Curso de Farmácia
Disciplina 0420136 – Integrado MIP (Noturno)

Imunidade aos Microrganismos - Dengue

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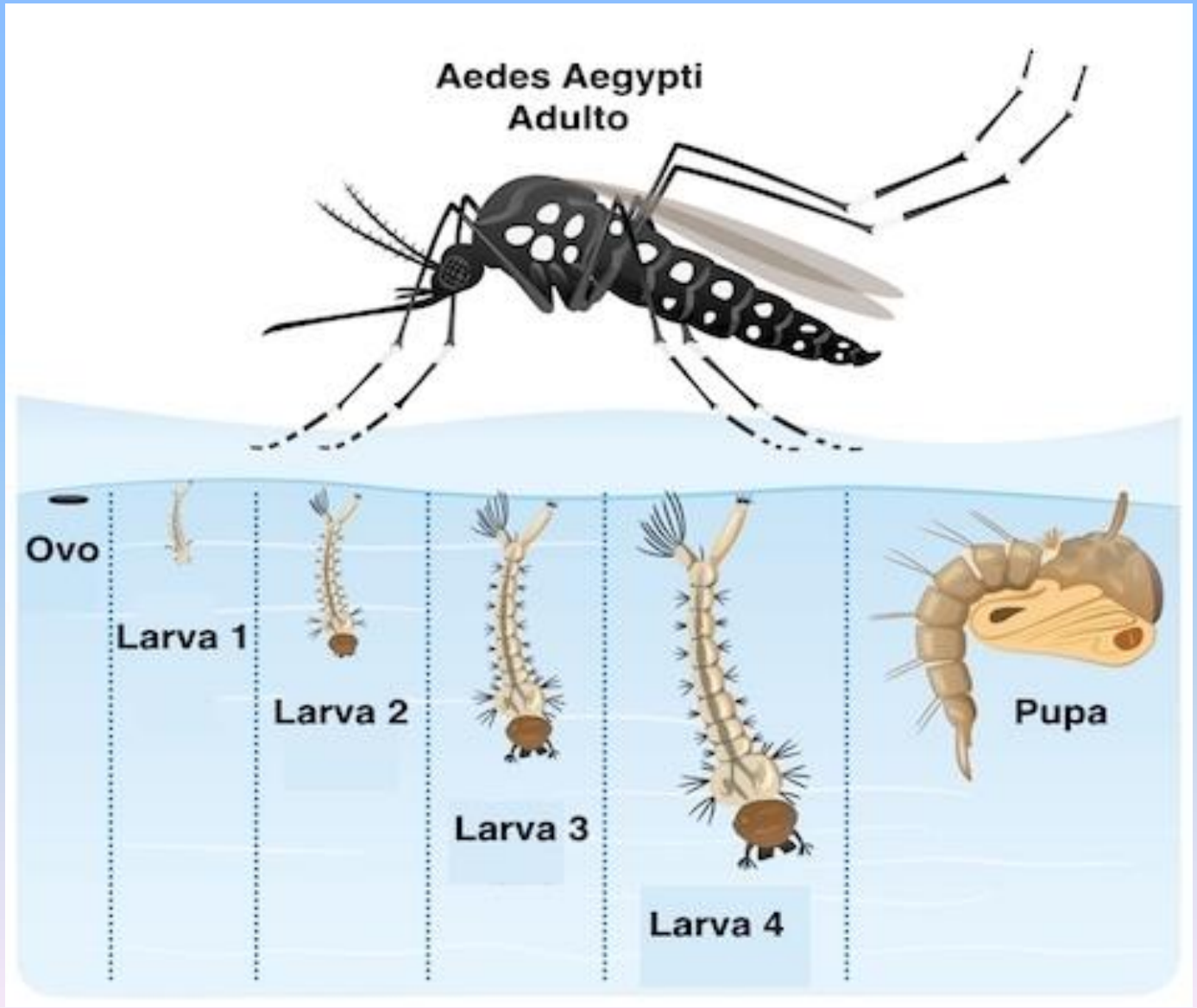
Tópicos Essenciais da Aula

1. **Discutir os mecanismos efetores da imunidade contra o virus da Dengue**

Vetores da Dengue:
Aedes aegypti e Aedes albopictus

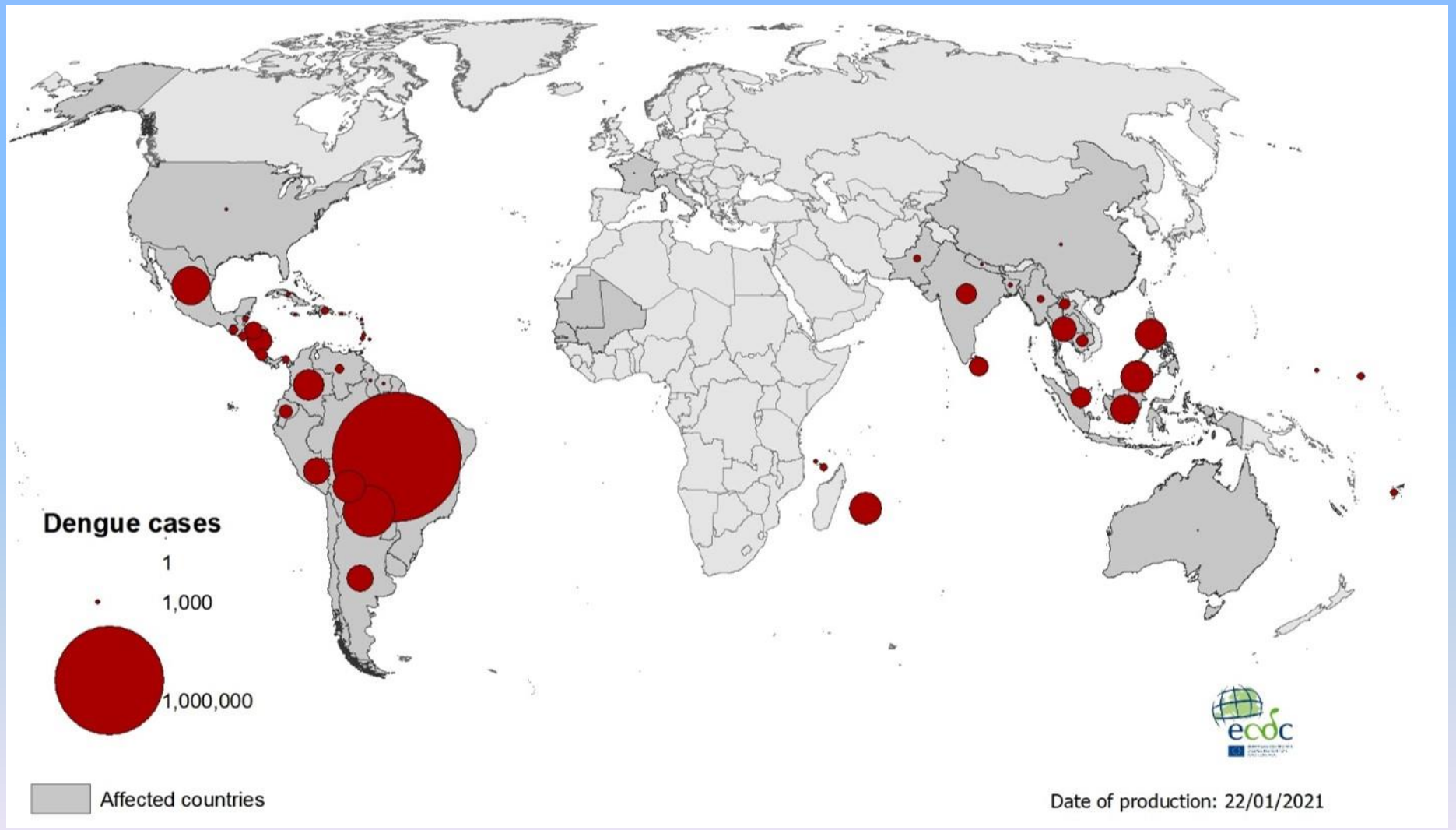
http://www.planetainvertebrados.com.br/index.asp?pagina=artigos_ver&id=119

Ciclo de Vida do Aedes aegypti



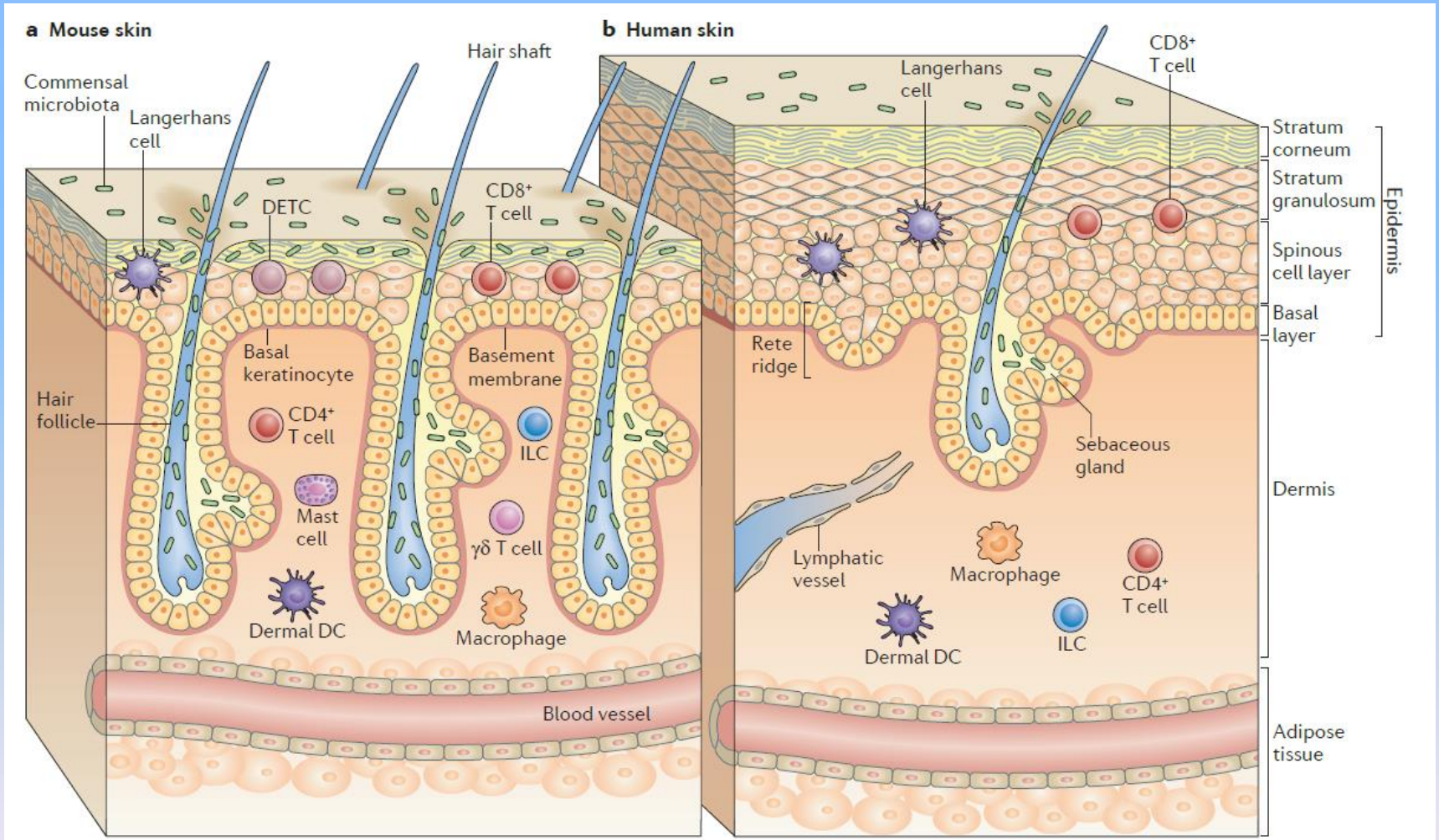
https://www.tuasaude.com/ciclo-de-vida-do-aedes-aegypti/

Distribuição Geográfica dos Casos de Dengue (2020)



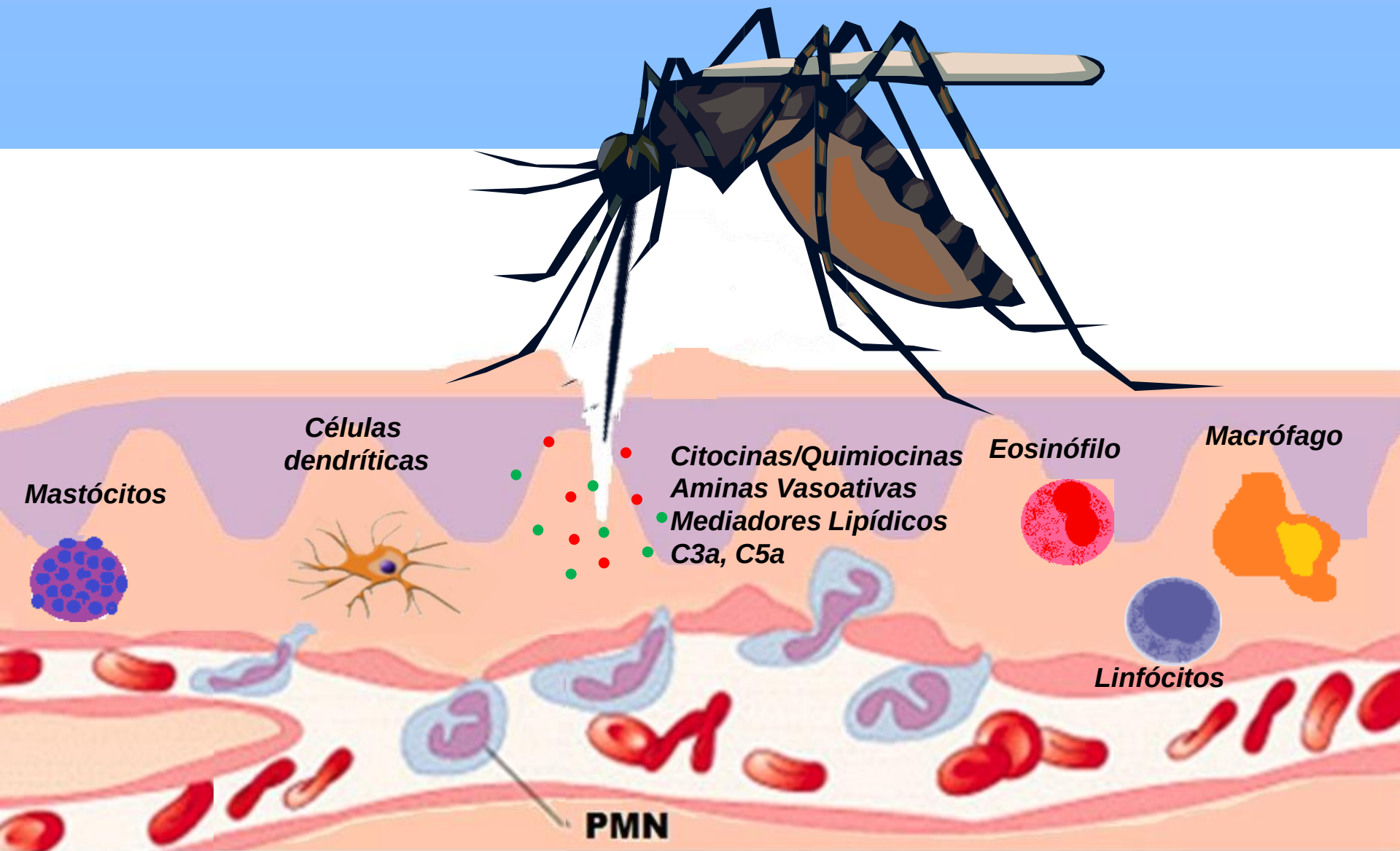
https://www.ecdc.europa.eu/en/publications-data/geographical-distribution-dengue-cases-reported-worldwide-2020

Sistema Imune Cutâneo

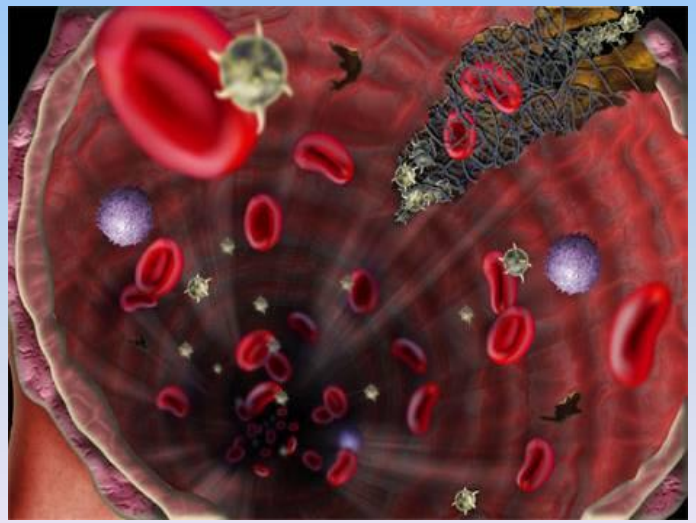


Pasparakis et al., Nat. Rev. Immunol., 14:289-301, 2014.

