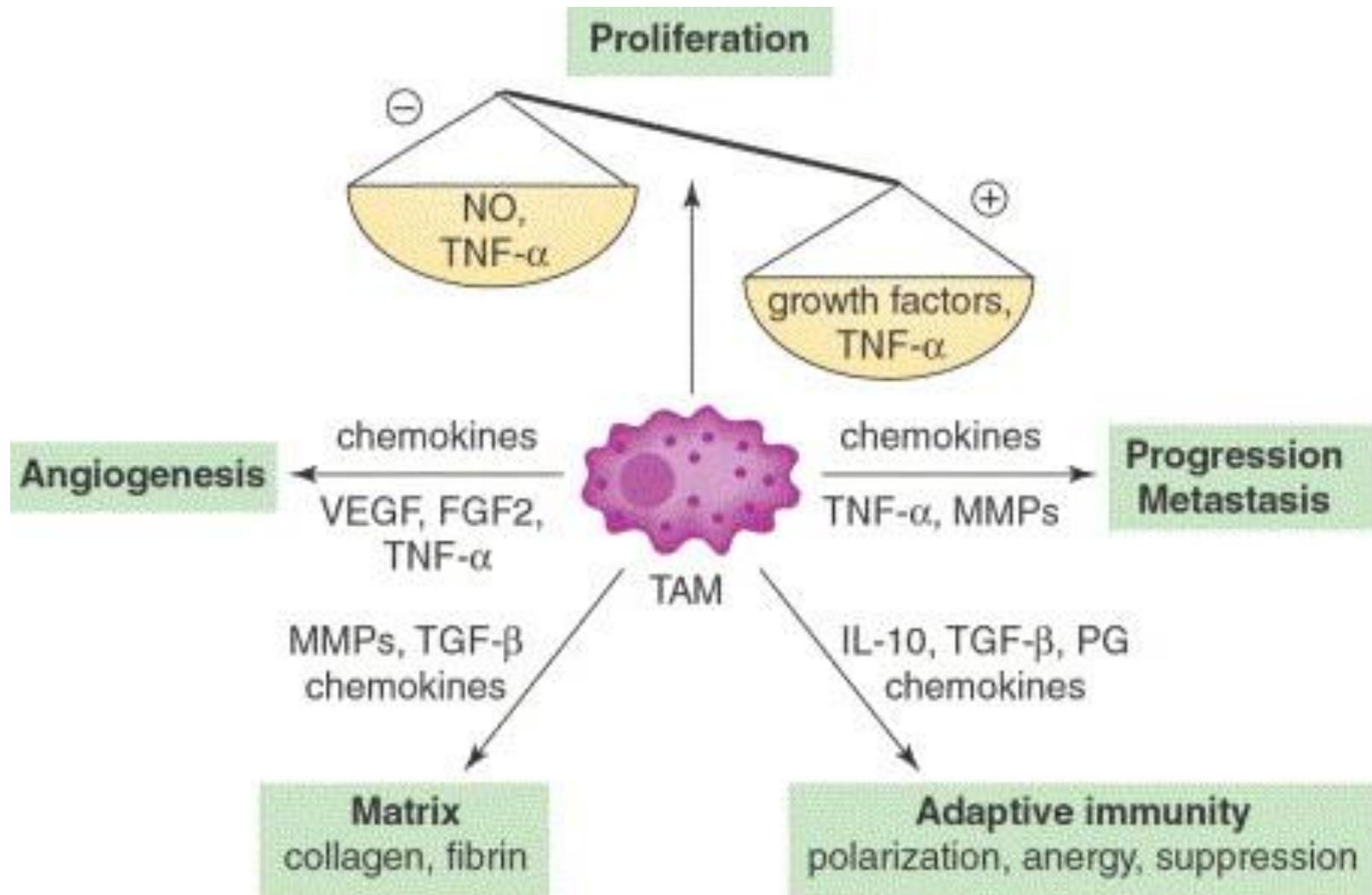


Myeloid-derived suppressor cells

