

A T SEJTEK TÍPUSAI ÉS AKTIVÁCIÓJA

Buzás Edit

Genetikai, Sejt- és Immunbiológiai Intézet

A T limfociták



1. A celluláris immunitás sejtjei
2. T sejt receptor van a felszínükön
3. A thymusban érnek
4. Típusaik:

$\alpha\beta$ T sejtek **T helper:** segítség a B sejteknek vagy makrofágoknak/NK sejteknek

T citotoxikus: vírusfertőzött vagy tumoros sejtek elpusztítása

T reguláló: más T sejtek működésének gátlása

MHC molekulával bemutatott epitópot ismernek fel

$\gamma\delta$ T sejtek

NKT sejtek

MAIT sejtek

T sejt receptor kompleks

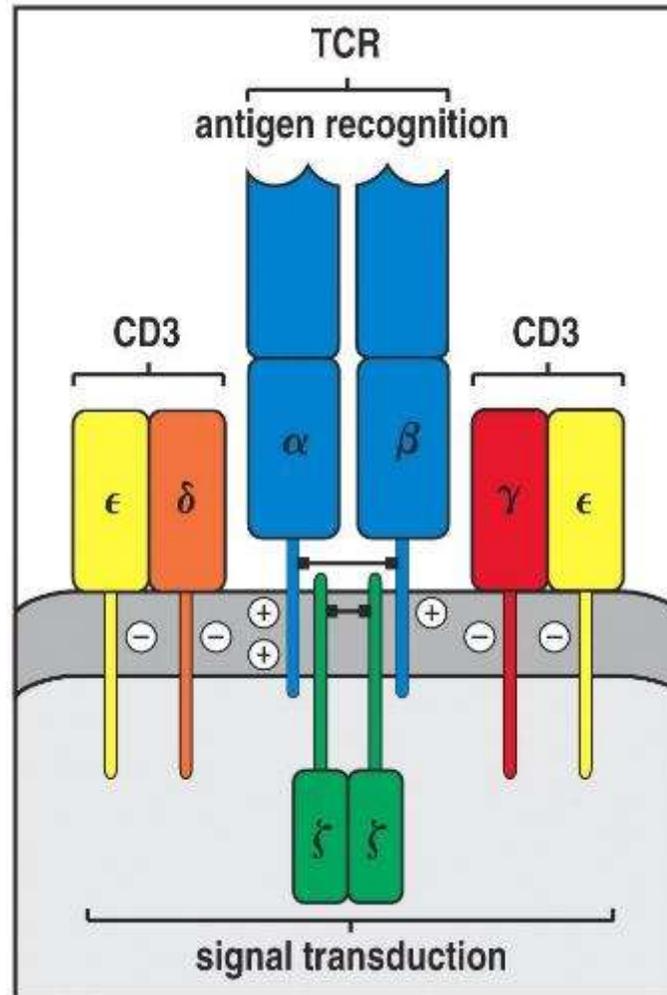


Figure 3-6 The Immune System, 2/e (© Garland Science 2005)

A T sejt CD3+ sejt

A T limfociták

- 1. T sejt ontogenezis (*thymus*)**
- 2. T sejt aktiváció (*szekunder nyirokszervek*)**
- 3. T sejttípusok és működésük (*szövetek*)**

Thymus

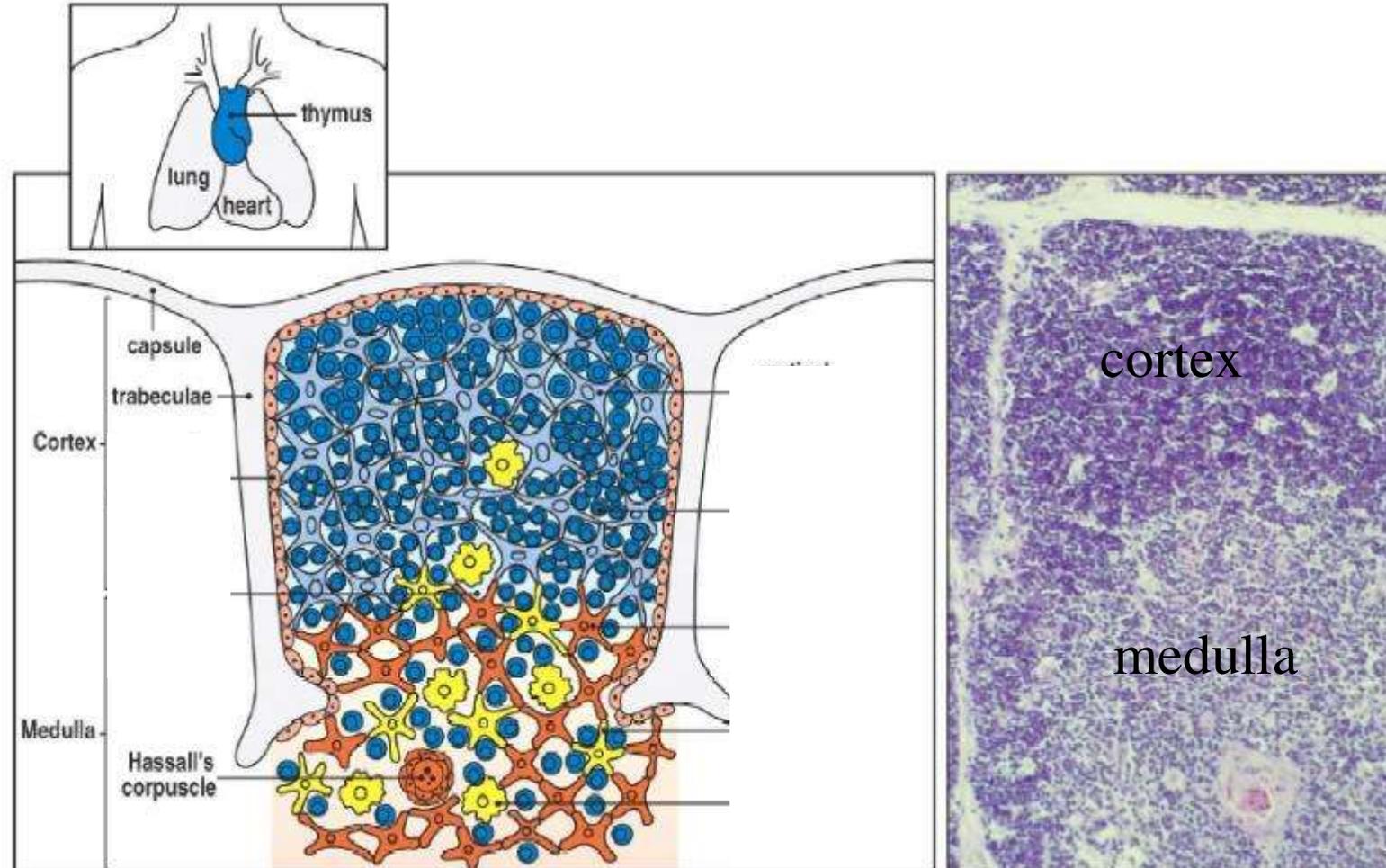
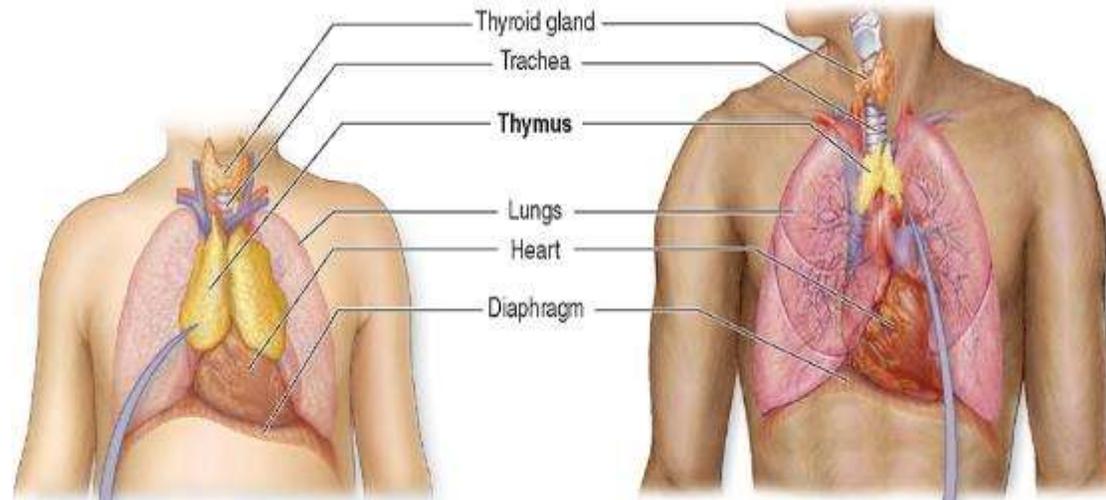
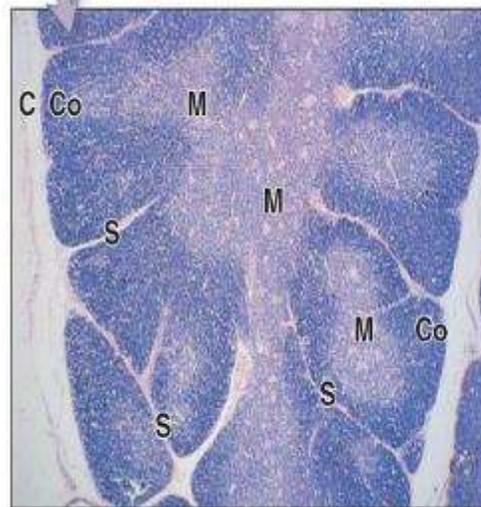