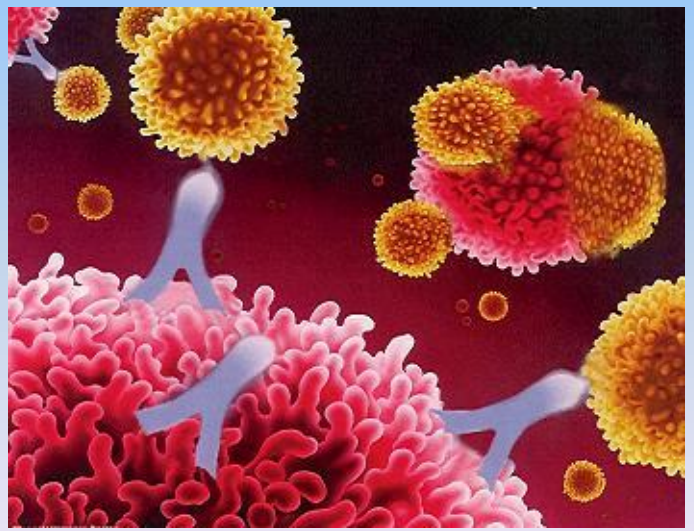
Pele: Células Residentes, Mediadores Inflamatórios e Células Inflamatórias



Desafios à Hematofagia



Sistema Vascular

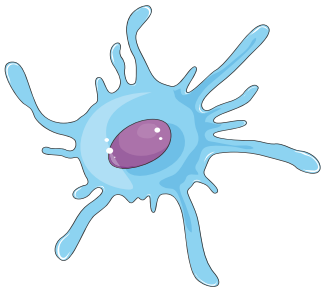


Sistema Imunológico

Fonte: várias.

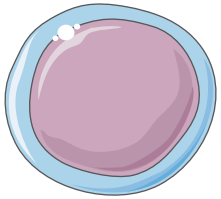
Efeitos da Saliva do Aedes aegypti em Células do Sistema Imunológico

Extrato Glândula Salivar (EGS)



Células Dendríticas
= Diferenciação
= Maturação
= Função

BIZZARRO et al., 2013



Viabilide de Linfócitos T e B
↓↓ Naïve
↓ Ativados
= Memória

BIZZARRO et al., 2013

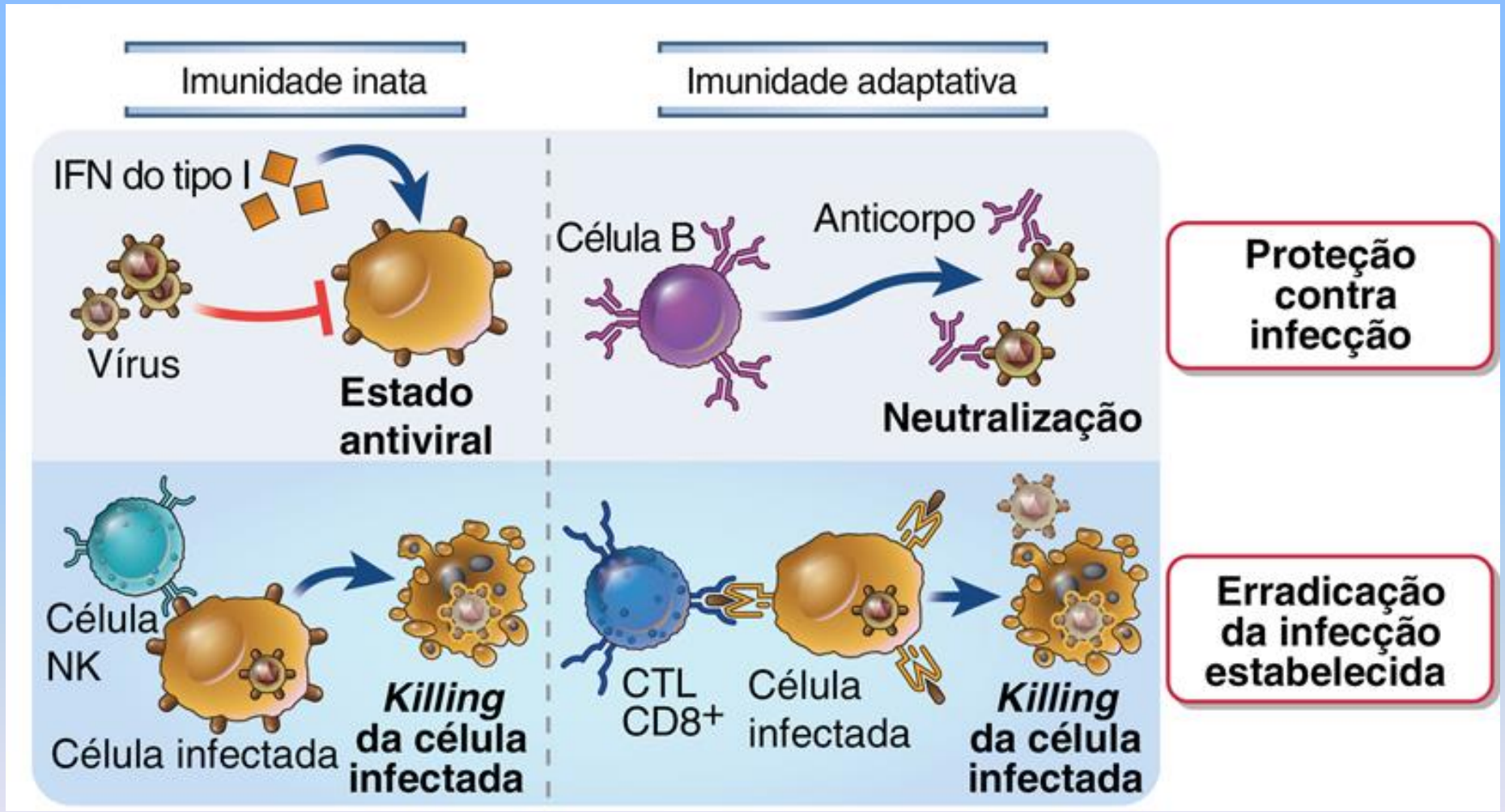
↓ NO, IL-6, IL-12
iNOS, NF-κB

↑ IL-10

↓ M1
= M2

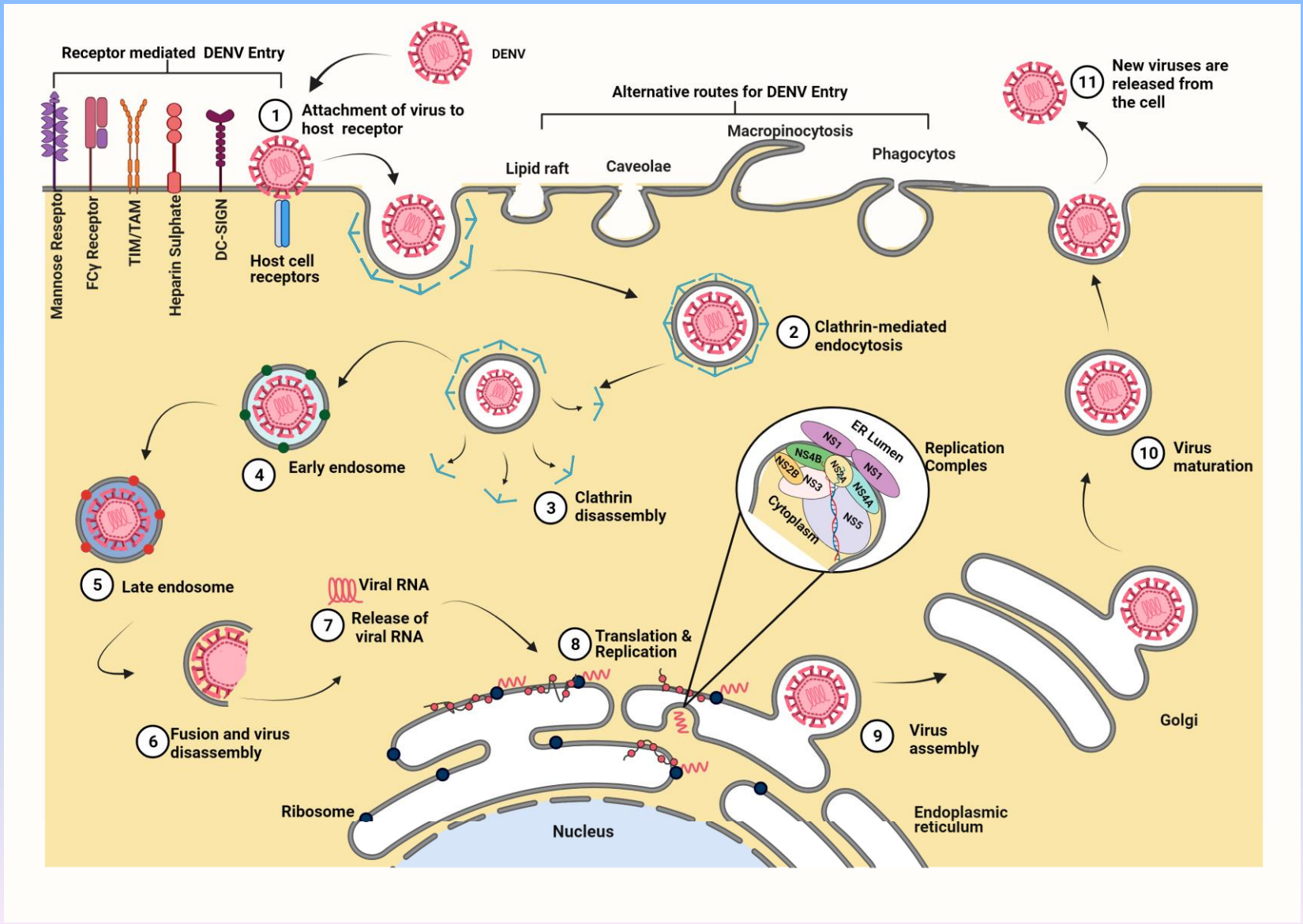
BARROS et al., 2019

Imunidade aos Vírus: Resumo



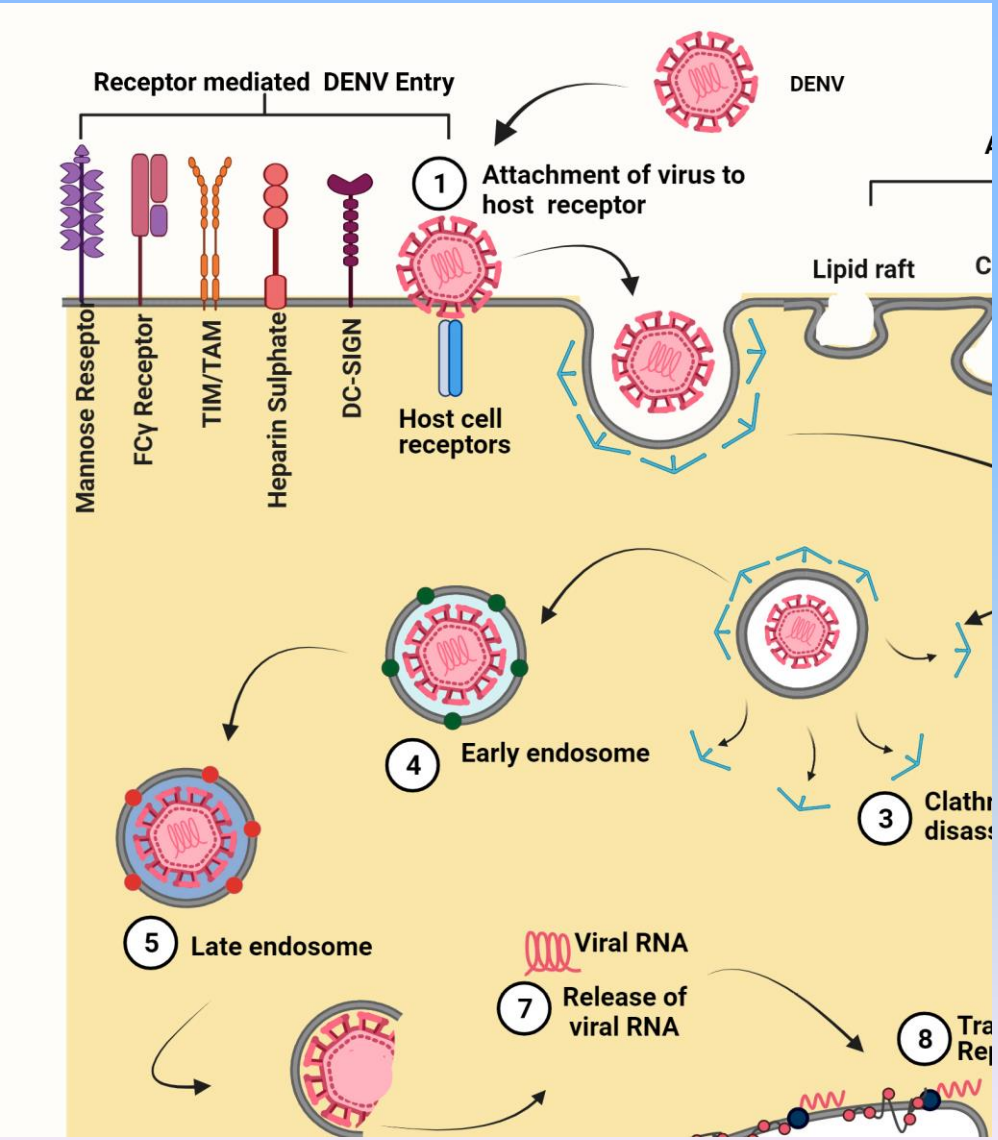
Abbas, Lichtman, Pillai, 9ª Edição, 2019.