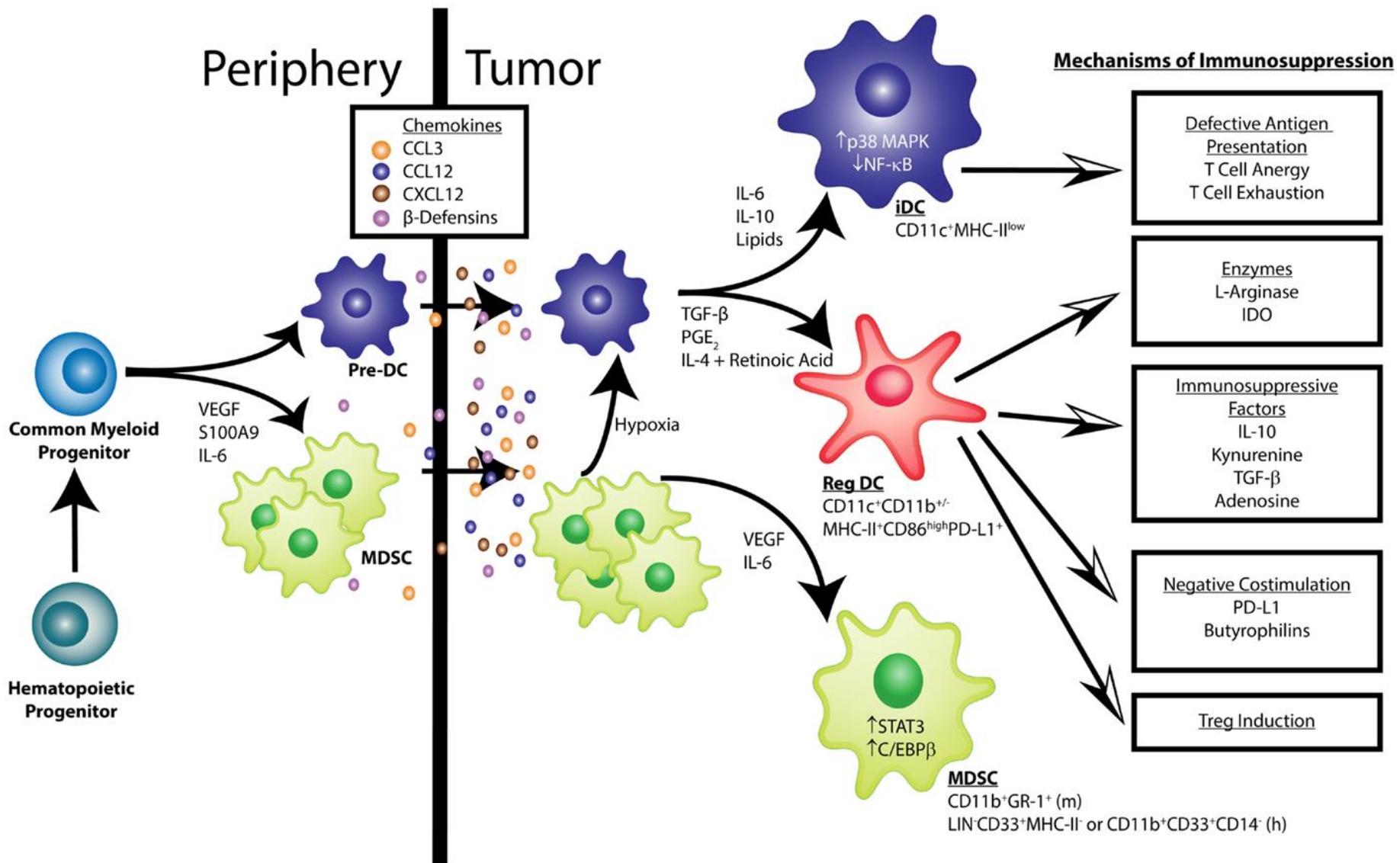


Gabrilovich DI et al. Nat Rev Immunol. 2009 Mar;9(3):162-74.