Figure 7-8 Immunobiology, 6/e. (© Garland Science 2005)

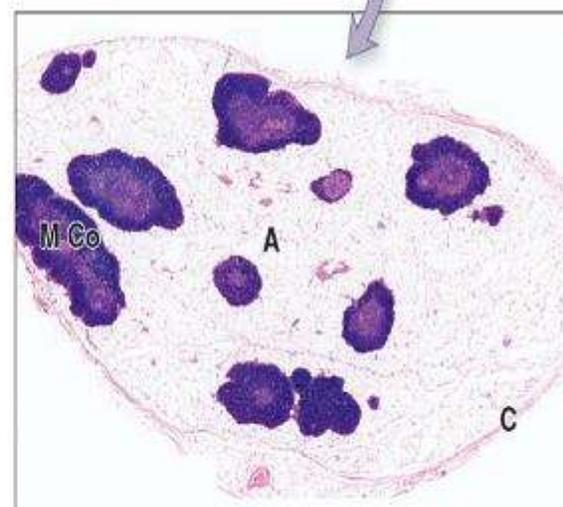
Thymus



a Child (left) and adult (right) thorax, anterior view



b Micrograph of child's thymus



c Micrograph of adult's thymus

Thymus stroma: entodermális citoretikulum

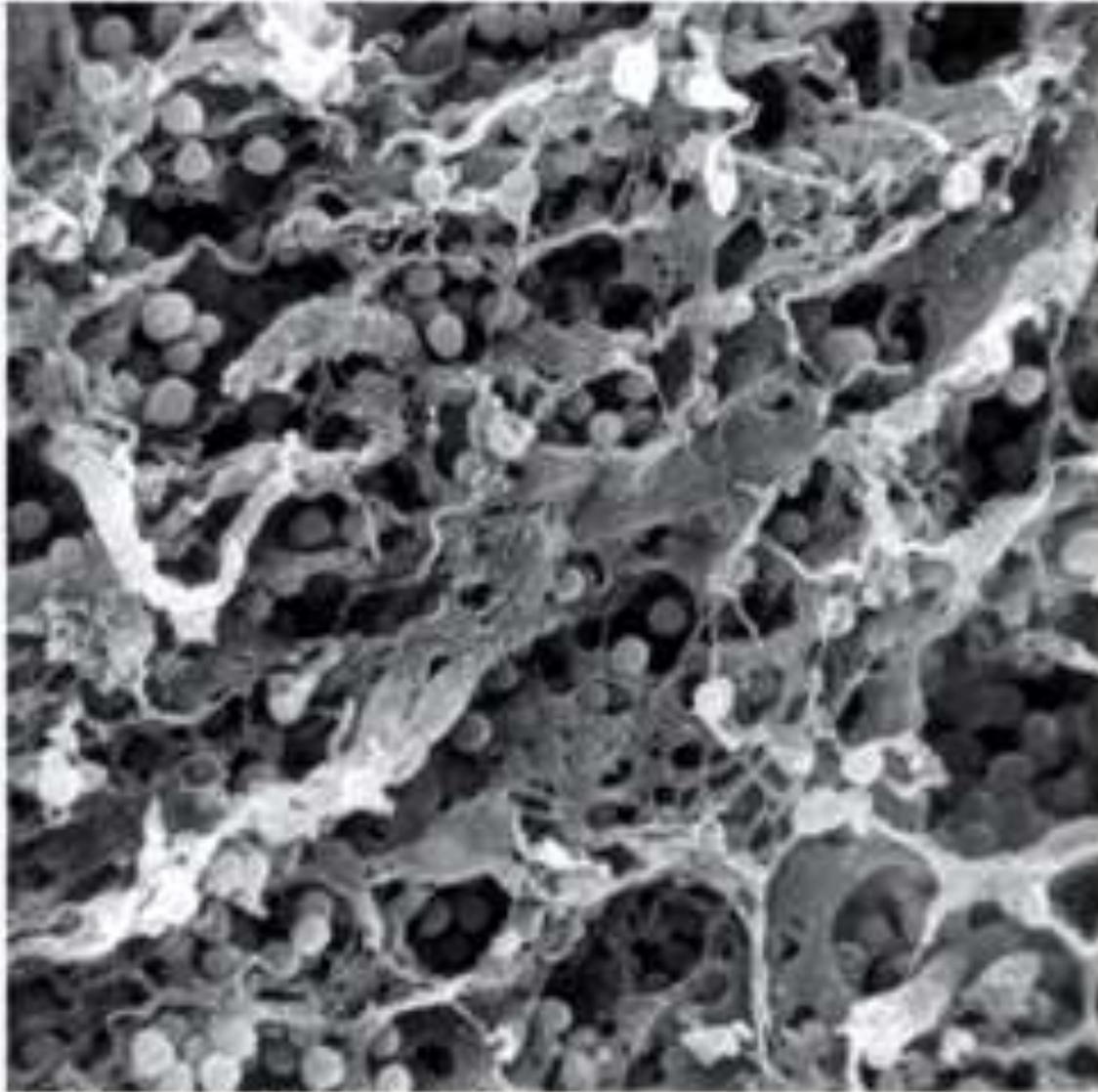
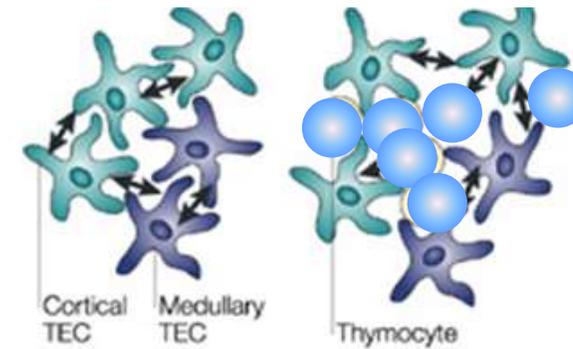
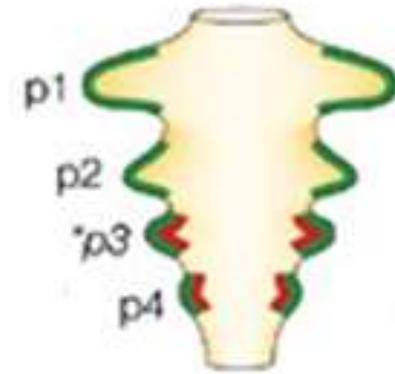
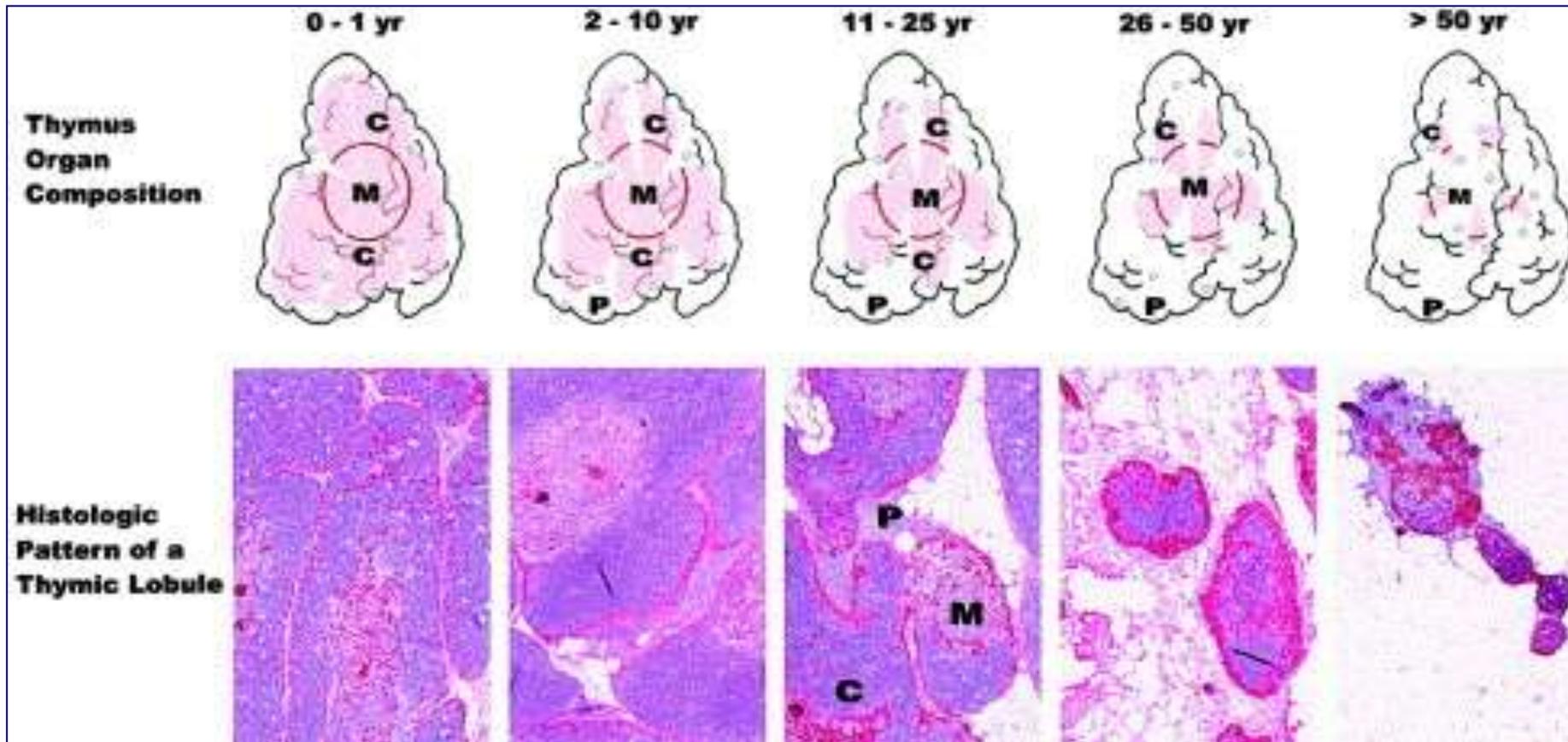