Entrada do Vírus da Dengue nas Células



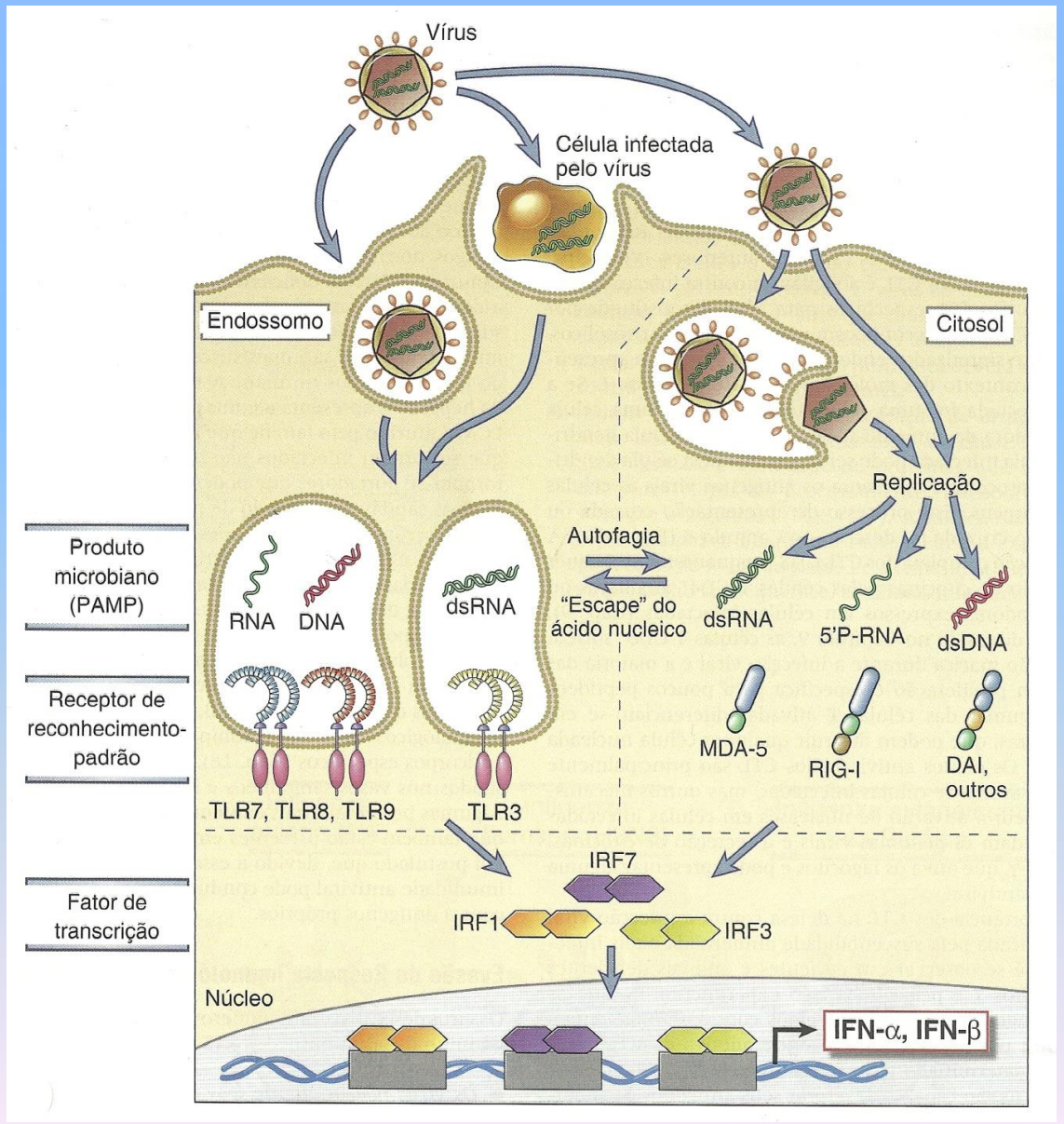
Nanaware et al., Viruses, 13(10):1967, 2021.

Entrada do Vírus da Dengue nas Células



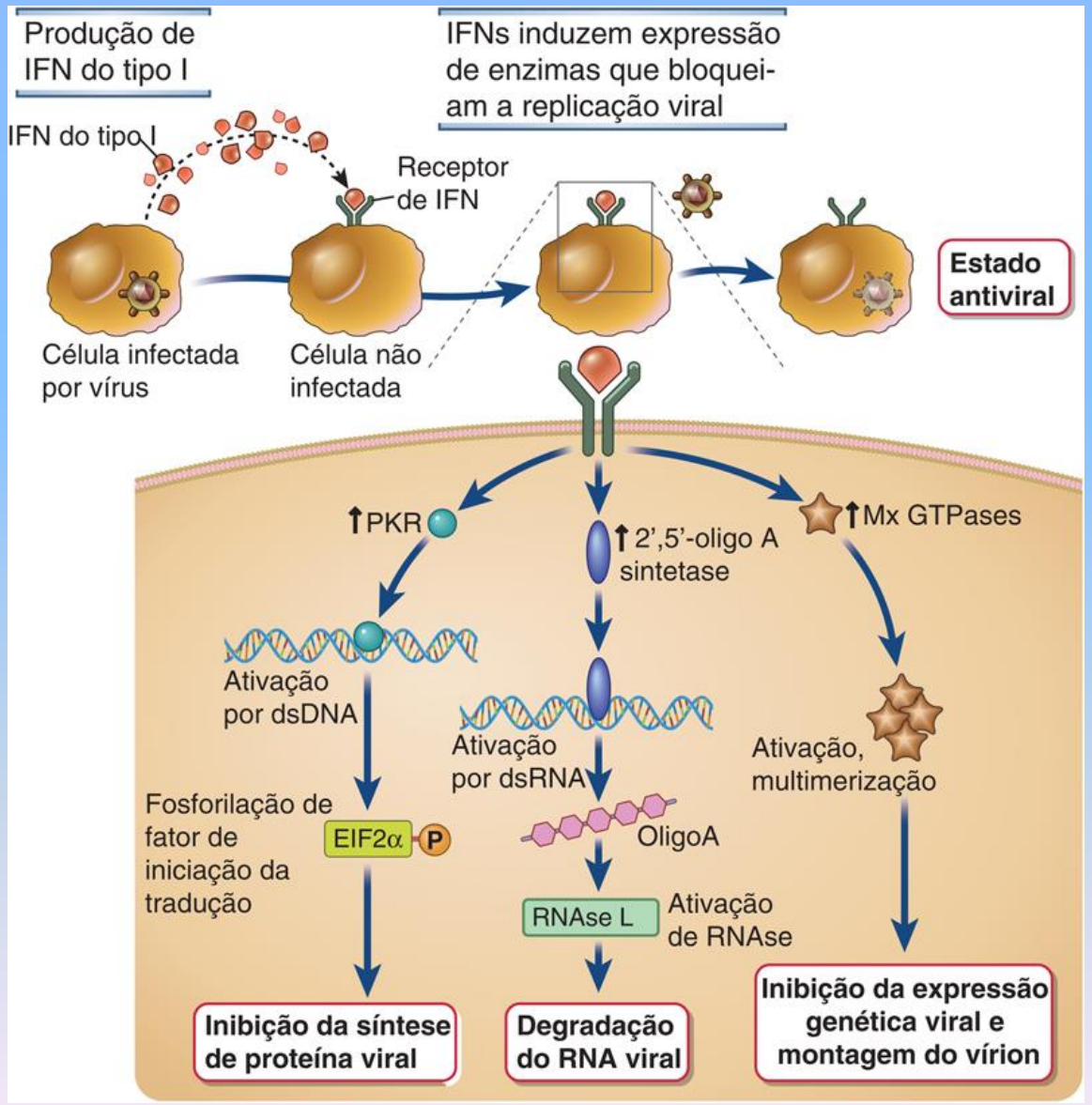
Nanaware et al., Viruses, 13(10):1967, 2021.

Reconhecimento Viral pela Imunidade Inata



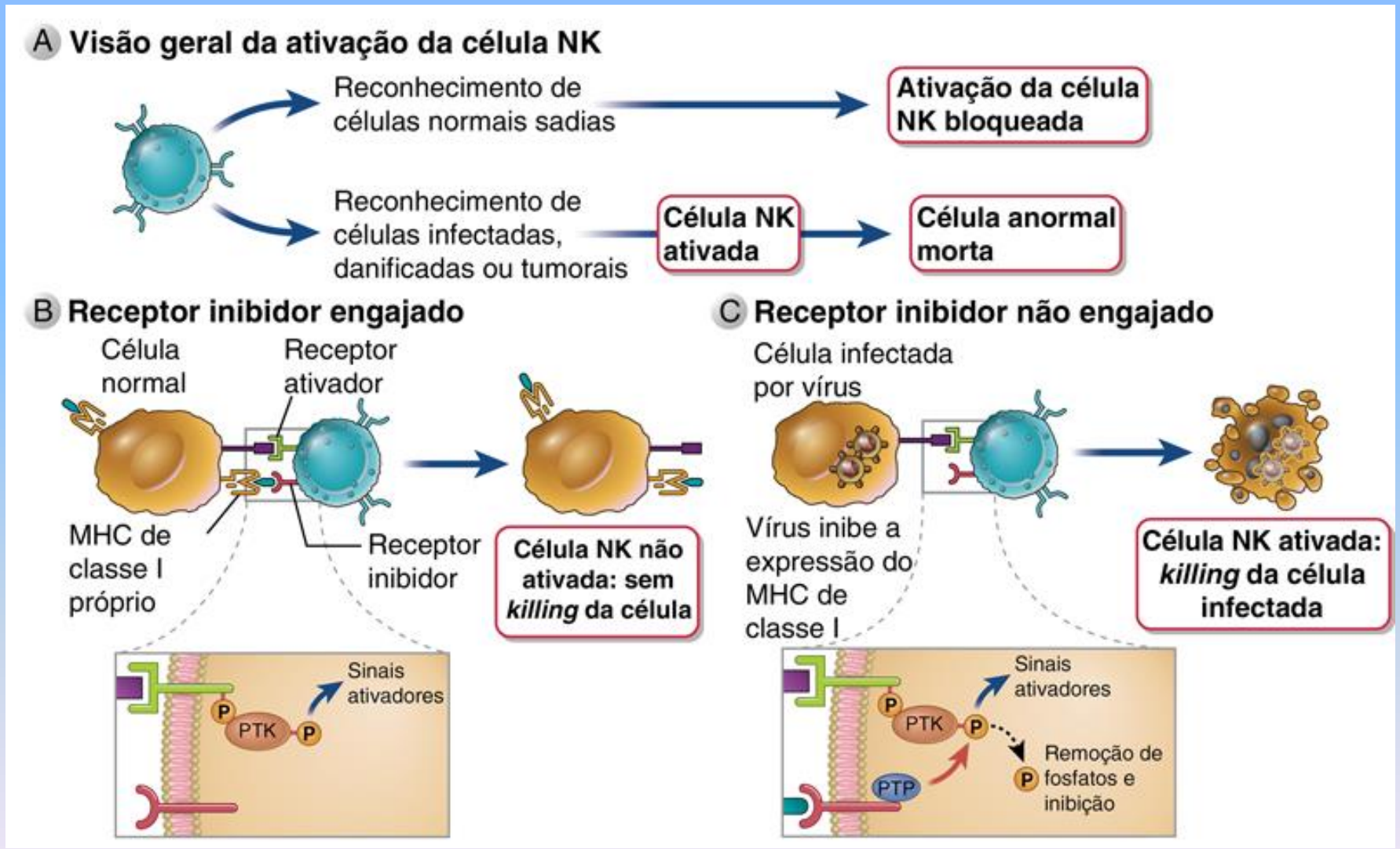
Abbas, Lichtman, Pillai, 7a. Edição, 2012.

Imunidade Inata contra Vírus: IFN do tipo I



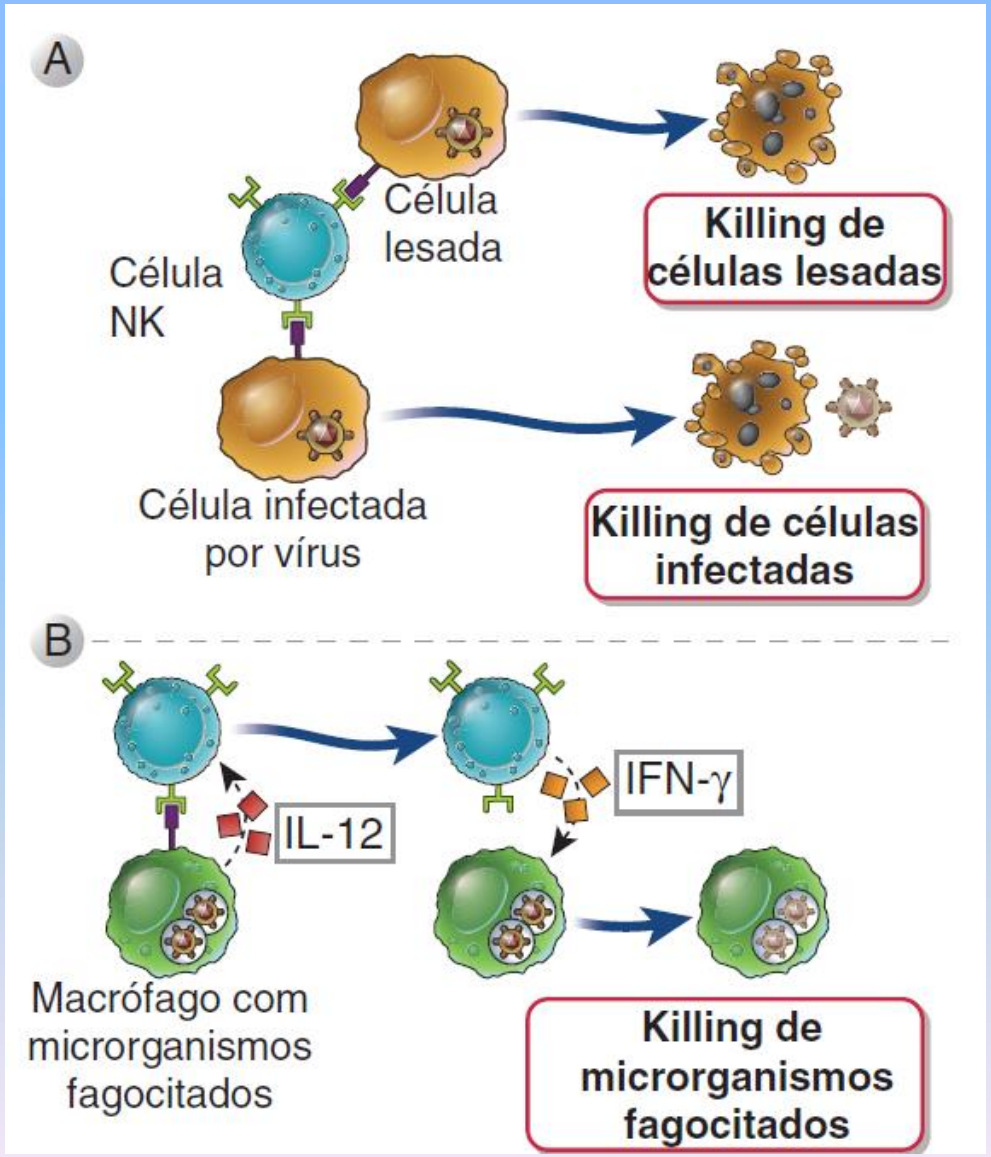
Abbas, Lichtman, Pillai, 9a. Edição, 2019.