Tumor-associated macrophages

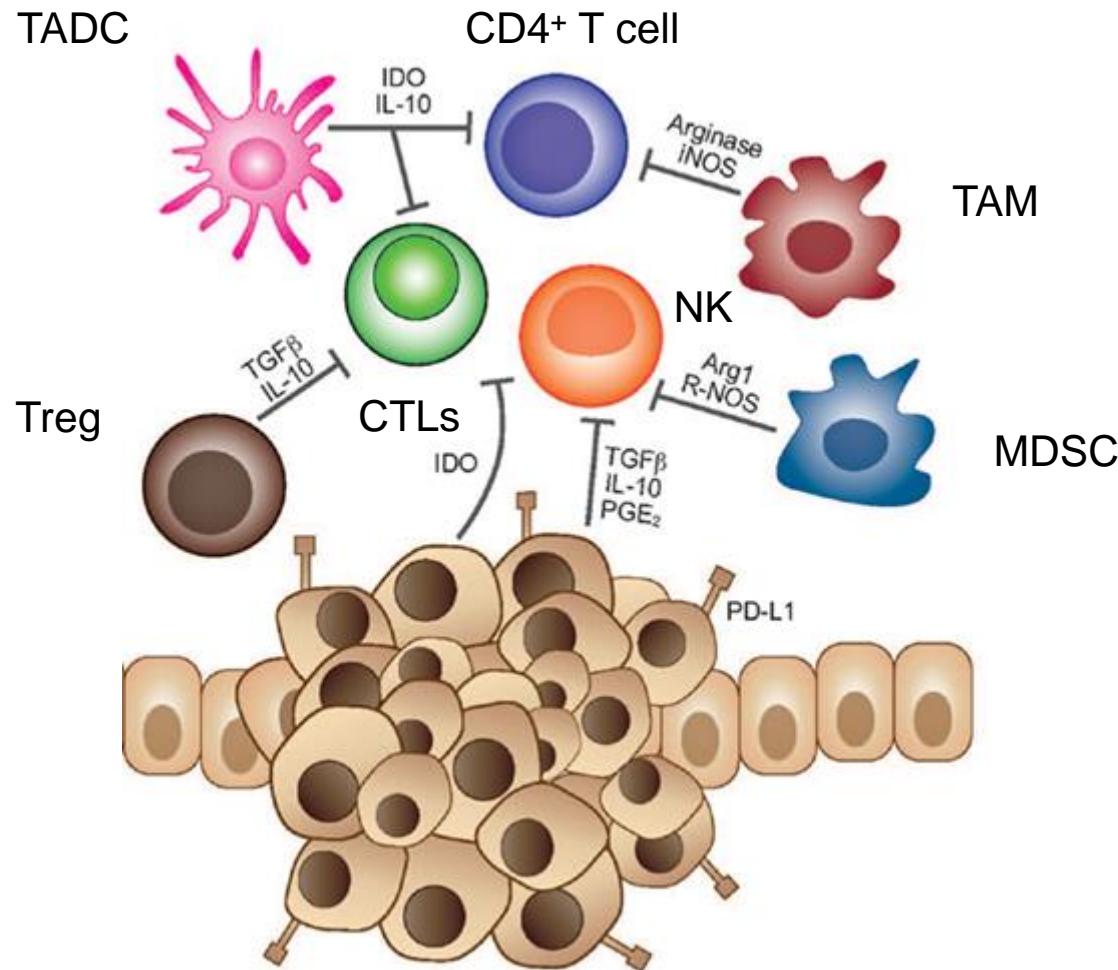


Tumor-associated dendritic cells

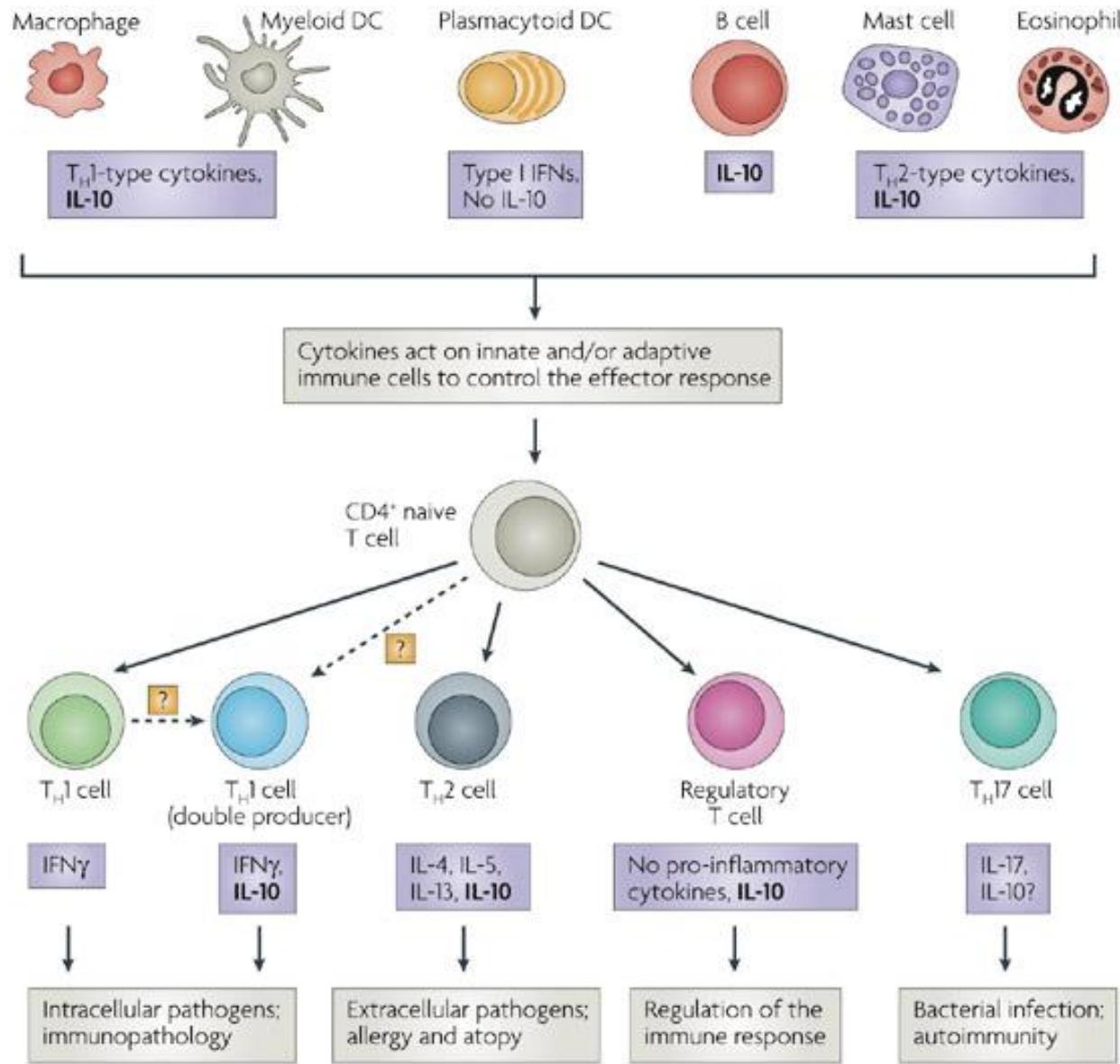