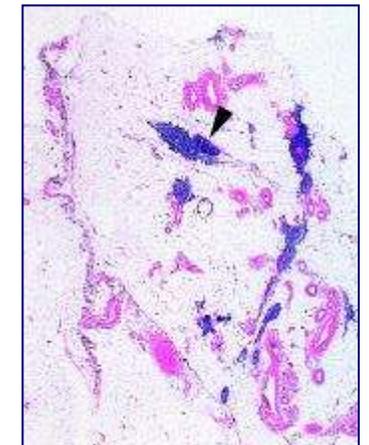
Figure 7-158 Immunobiology, 7th ed. (© Garland Science 2018)



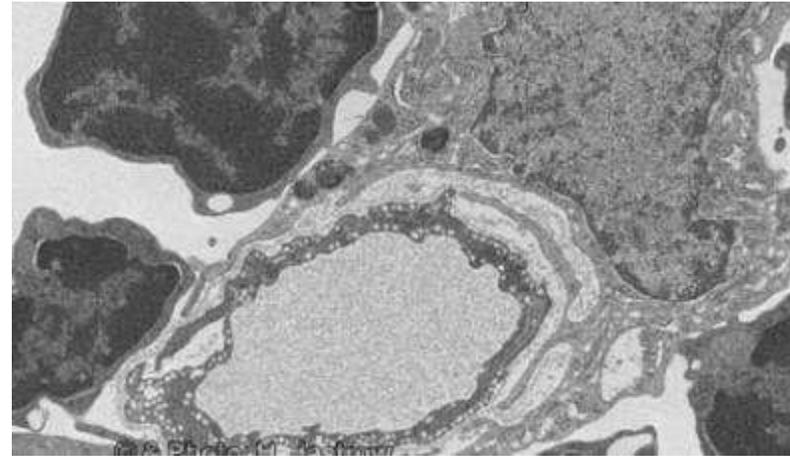
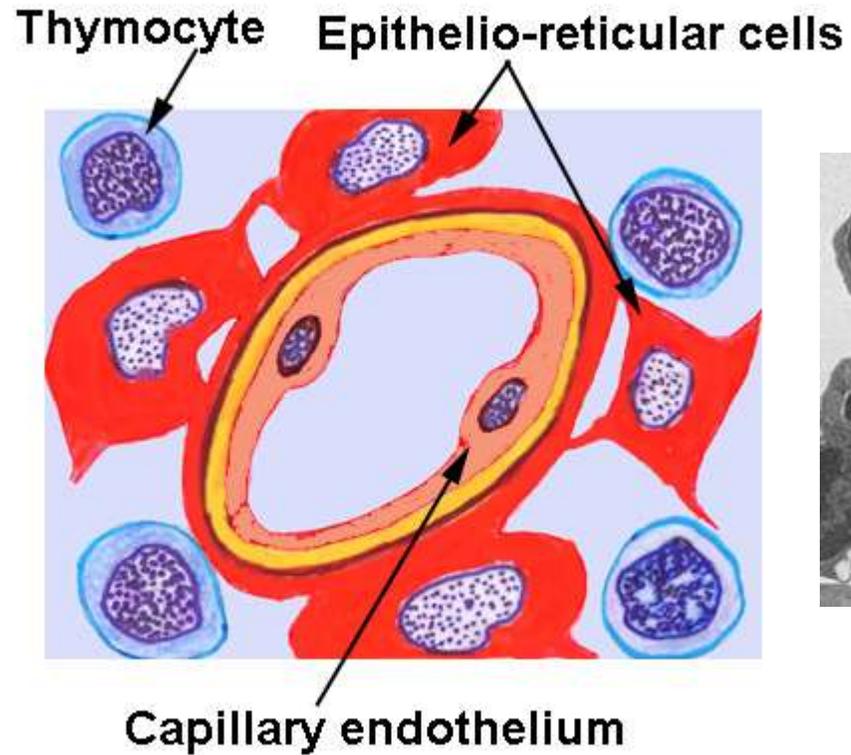
A thymus ontogenezise