Imunidade Inata contra Vírus: Células NK



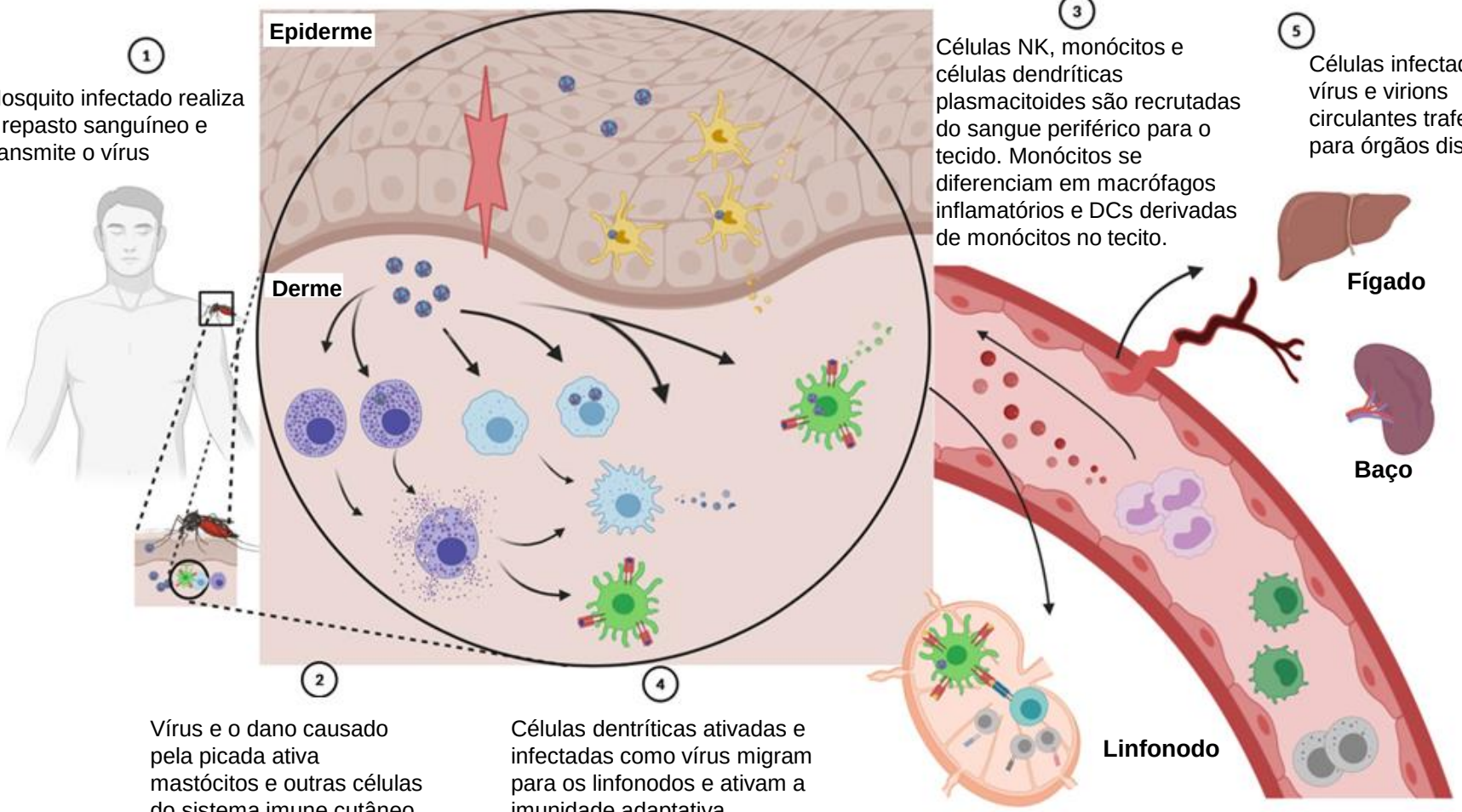
Abbas, Lichtman, Pillai, 7a. Edição, 2012.

Imunidade Inata contra Vírus: Células NK



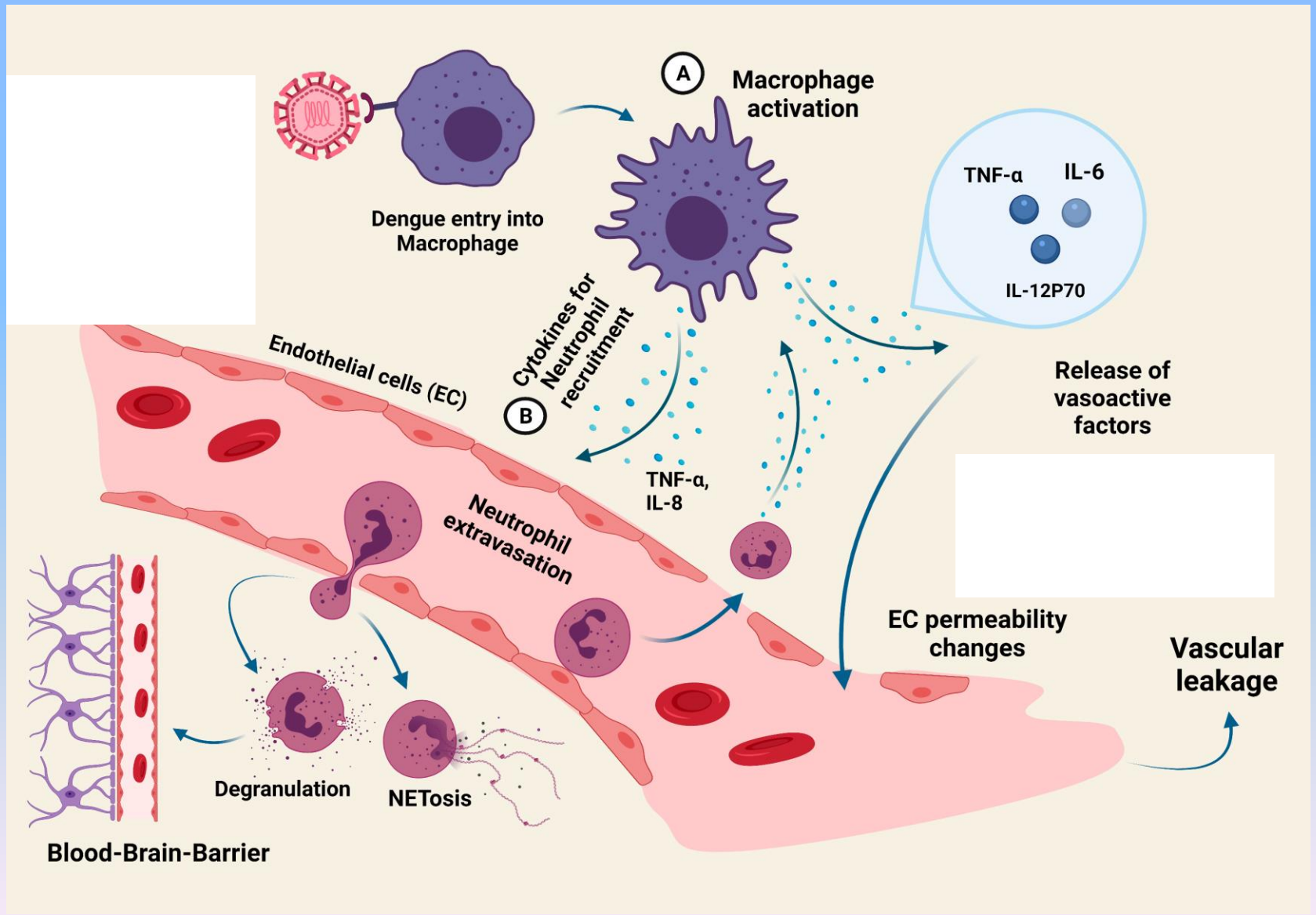
Abbas, Lichtman, Pillai, 9ª Edição, 2019.

Eventos Imunológicos da Infecção por Vírus da Dengue



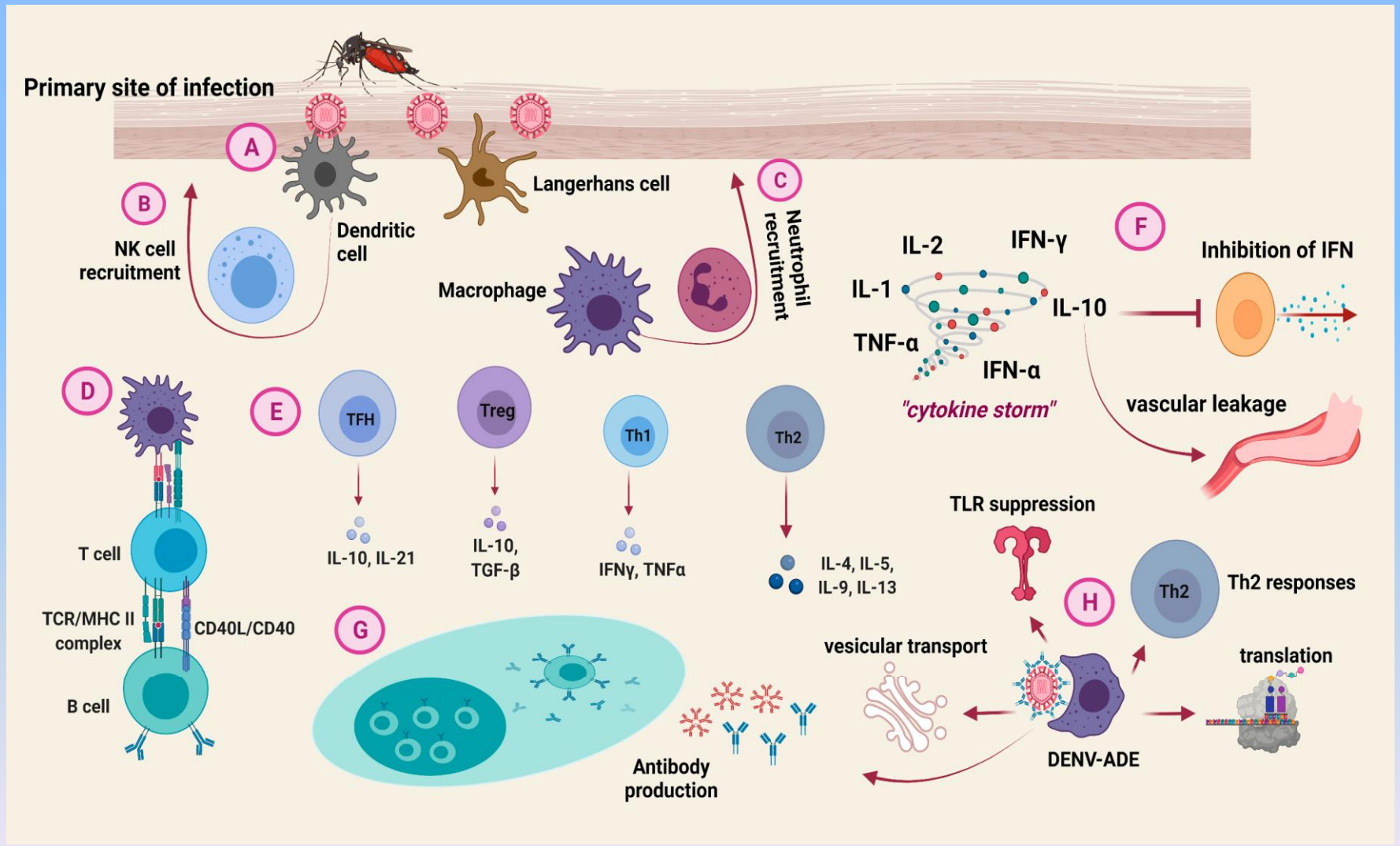
Adaptado de: King et al., Front Cell Infect Microbiol., 10:574417, 2020.

Resposta Inflamatória Durante a Infecção pelo Vírus da Dengue



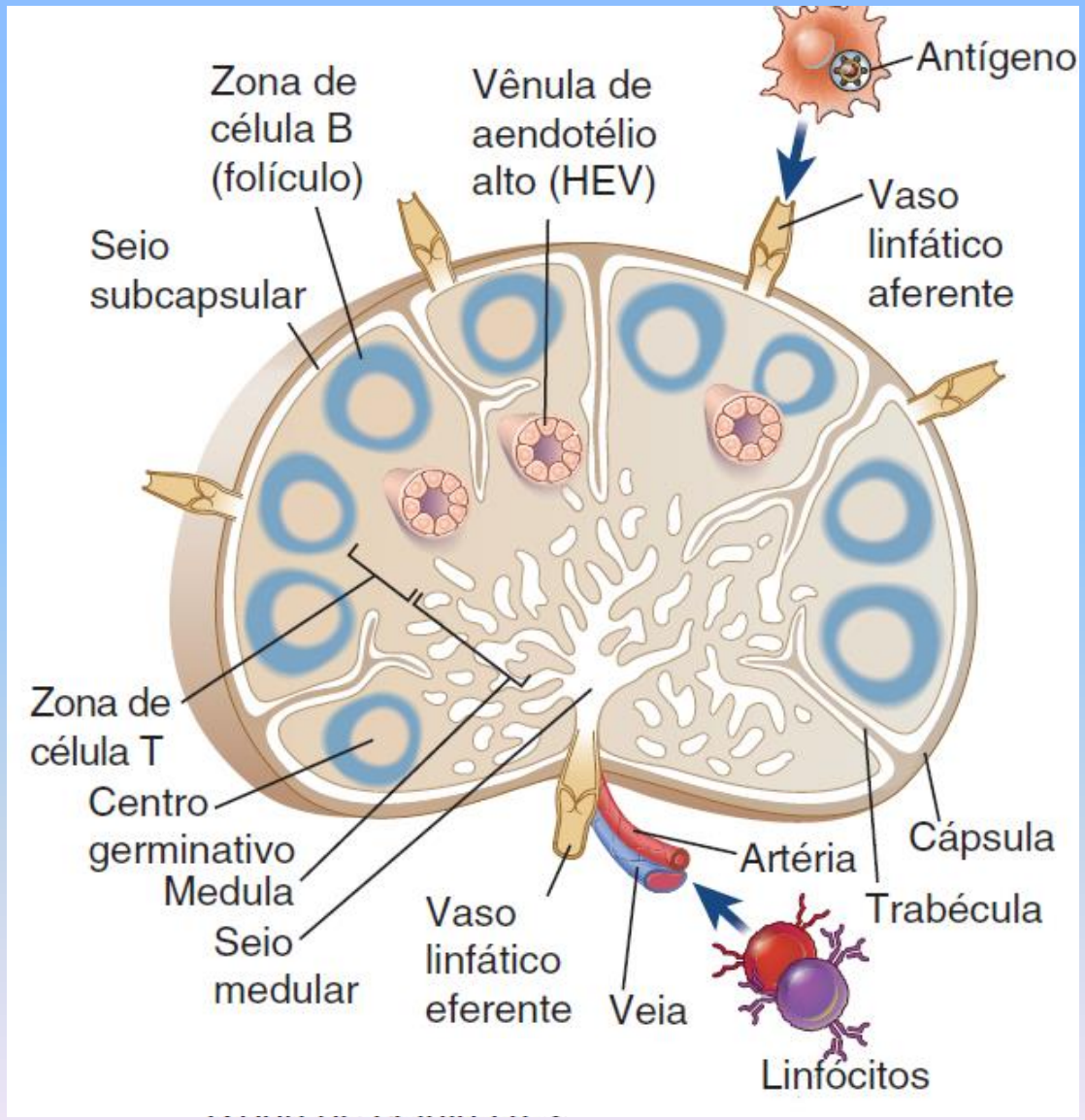
Nanaware et al., Viruses, 13(10):1967, 2021.