Production of immunosuppressive factors

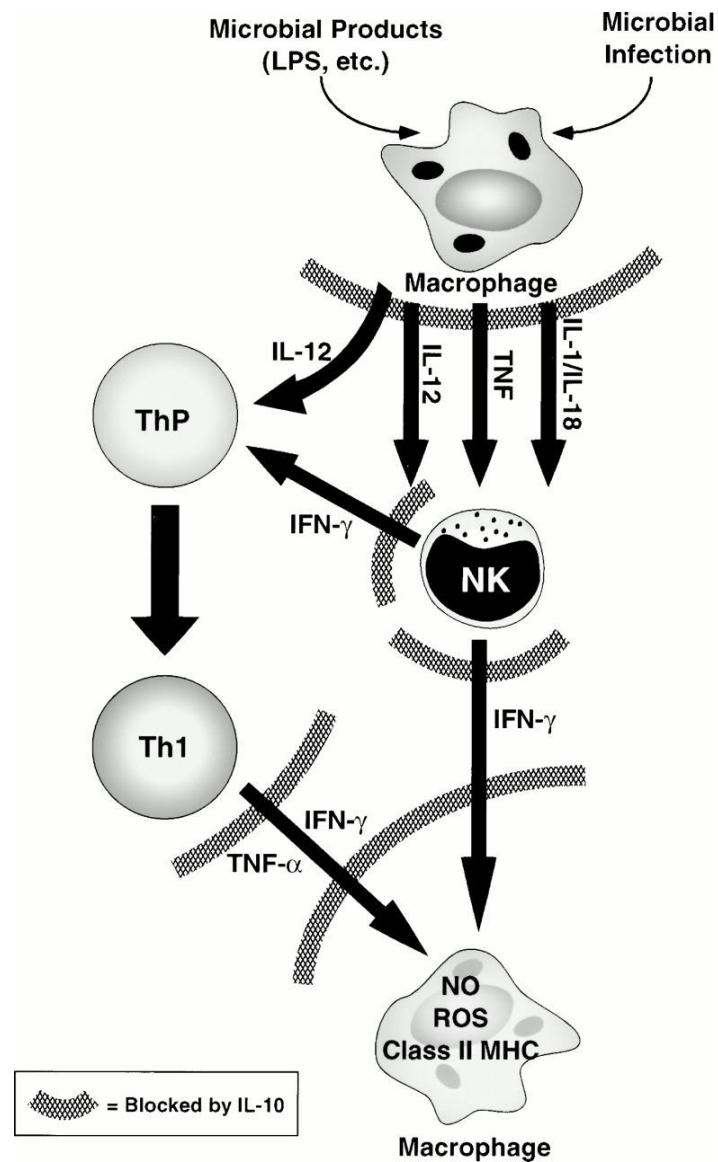
Cytokines, Enzymes and Co-inhibitory molecules