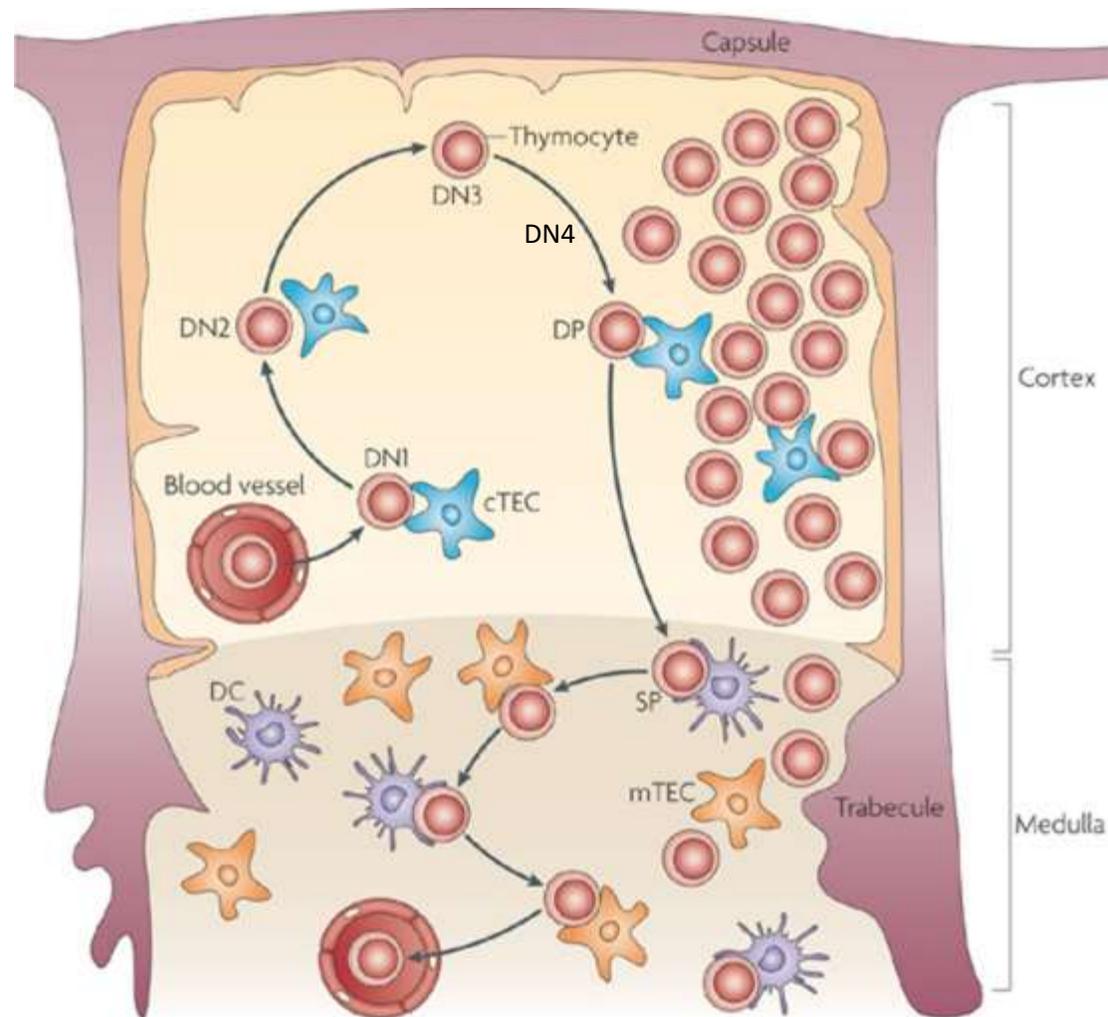
78 éves nő thymusa



Vér-thymus gát



T sejt érés a thymusban

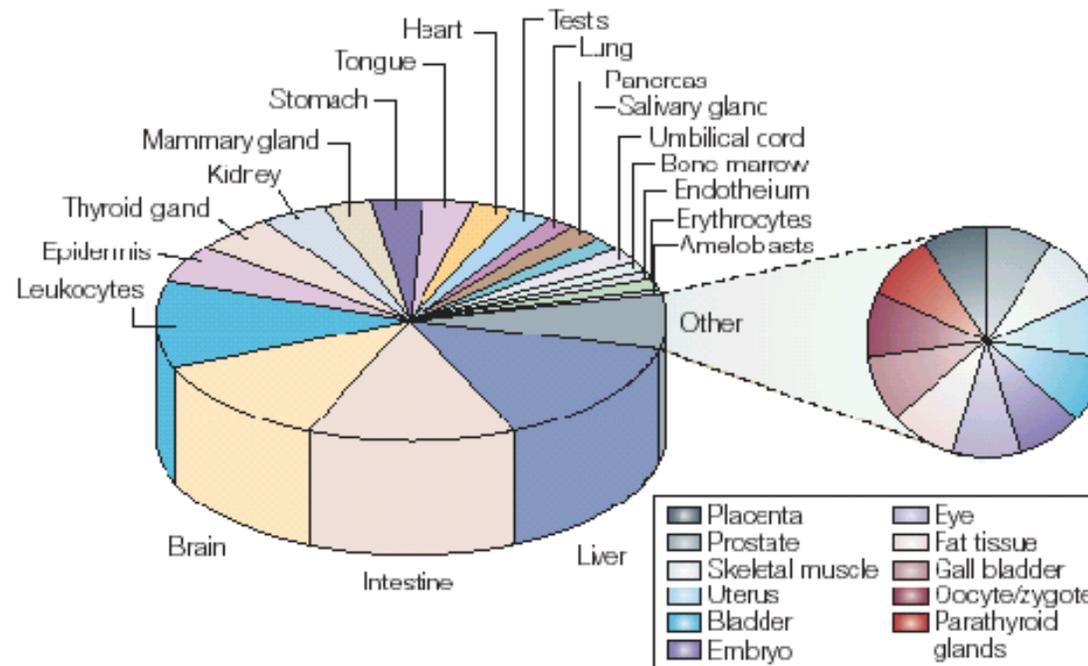


R.N. Germain, Nature Review 2002

mTEC: saját antigének kerülnek bemutatásra a thymusban: promiszkuus génexpresszió

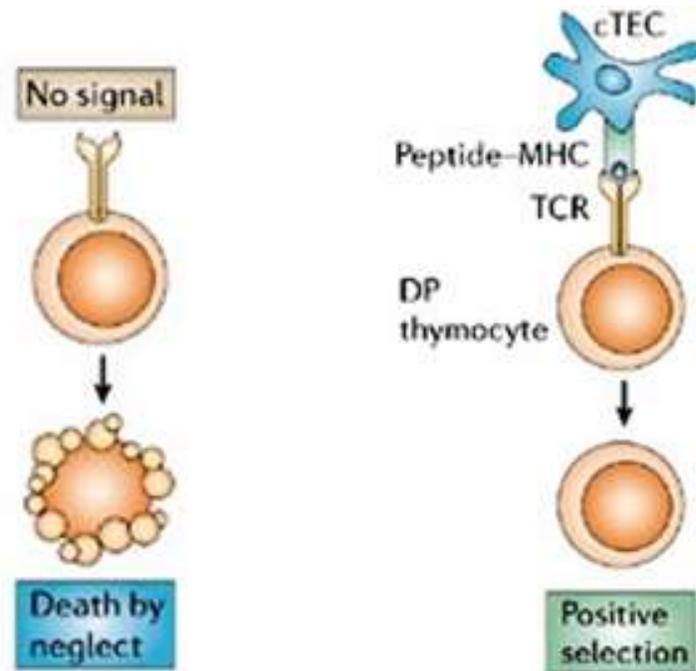
5-10%-a (~3000 gén) expresszálódik:

Fő szabályozói az AIRE és a FEZF2 transzkripciós faktorok

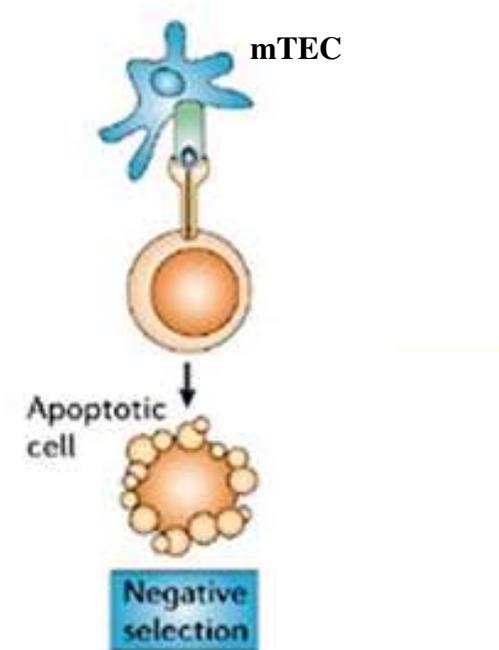


A saját peptid-saját MHC kötődés próbái

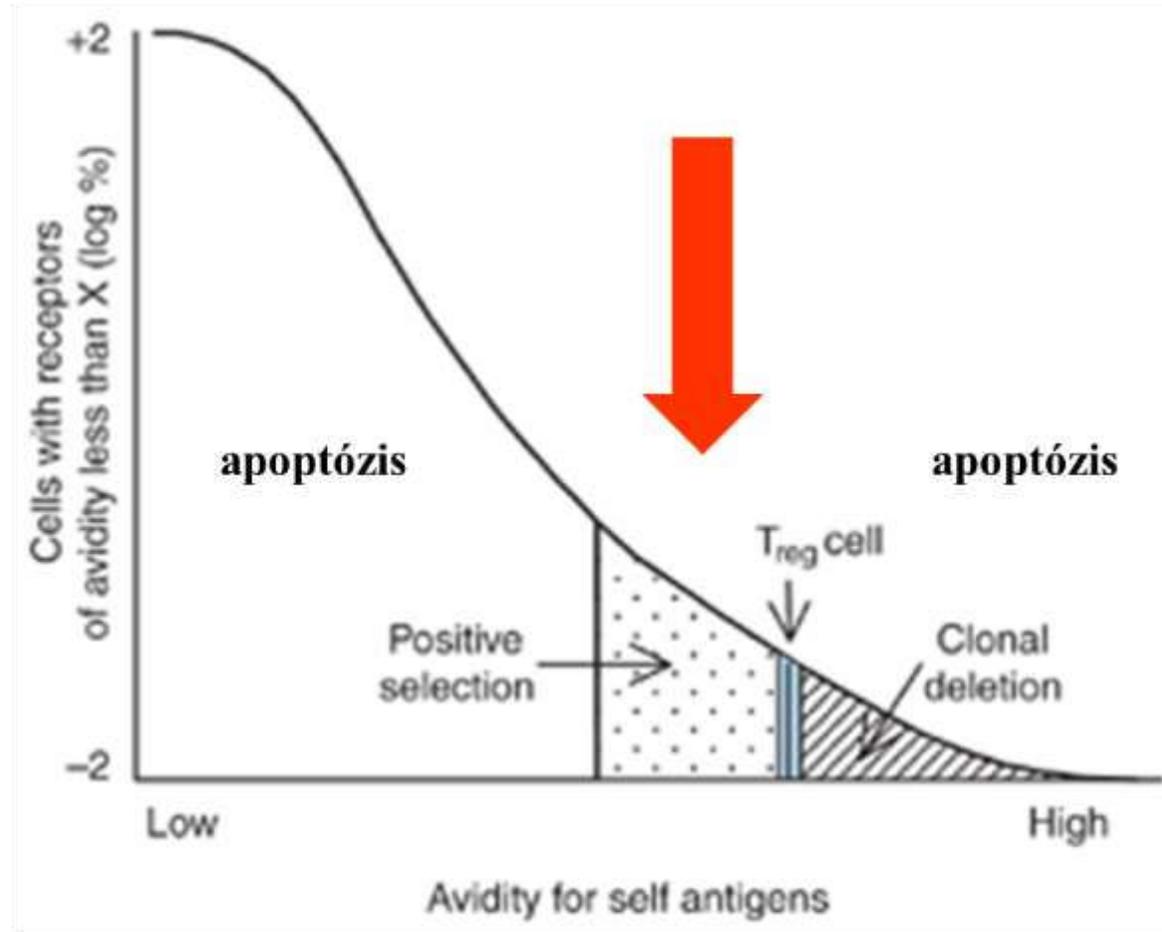
Pozitív szelekció

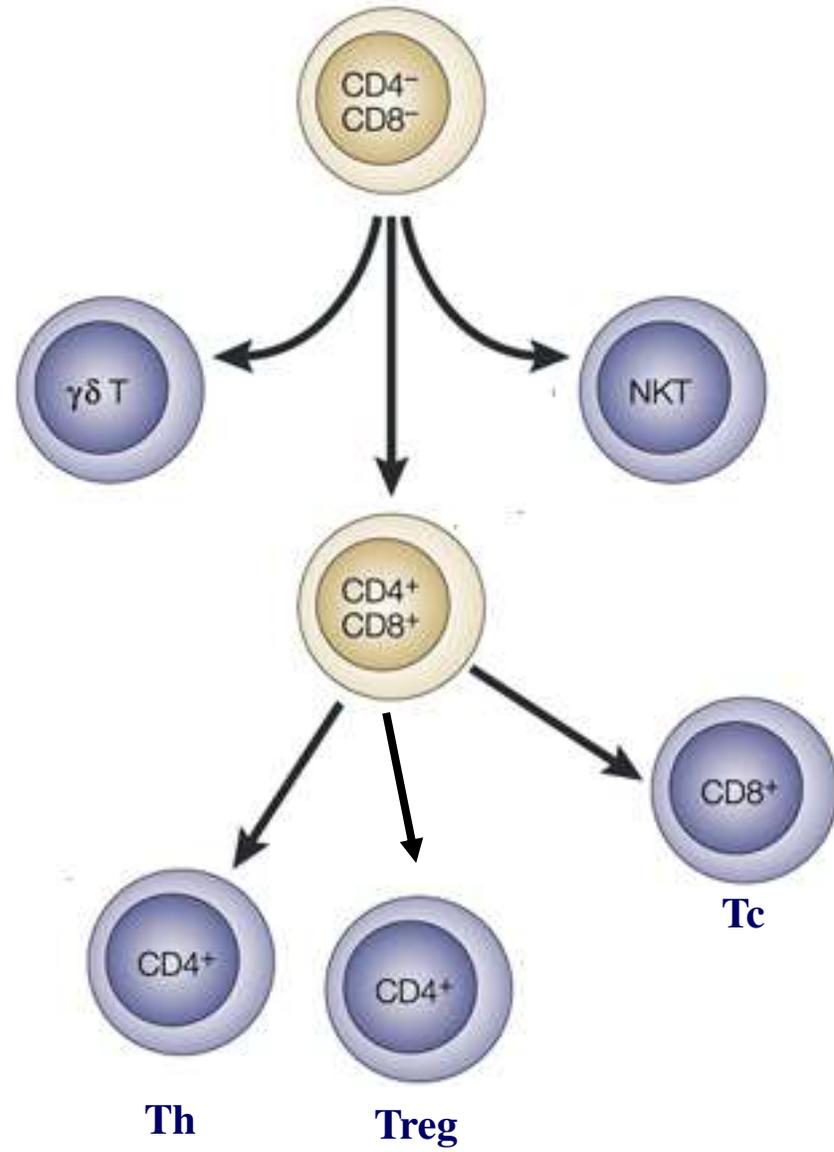


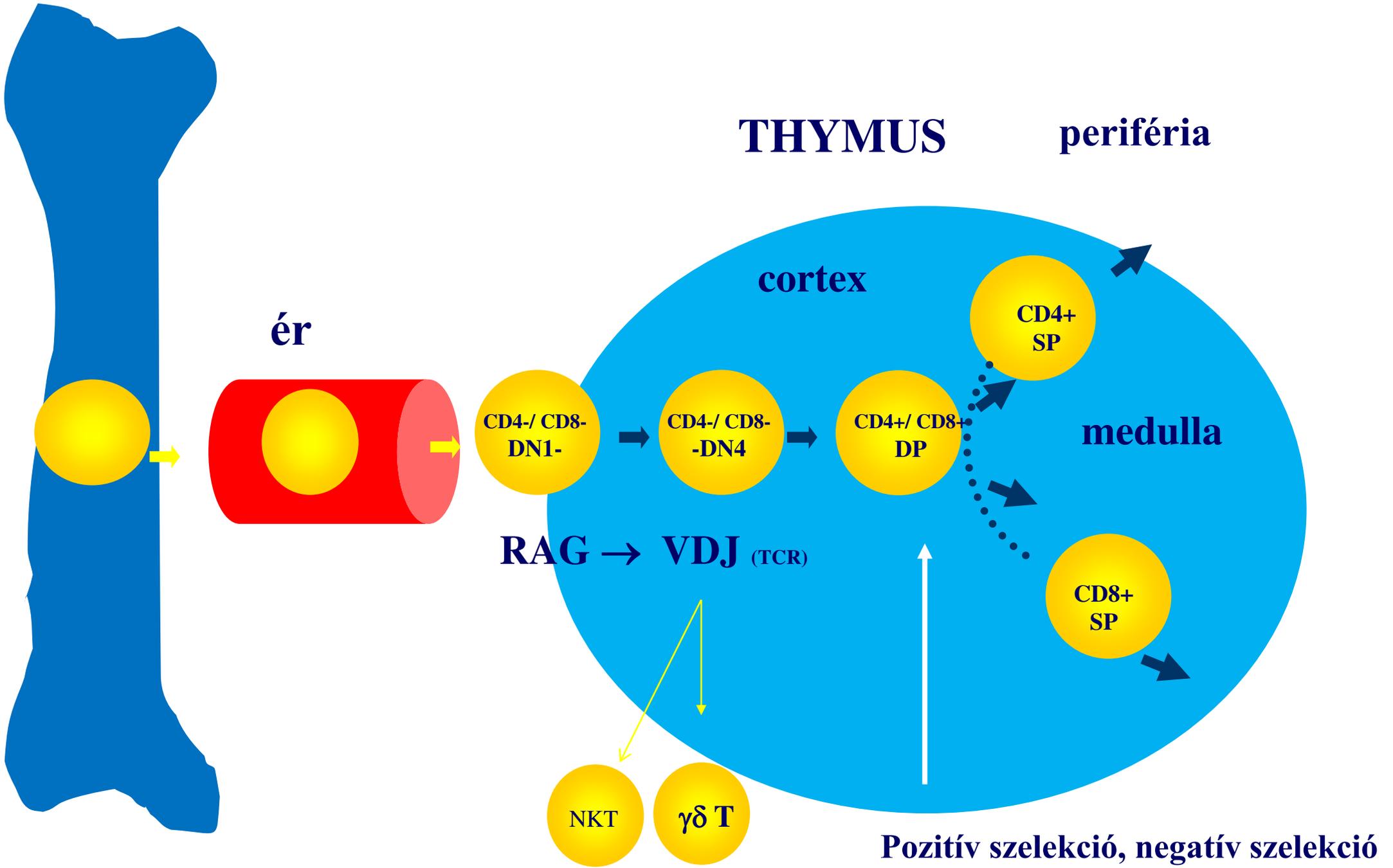
Negatív szelekció



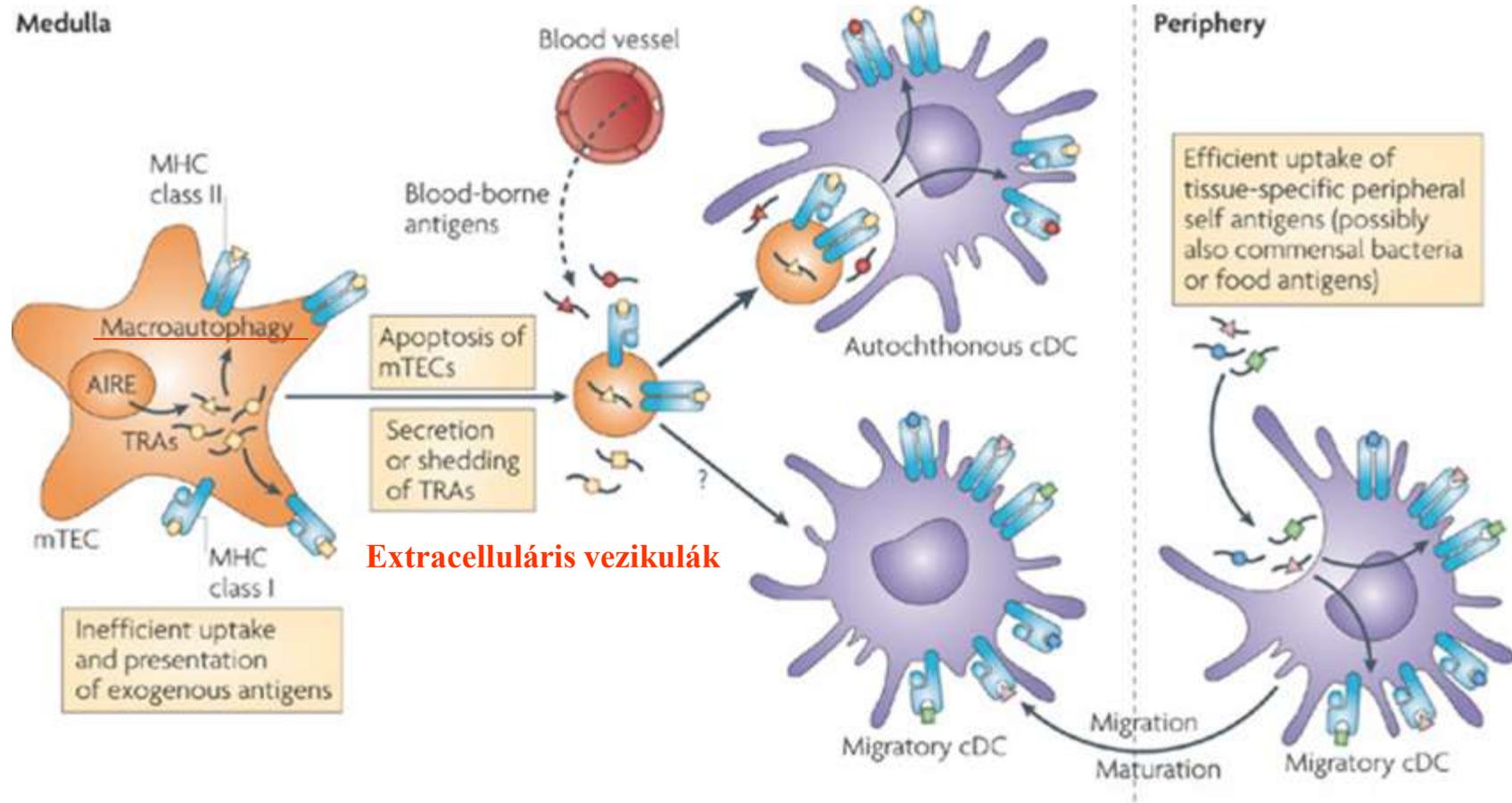
Szelekció a TCR MHC_saját peptid komplex aviditása alapján a thymusban







A saját peptid-saját MHC kötődés próbái



TRA: tissue-restricted antigen