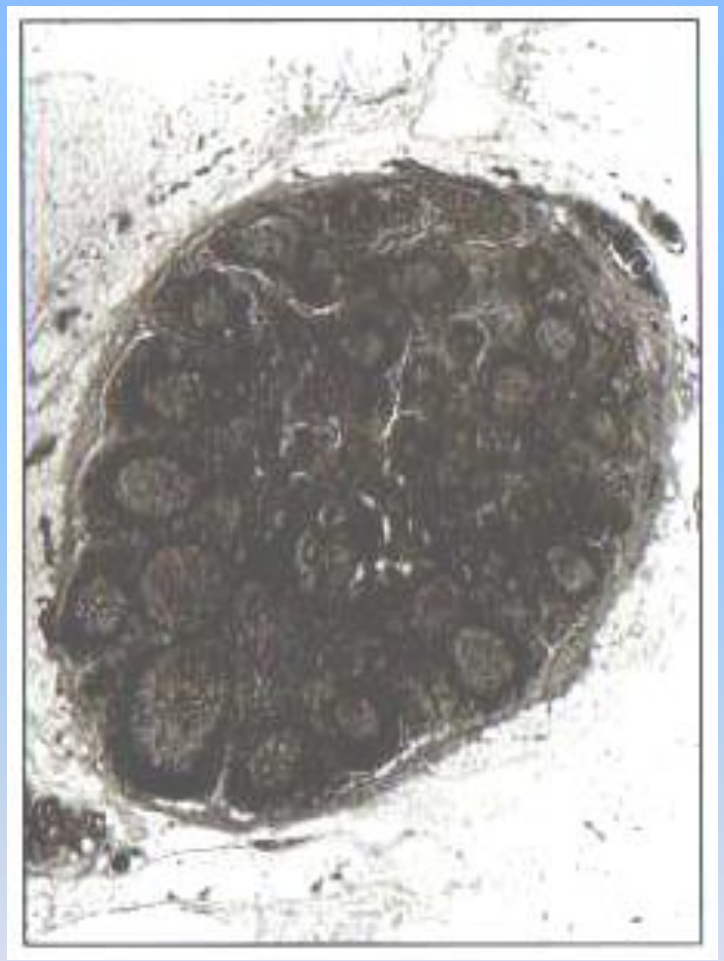
Resposta Imune Durante a Infecção pelo Vírus da Dengue



Nanaware et al., Viruses, 13(10):1967, 2021.

Linfonodos

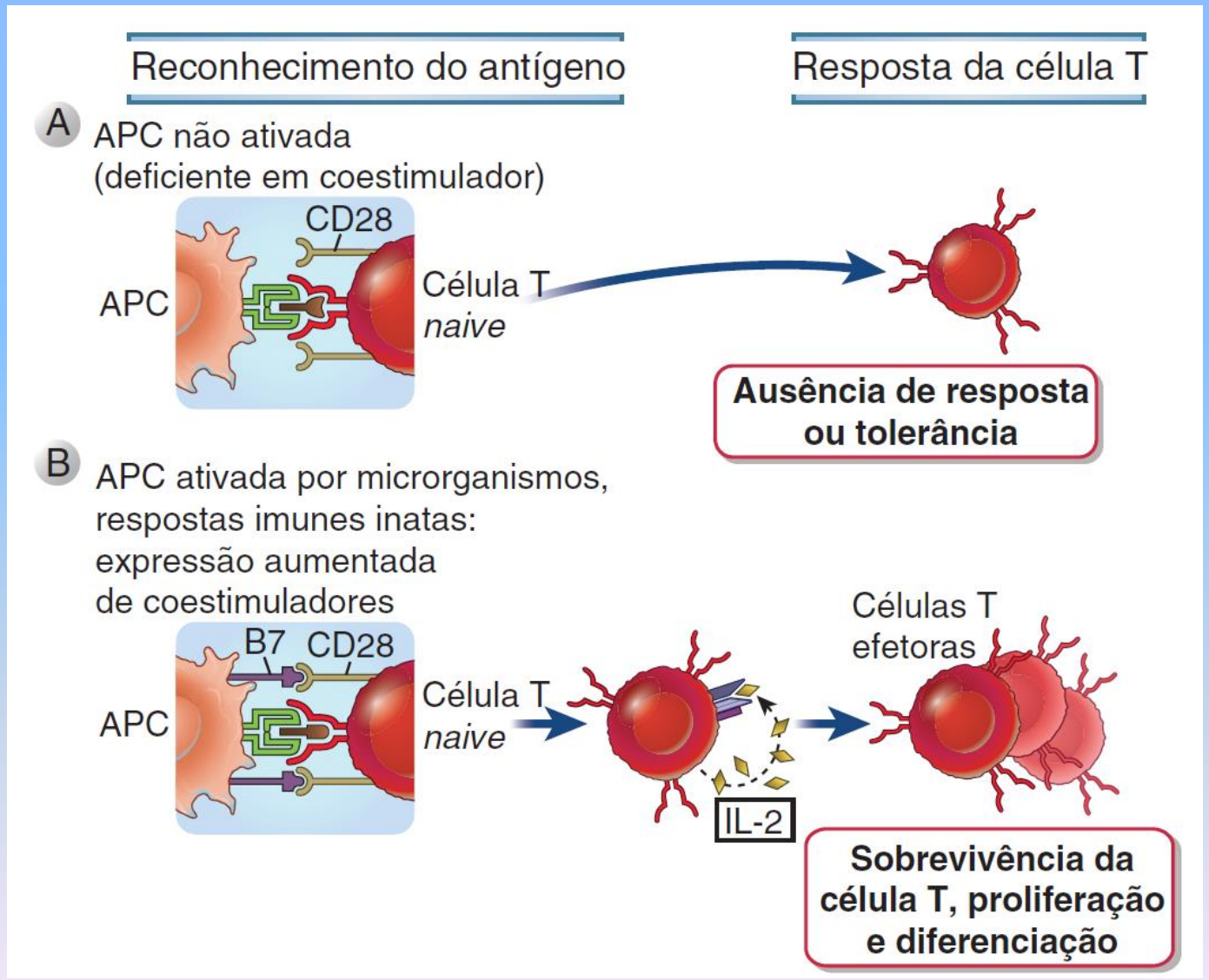




Abbas, Lichtman, Pillai, 6a. Edição, 2008.

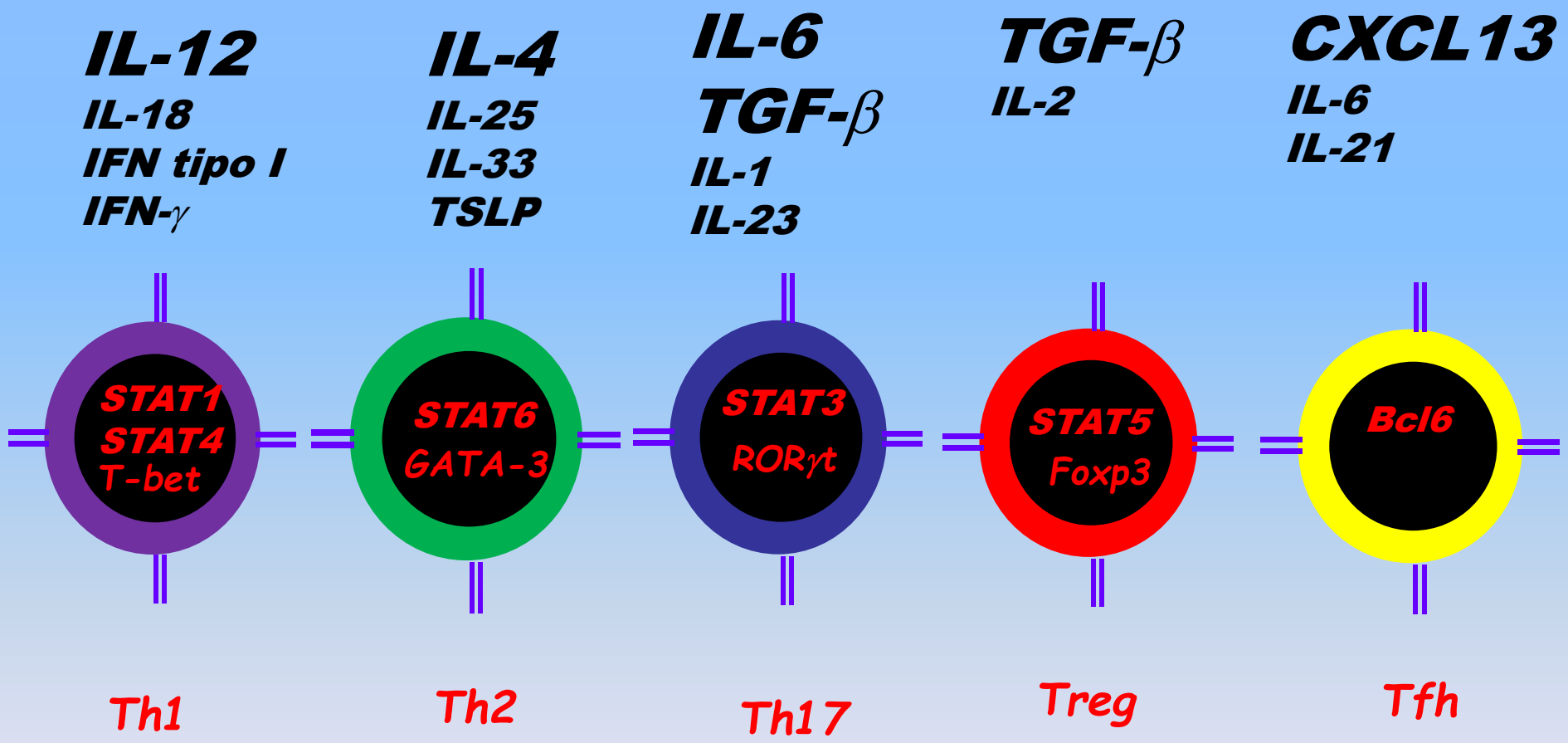
Abbas, Lichtman, Pillai, 9ª Edição, 2019.

Moléculas Co-Estimuladoras: 2º sinal

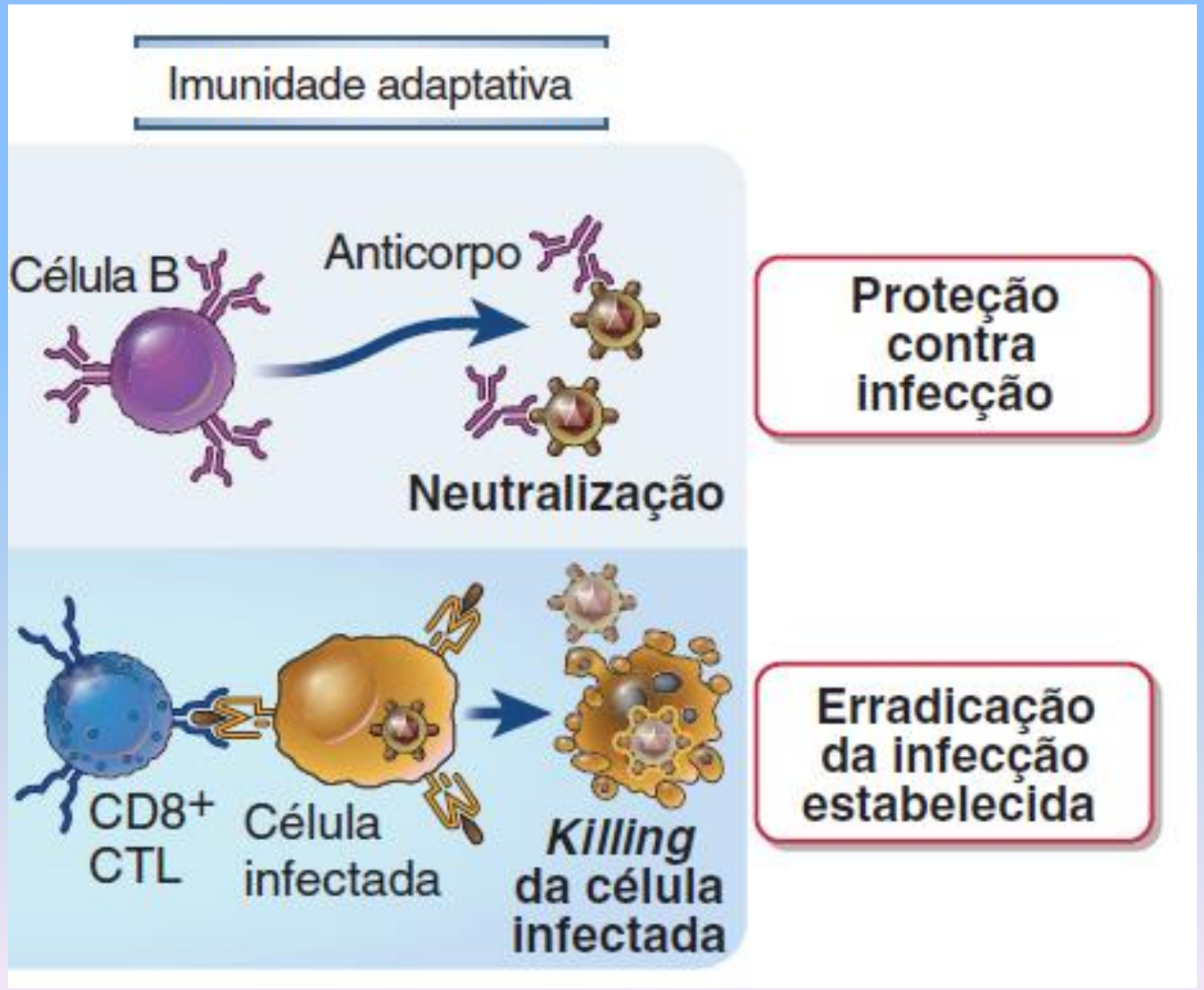


Abbas, Lichtman, Pillai, 9ª Edição, 2019.