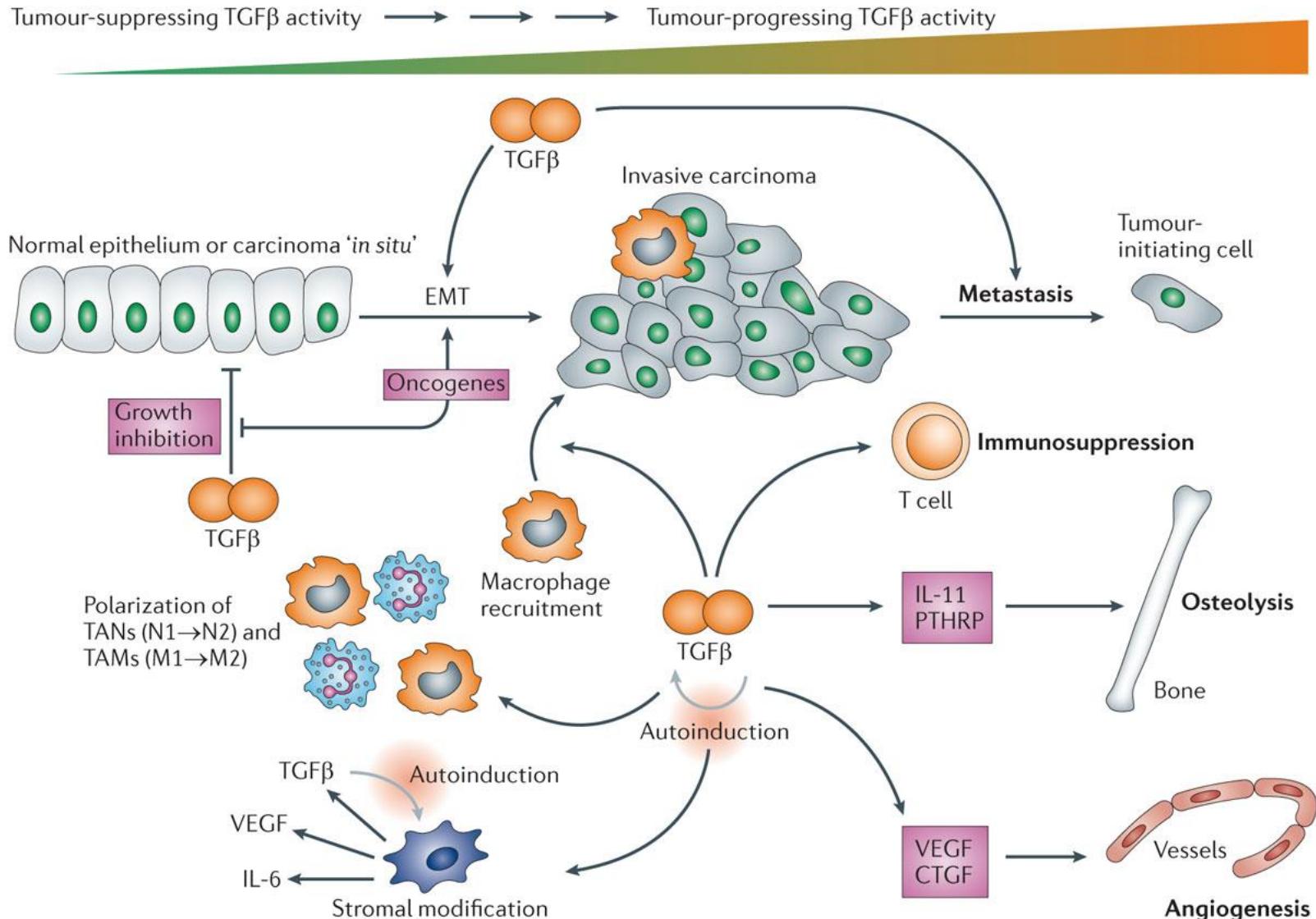
IL-10



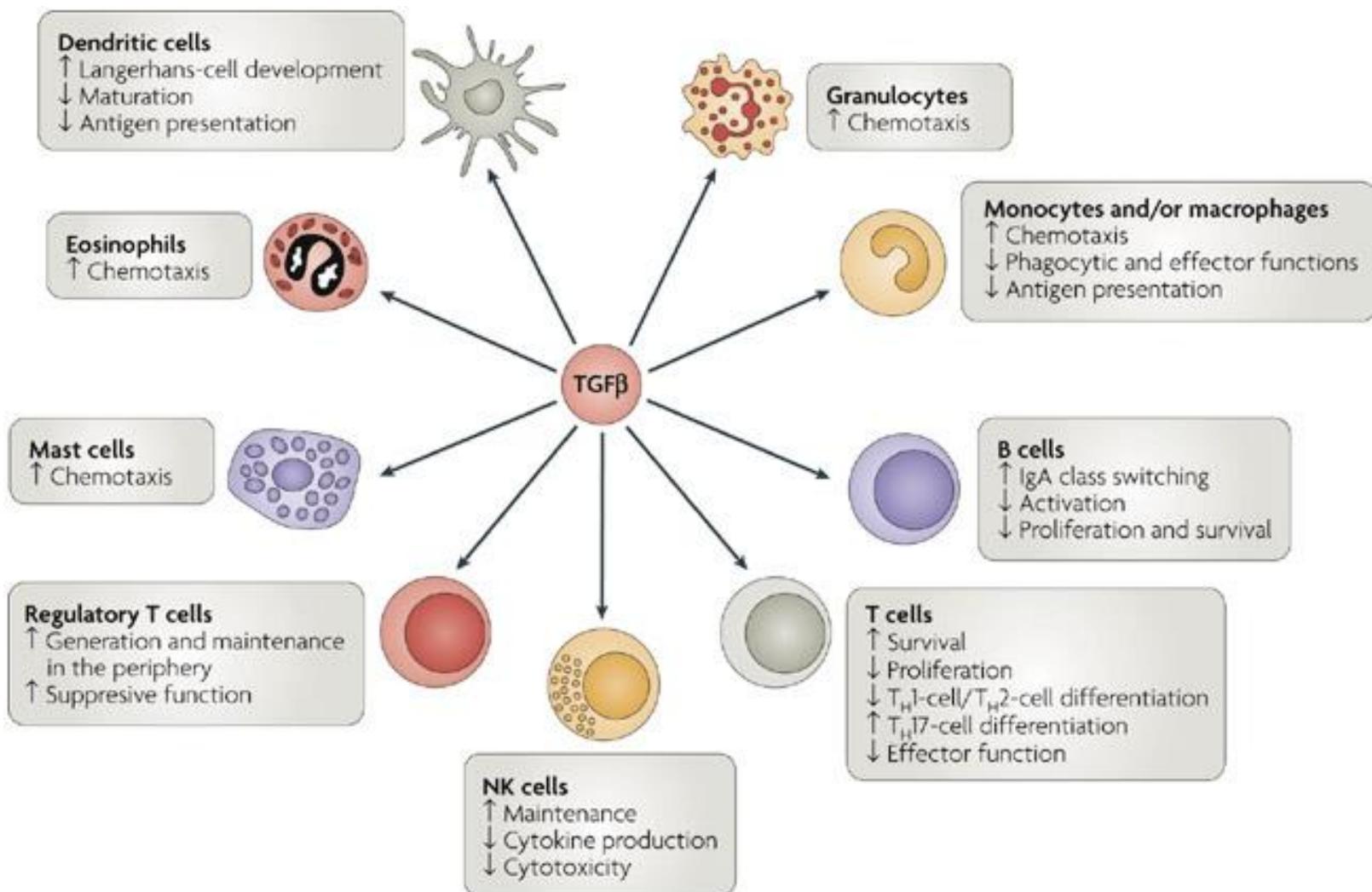
IL-10



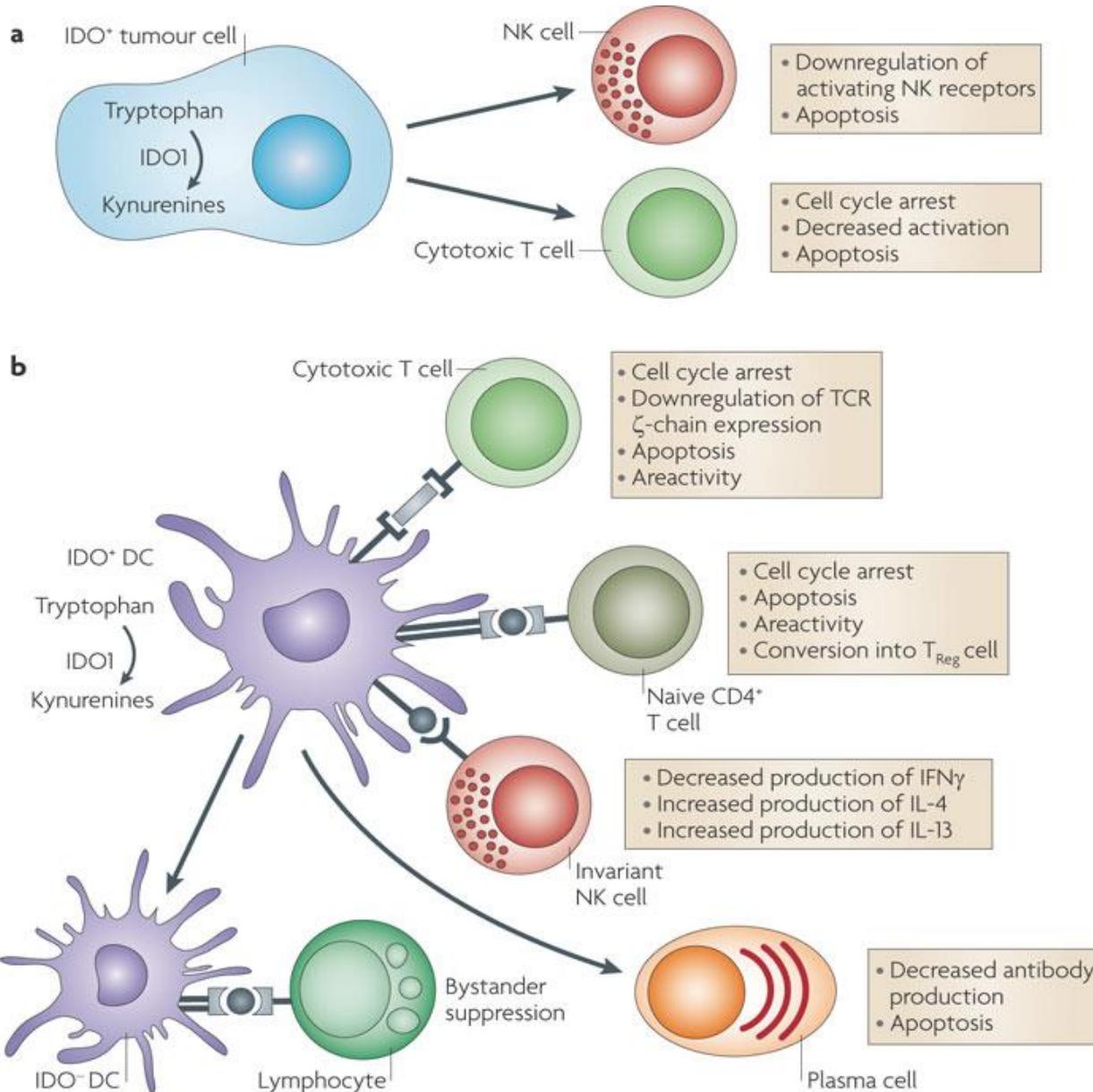