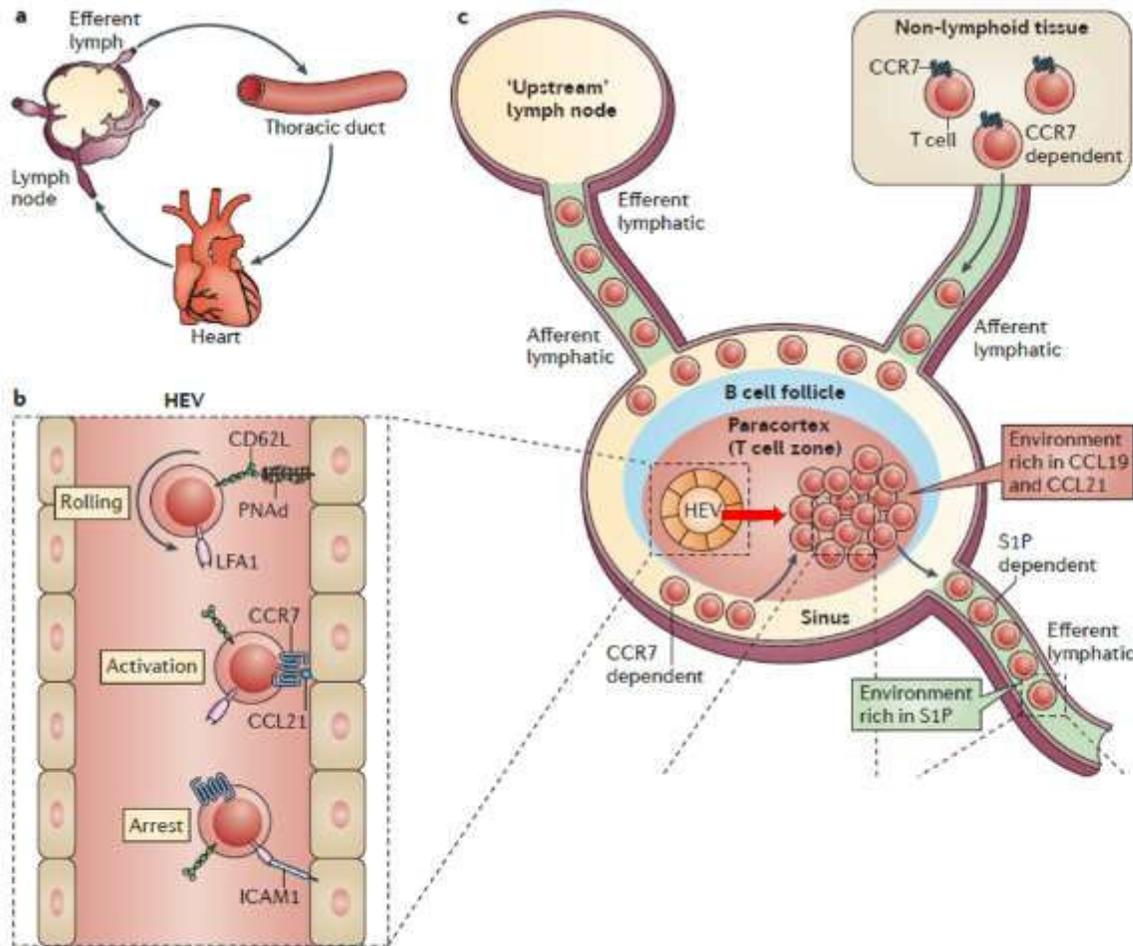
A pozitív és negatív szelekciót a keletkezett T sejtek 5%-a éli túl



A pozitív és negatív szelekciót túlélő T sejtek elhagyják a thymust és csatlakoznak a recirkuláló limfocita tömeghez



A naiv T sejtek migrációja a nyirokcsomókba



A naiv T sejteken L-szelektin (CD62L) és CCR7 homing receptorok vannak

A nyirokcsomókban addresszin molekulák expresszálódnak (CCL19 és CCL21)

Az éretlen dendritikus sejtek a perifériáról a nyirokcsomókba szállítják a felvett antigént