Citocinas: "3 º sinal": diferenciação

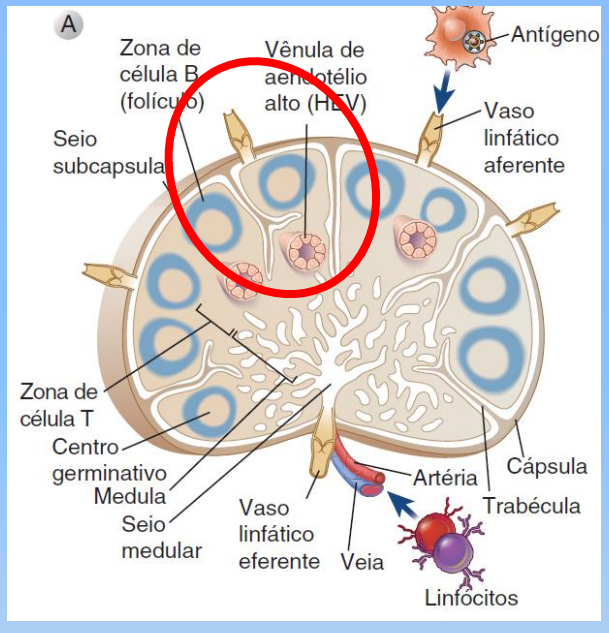


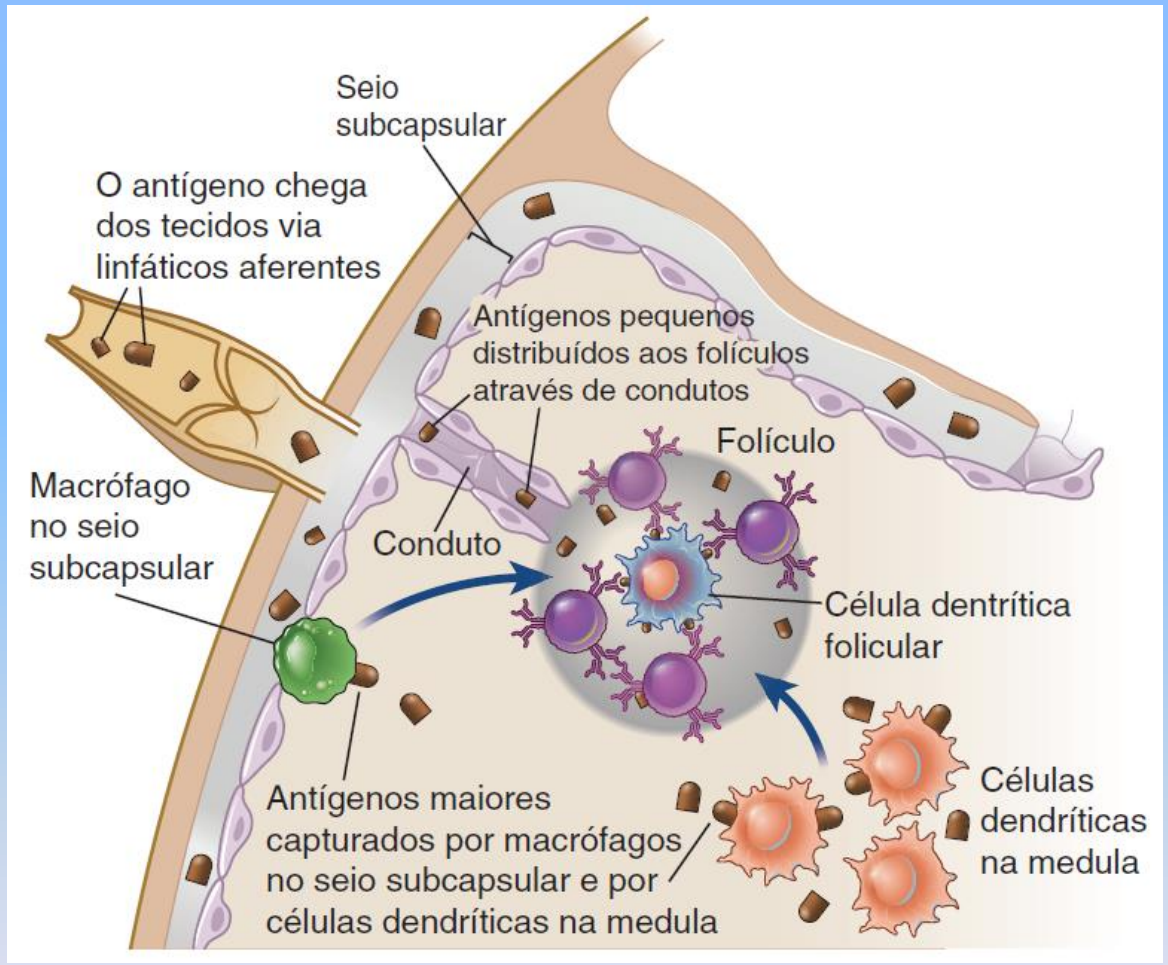
Imunidade Adaptativa contra Vírus: Anticorpos e Linfócitos T CD8+



Abbas, Lichtman, Pillai, 9a. Edição, 2019.

Vias de acesso do antígeno a células B foliculares

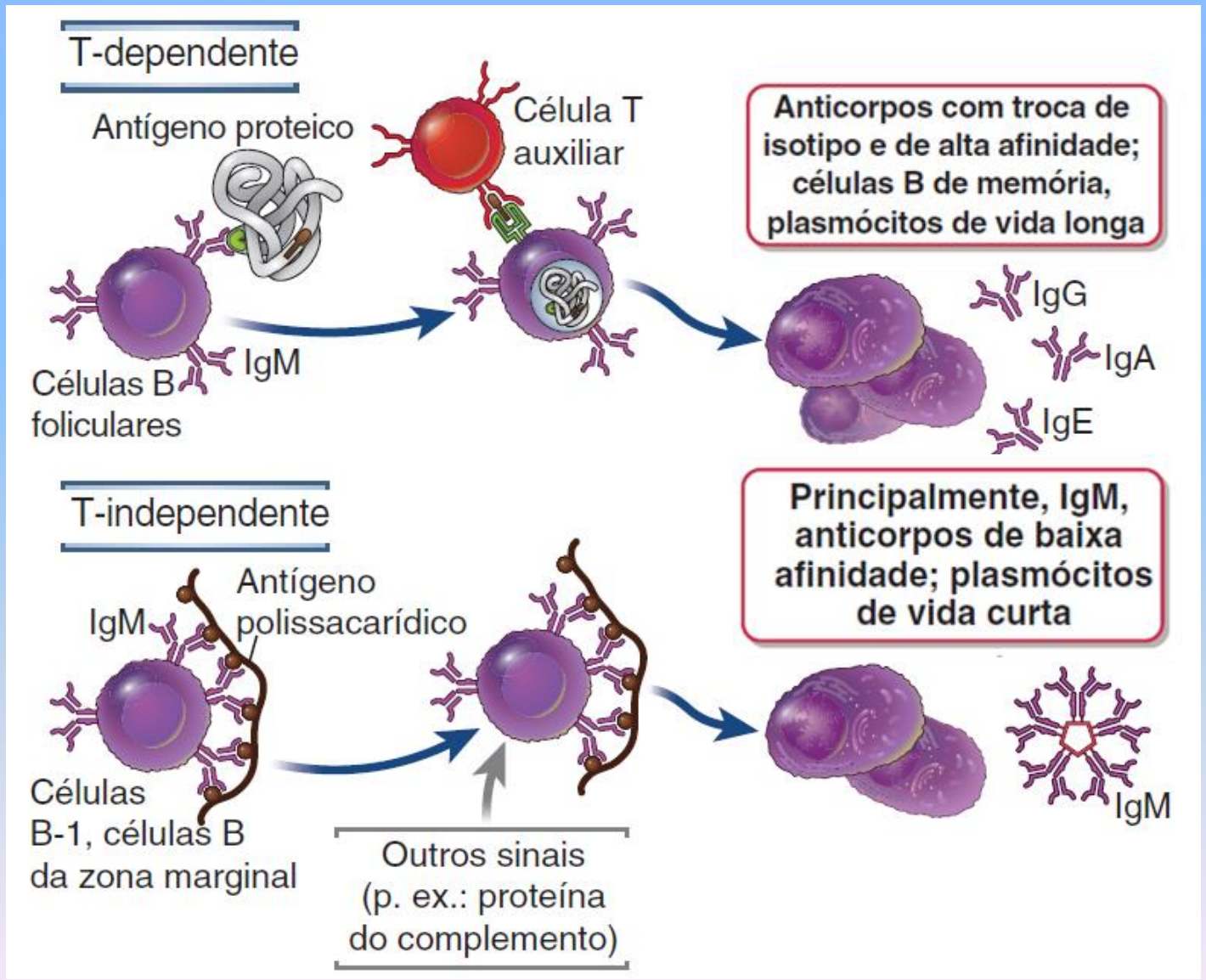




- ***Células dendríticas foliculares* e estroma folicular produzem CXCL13: liga CXCR5**
- ***Antígenos solúveis (menores que 70 kDa): alcançam folículos diretamente***
- ***Antígenos grandes ou microorganismos: capturados por outras células***

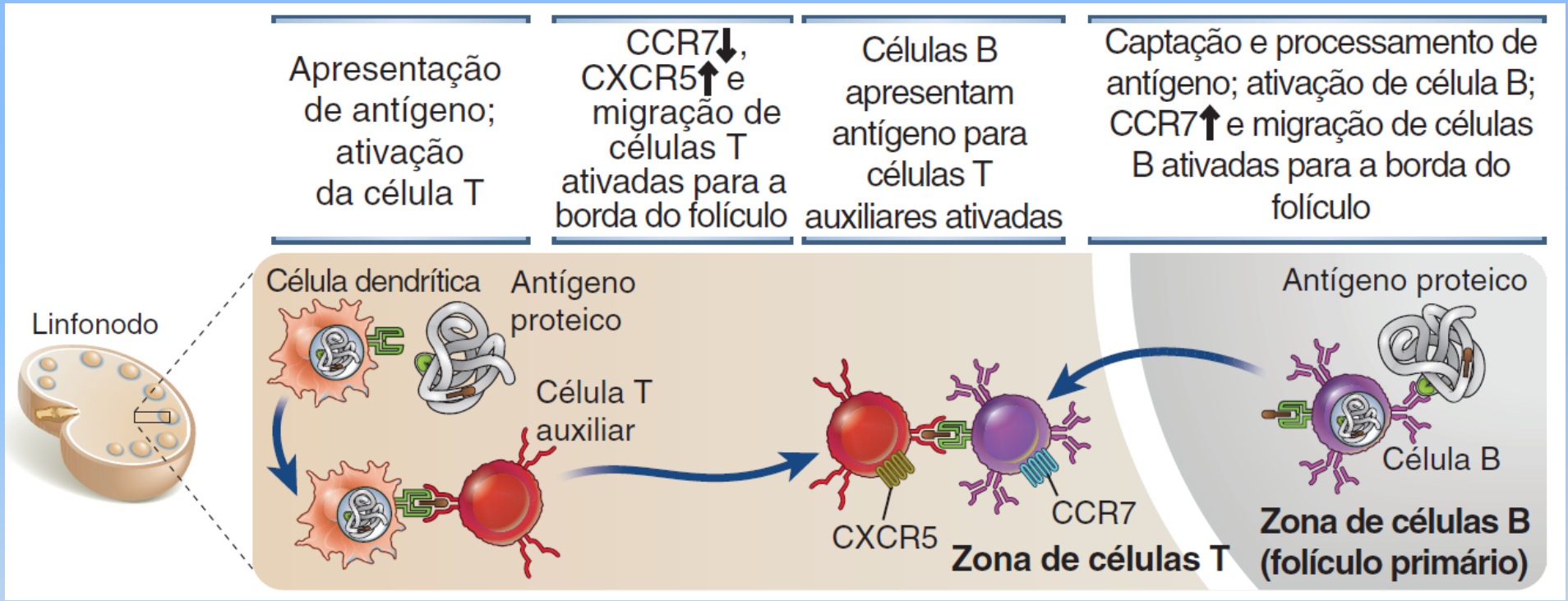
Abbas, Lichtman, Pillai, 9ª Edição, 2019.

Subpopulações de Linfócitos B são Ativados de Maneiras Diferentes



Abbas, Lichtman, Pillai, 9ª Edição, 2019.

Importância das Quimiocinas para as Interações B:T



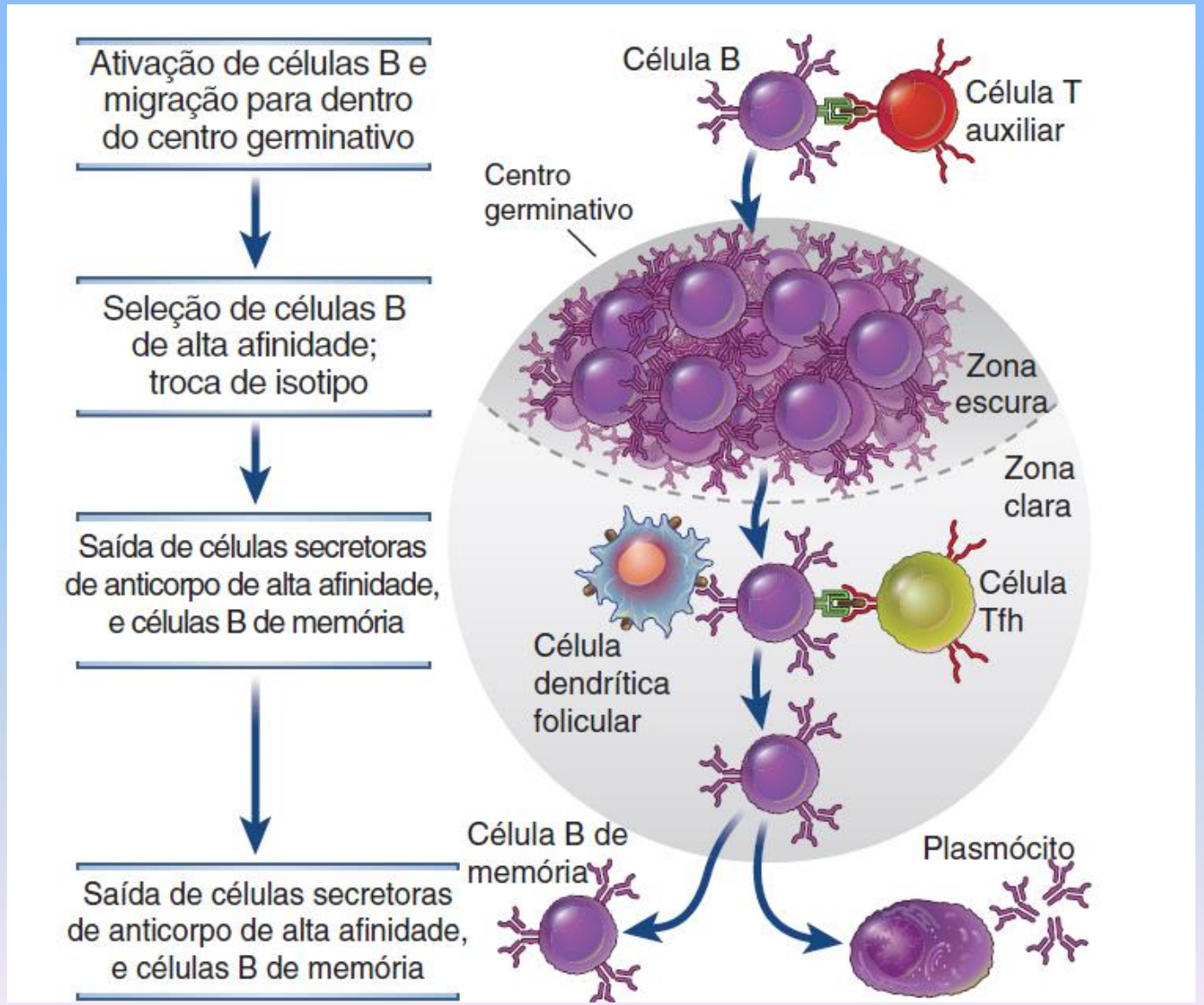
- ***CXCL13: liga CXCR5 (folículo)***

- ***CCL19 e CCL21: ligam CCR7 (região parafolicular/paracortical)***

https://www.youtube.com/watch?v=GZv6jpsBO1I

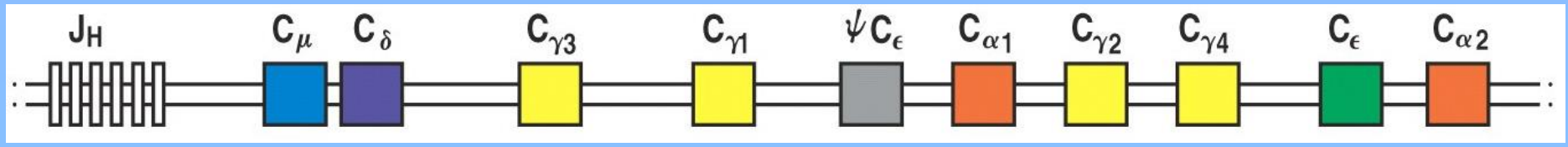
Abbas, Lichtman, Pillai, 9ª Edição, 2019.