TGF β



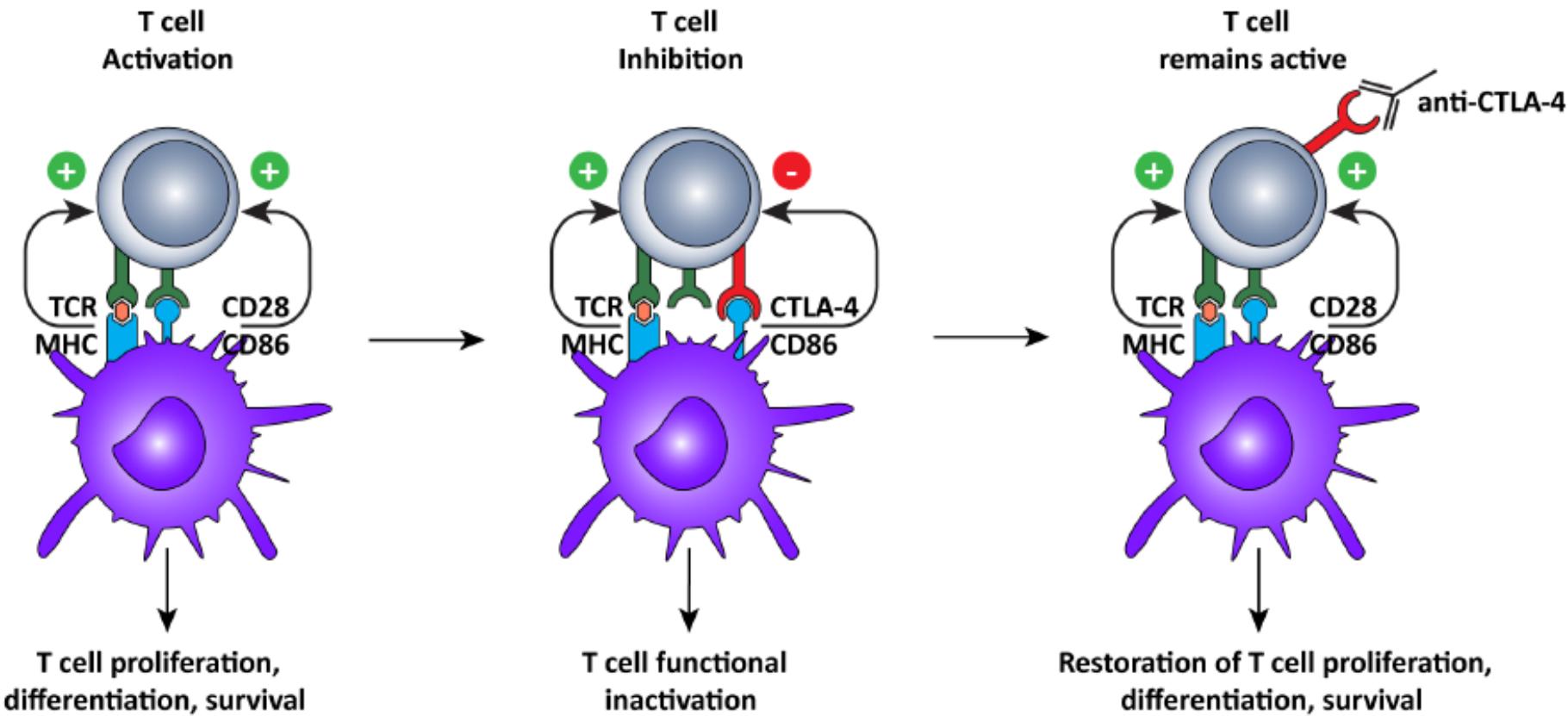
TGF β



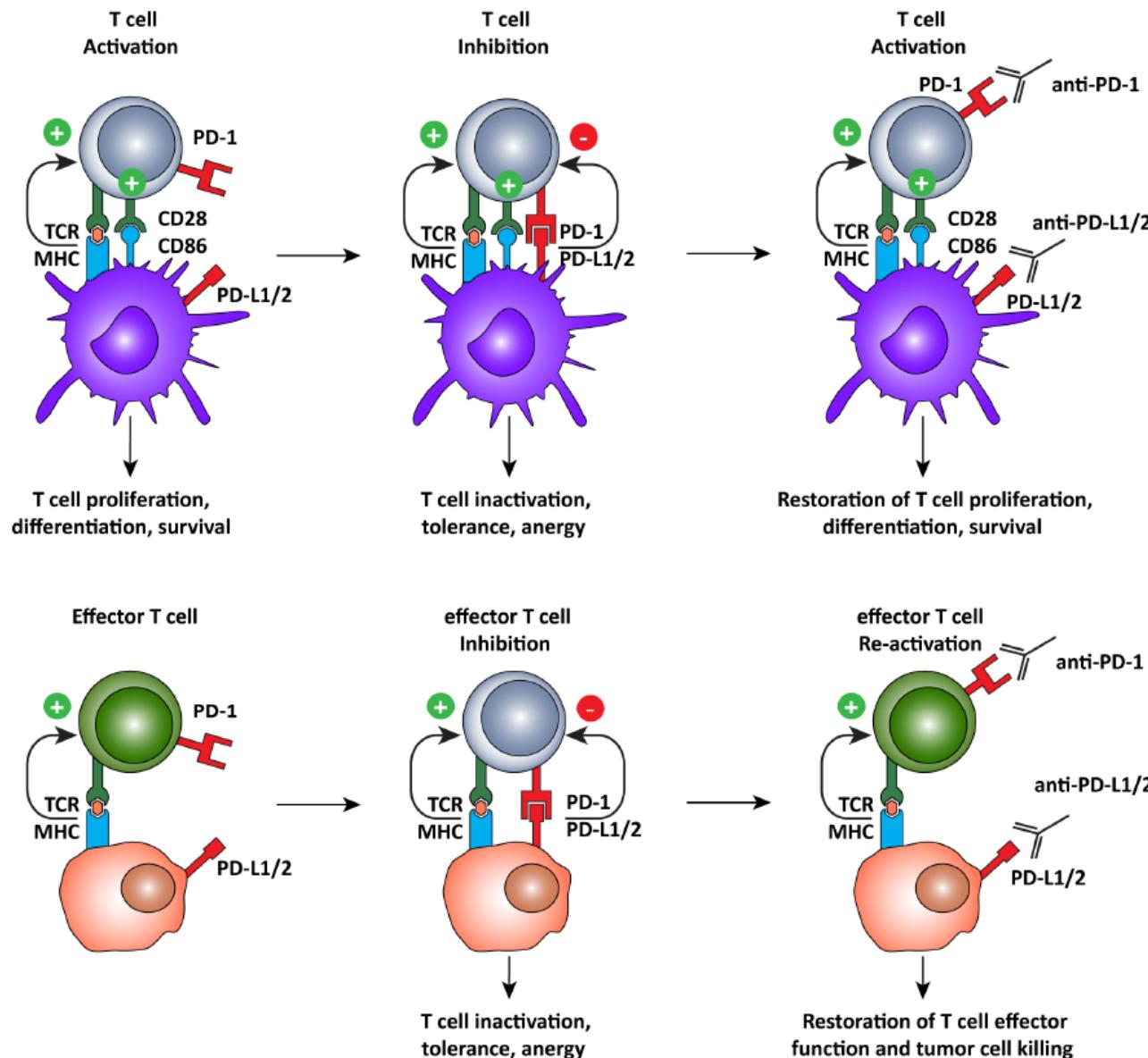
Indoleamine-2,3-dioxygenase (IDO)



CTLA-4



PD-1



Conclusions

- Tumor evasion is an emerging hallmark of cancer.
- Tumor variants become invisible to the immune system.
- Tumor and immune cells in the tumor stroma suppress antitumor immune response.

Myeloid derived suppressor cells