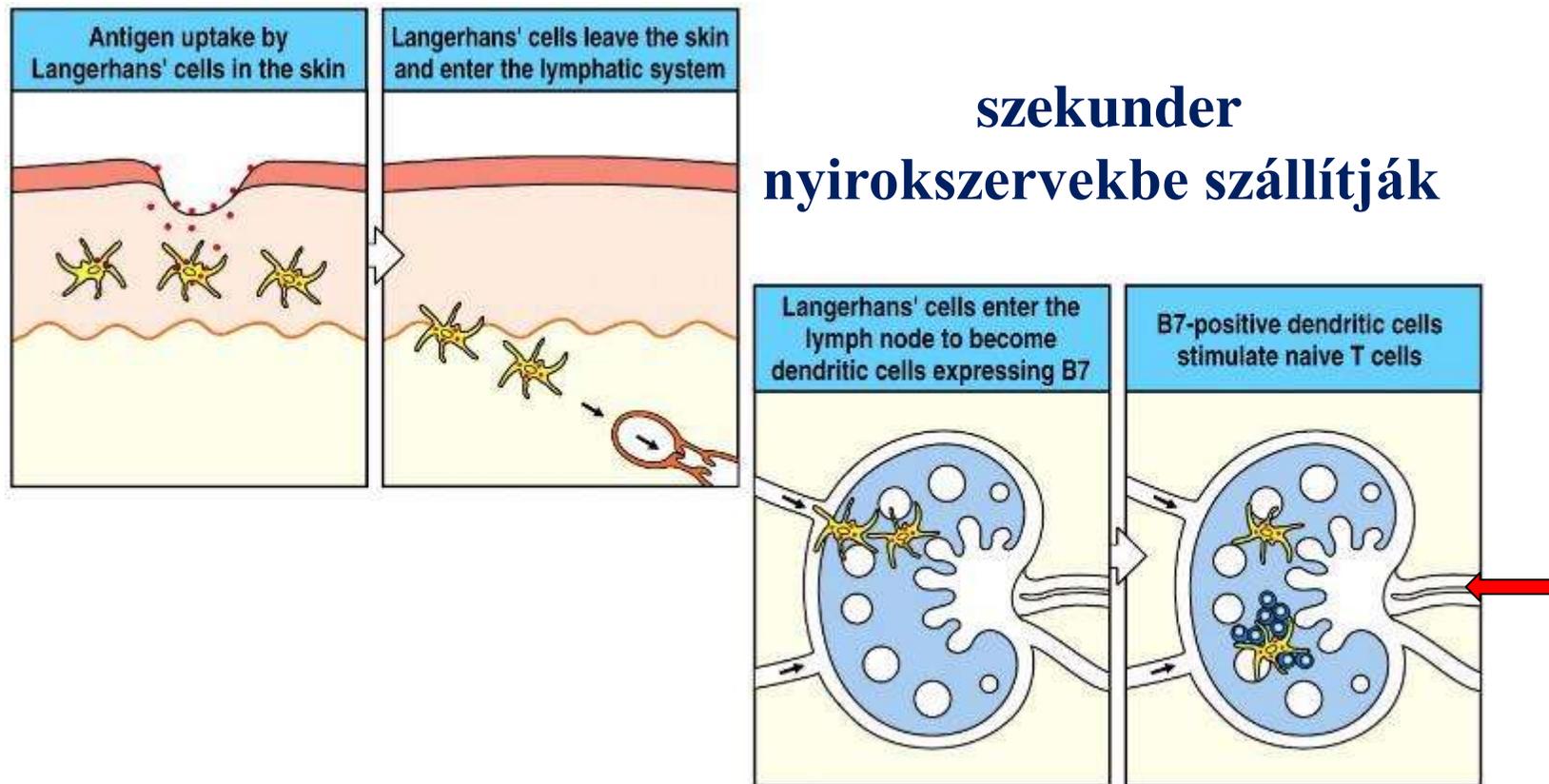
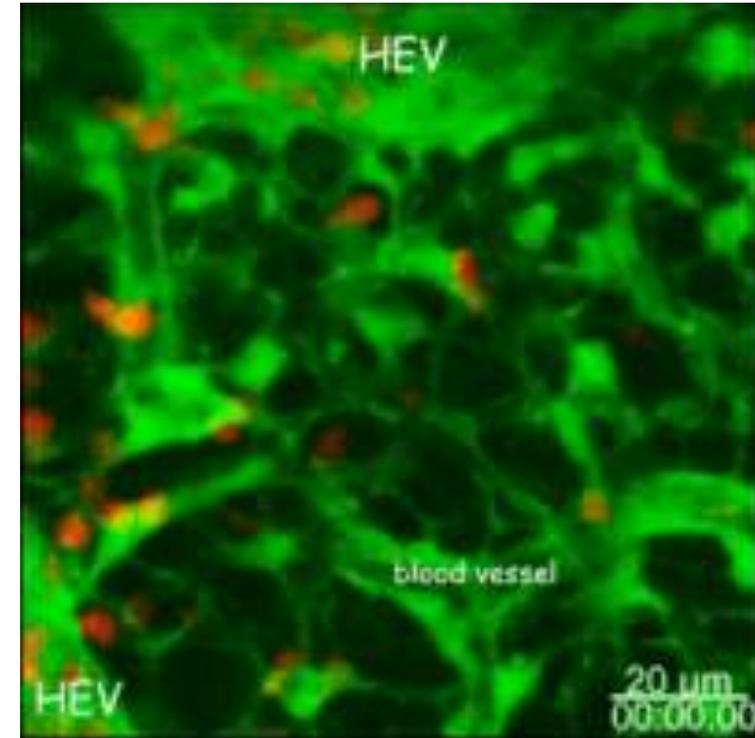
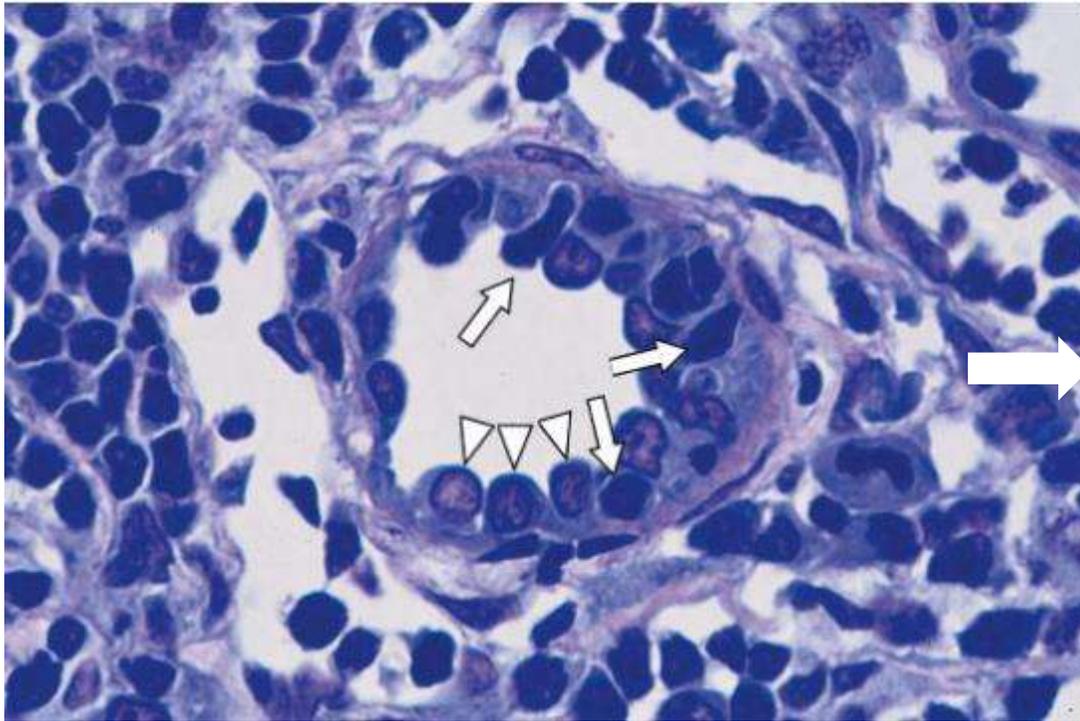


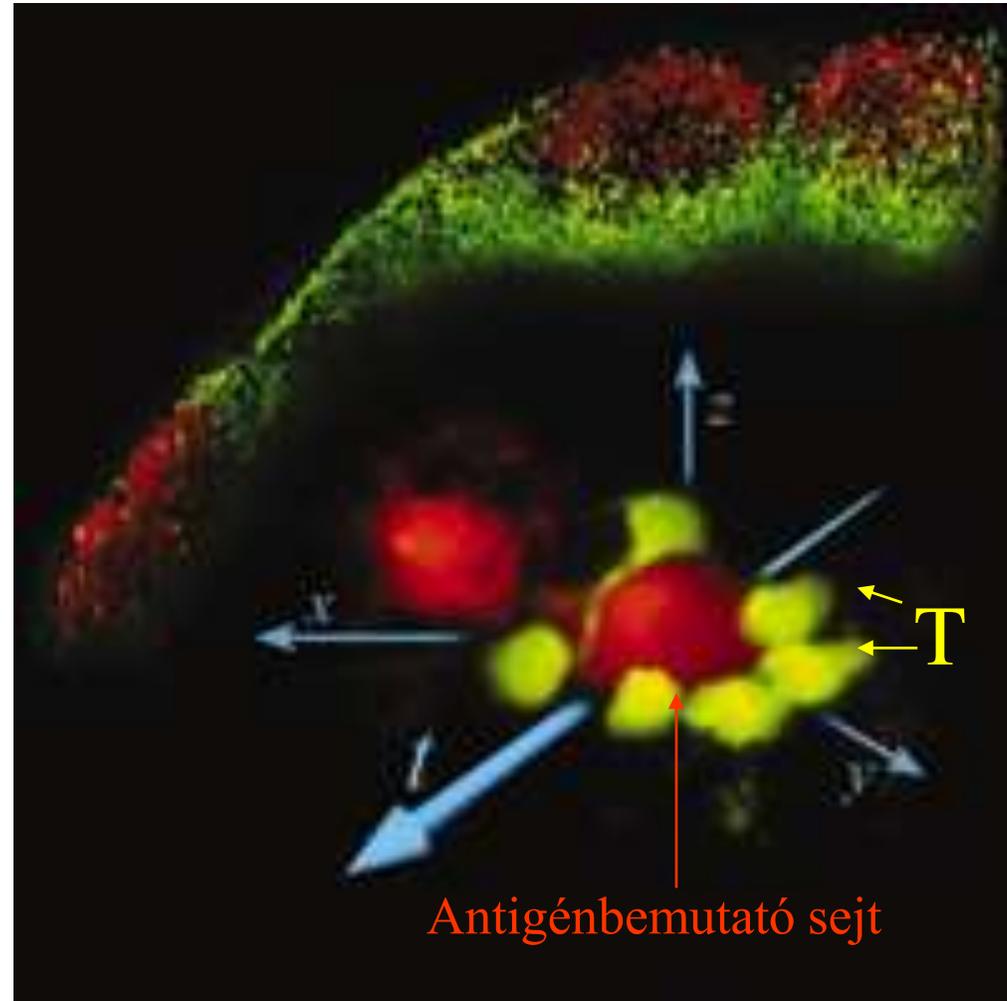
Figure 8-15 Immunobiology, 6/e. (© Garland Science 2005)