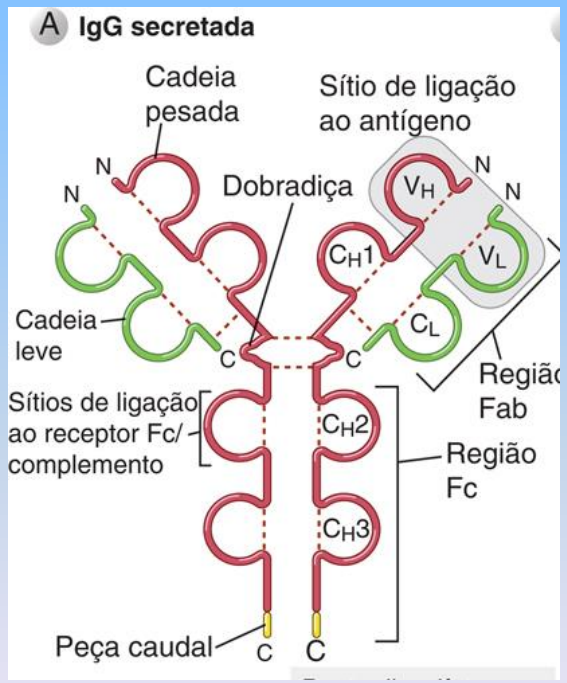
Reação de Centro Germinativo



Abbas, Lichtman, Pillai, 9ª Edição, 2019.

Troca de isotipo ("switch" de classe)





Abbas, Lichtman, Pillai, 9ª Edição, 2019.

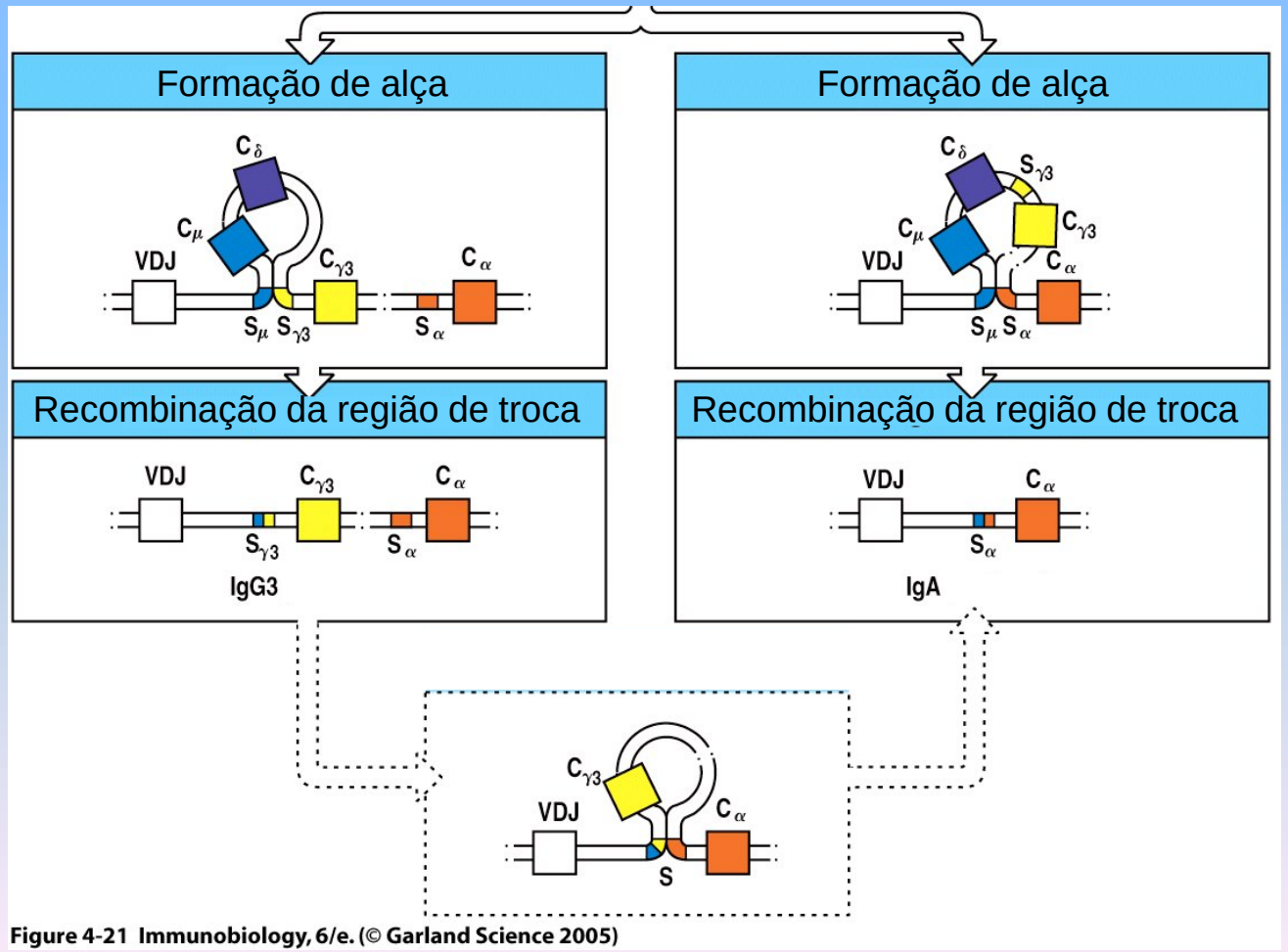
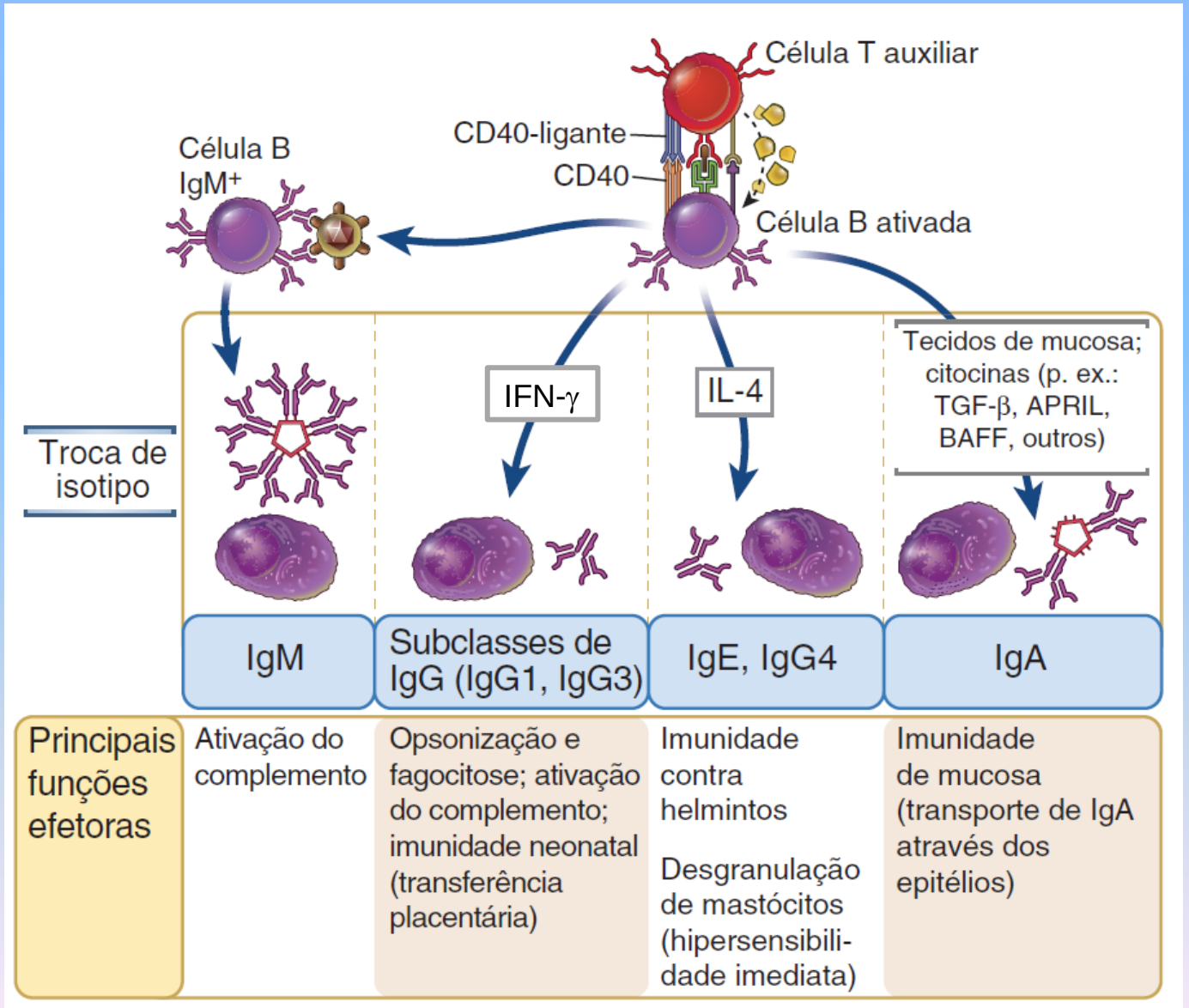


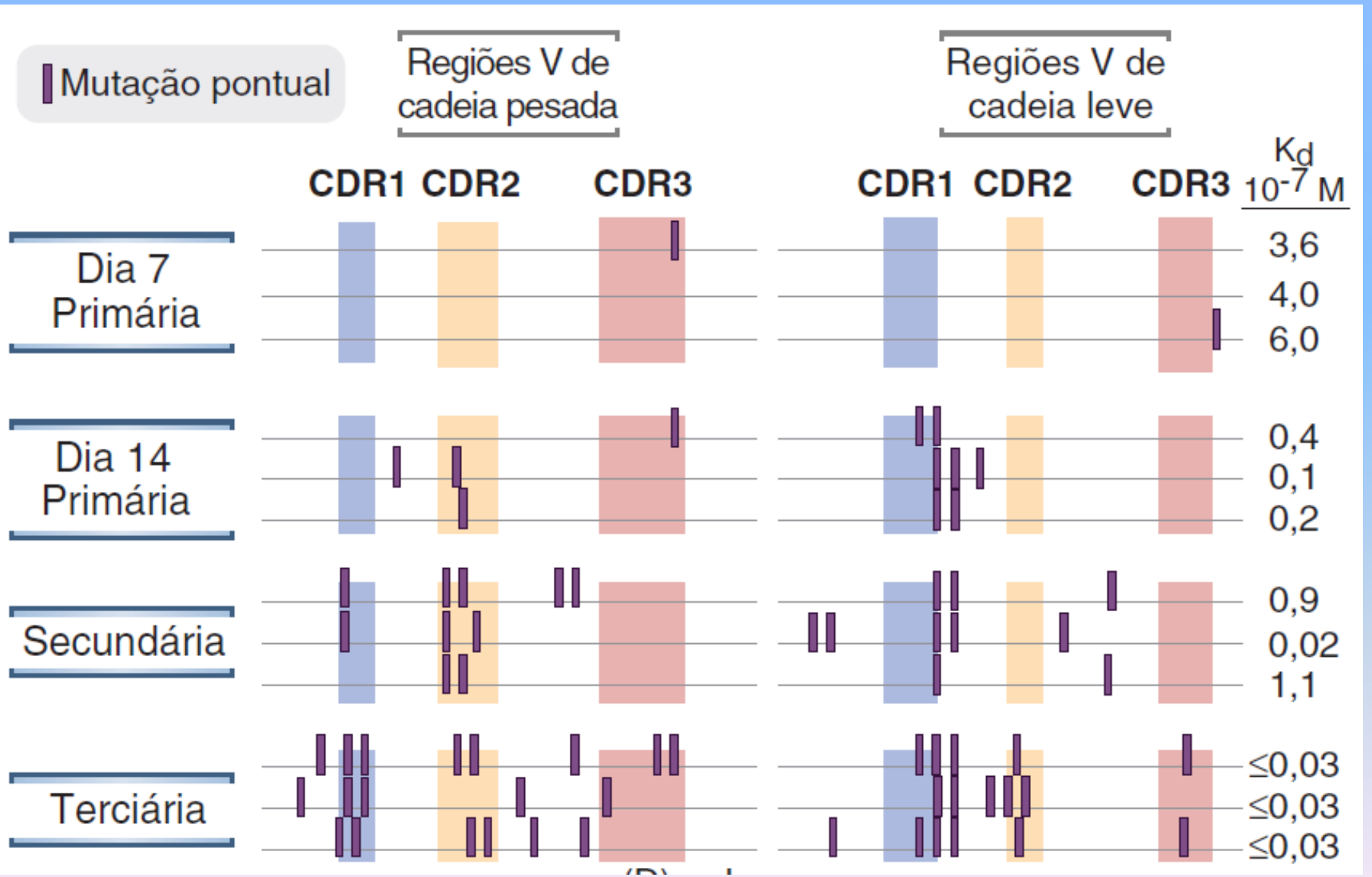
Figure 4-21 Immunobiology, 6/e. (© Garland Science 2005)

Mudanças de Isotipo da Cadeia Pesada



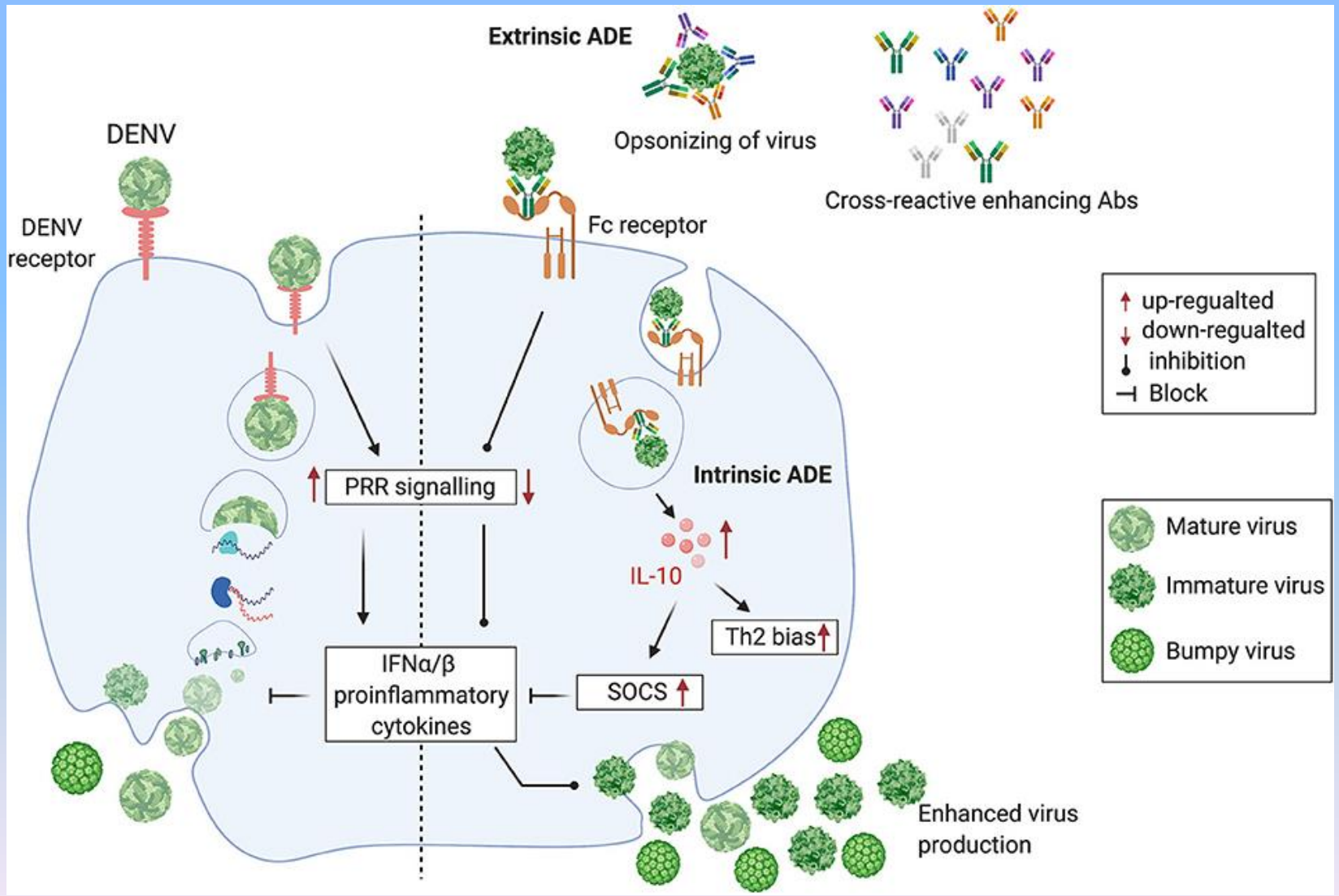
Abbas, Lichtman, Pillai, 9ª Edição, 2019.

Hipermutações somáticas



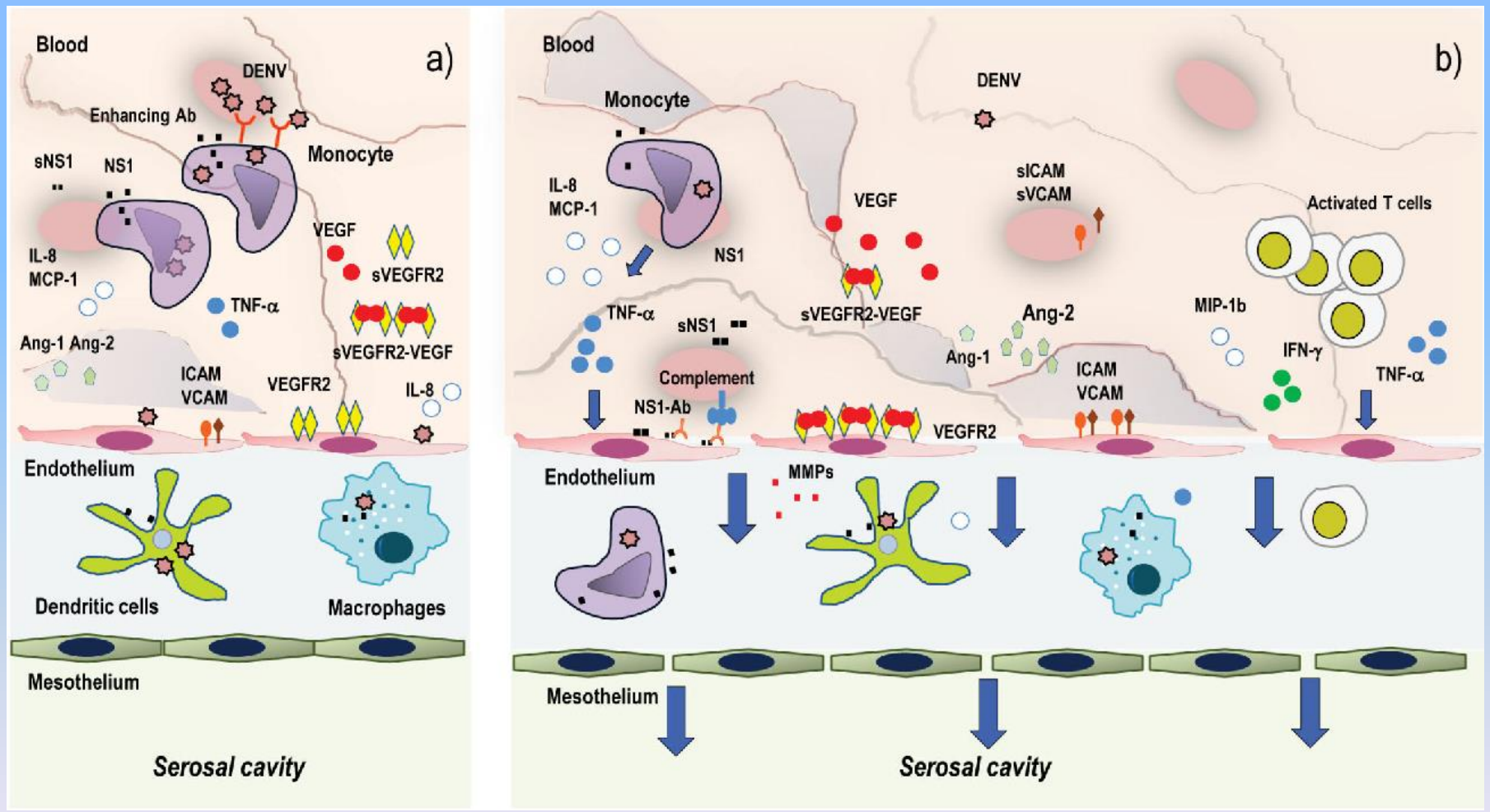
Abbas, Lichtman, Pillai, 9ª Edição, 2019.

Antibody-Dependent Enhancement (ADE) (Amplificação Dependente de Anticorpos)



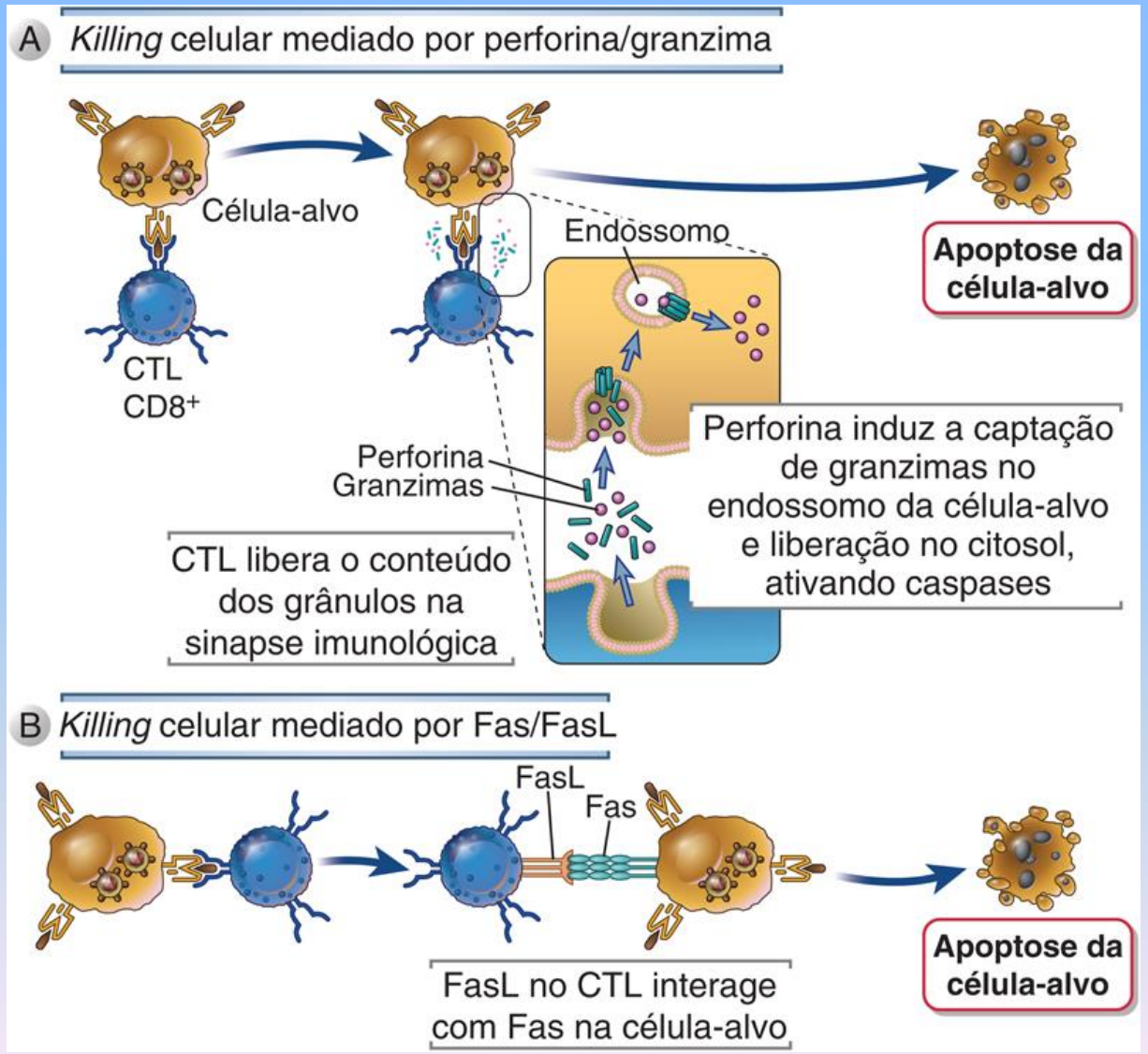
Shukla et al., Front. Cell. Infect. Microbiol., 22, 2020.

Alterações Vasculares Associadas à Dengue Hemorrágica



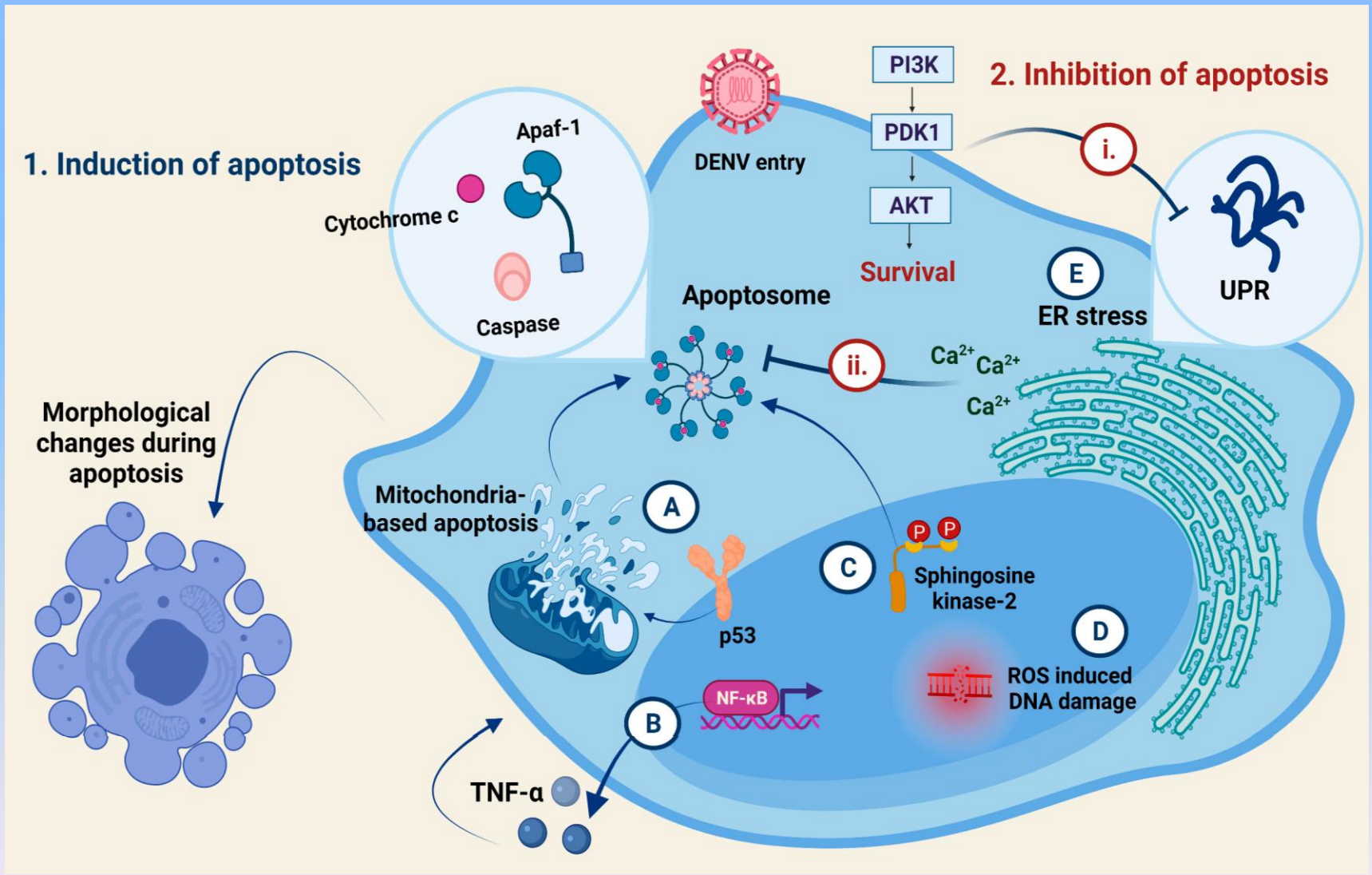
Sriikiatkhachorn & Kelley, Antiviral Research, 109:160-70, 2014.

Imunidade Adaptativa contra Vírus: Mecanismos Efetores dos Linfócitos T CD8+



Abbas, Lichtman, Pillai, 8a. Edição, 2015.

Regulação de Morte Celular pelo Vírus da Dengue



Nanaware et al., Viruses, 13(10):1967, 2021.

Mecanismos de Evasão do Vírus da Dengue

DENV factors	Target pathway	Actions
sfRNA	RNA-sensing	Binds to TRIM25 to inhibit viral RNA recognition by RIG-I
NS2A	IFN induction	Antagonizes the phosphorylation of TBK1 and RIG-I-induced IRF3
	IFN signaling	Inhibits IFN-triggered antiviral actions
NS2B	DNA-sensing	Targets cGAS for degradation
NS2B3	DNA-sensing	Cleaves STING through protease-dependent manner
	IFN induction	Interacts with IKKε to mask part of its kinase domain to prevent the phosphorylation of IRF3
	Mitochondrial dynamics	Cleaves MFN1 and MFN2 to modulate the MFN-mediated host antiviral defense
NS3	RNA-sensing	Competes with RIG-I for 14-3-3ε binding to block RIG-I activation
NS4A	RNA-sensing	Translocates to mitochondrion-associated endoplasmic reticulum membranes to prevent the binding between RIG-I and MAVS.
	IFN induction	Blocks TBK1 activation
	IFN signaling	Inhibits of IFN-triggered gene expressions
NS4B	IFN induction	Antagonizes the phosphorylation of TBK1 and RIG-I-induced IRF3
	IFN signaling	Inhibits STAT1 phosphorylation and transcriptional activation
NS5	RNA-sensing	Catalyzes DENV genomic RNA 2'-O methylation mimicking cellular mRNA
	IFN signaling	Binds and degrades STAT2

sfRNA, subgenomic flaviviral RNA; TRIM25, tripartite motif protein 25; RIG-I, retinoic acid-inducible gene-I; TBK1, TANK binding kinase-1; IRF, interf transducer and activator of transcription; cGAS, cyclic GMP-AMP synthase; STING, stimulator of interferon genes; IKKε, IκB kinase epsilon; MF antiviral signaling protein.

Kao et al., Front. Immunol., 2018.