A megérett dendritikus sejtek
bemutatják az antigént

A nyirokcsomó állományába a HEV-ek falán át lépnek be a T sejtek



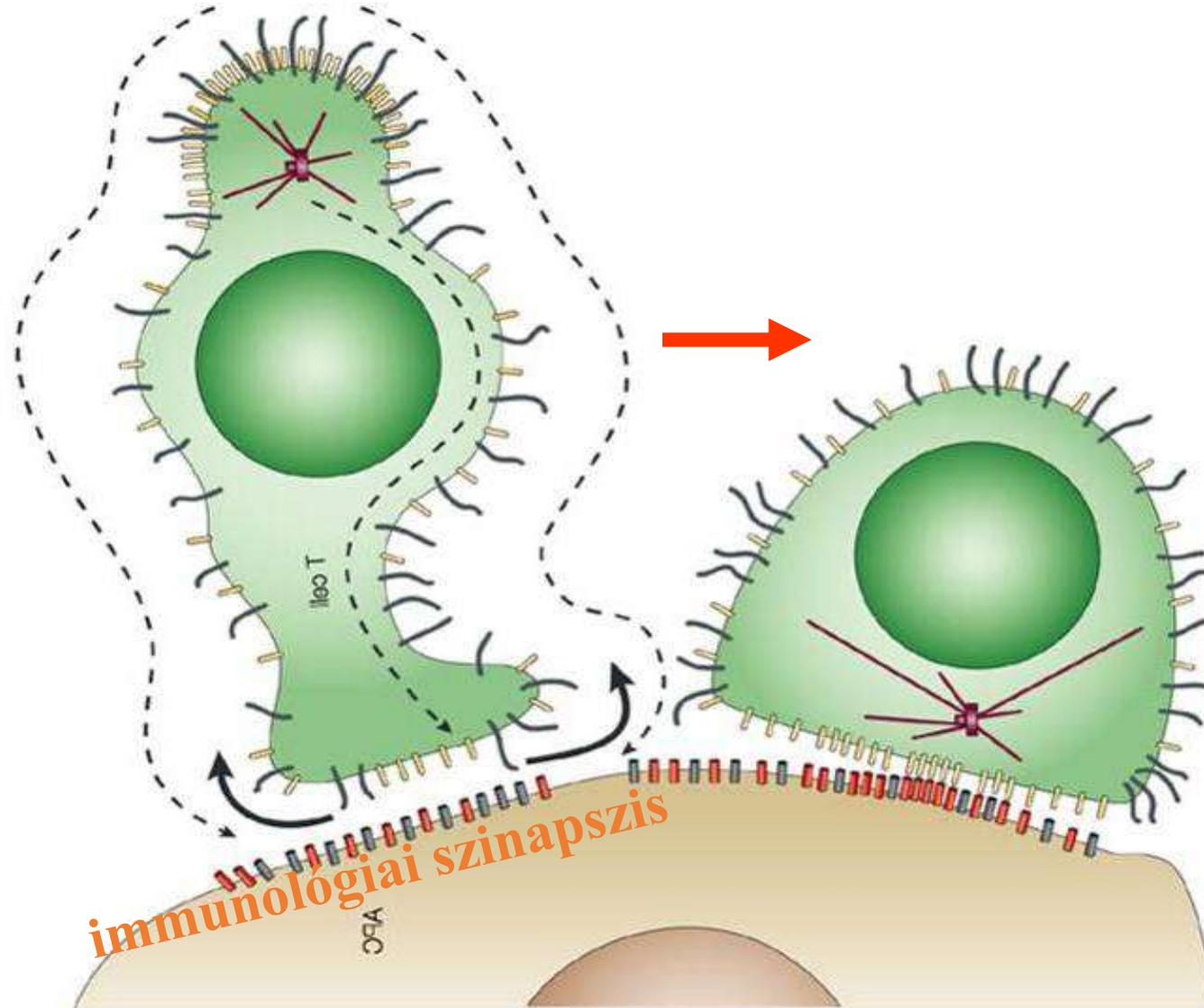
A nyirokcsomó paracortexébe a HEV-ek falán át lépnek a véráram útján érkezett T sejtek



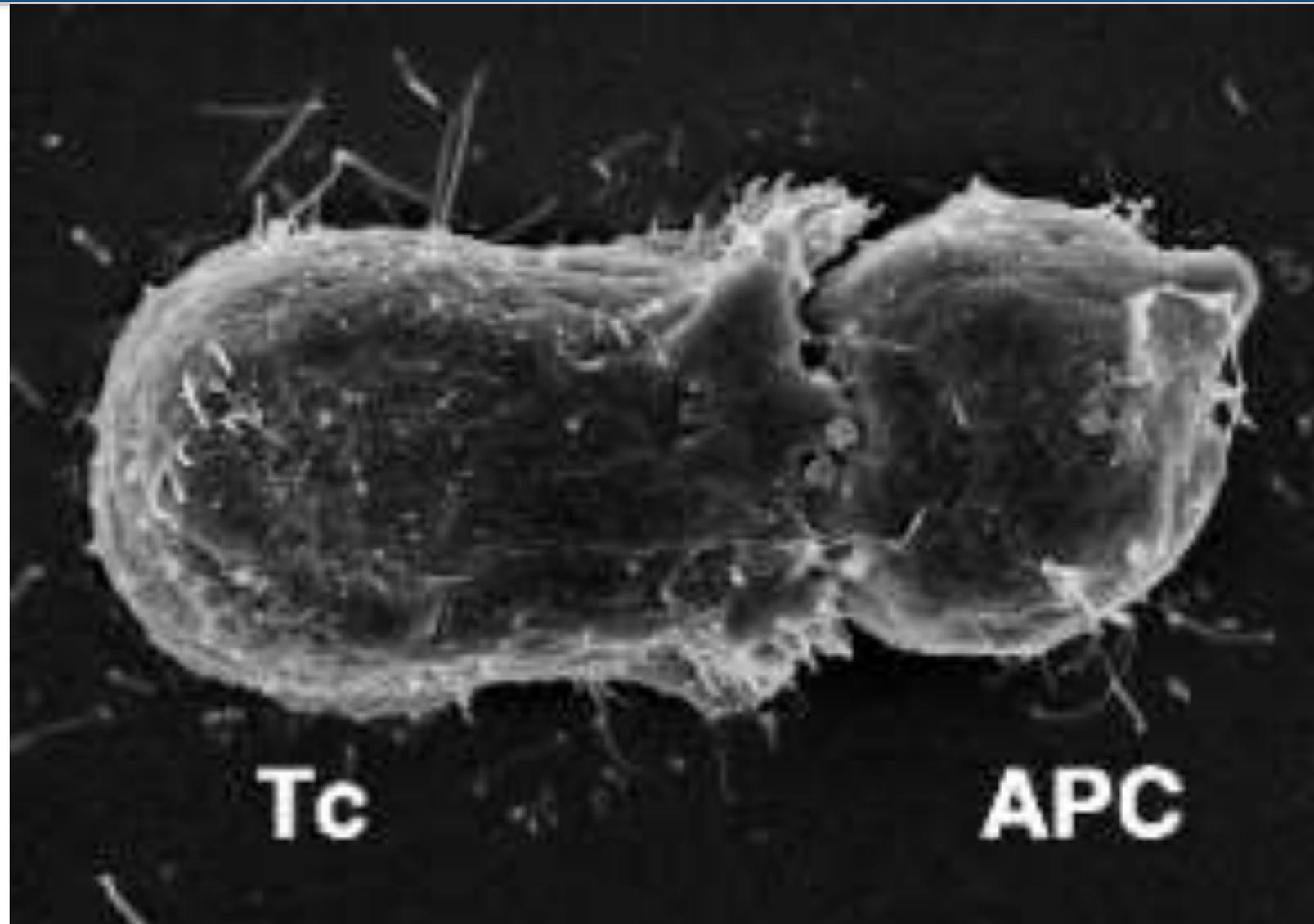




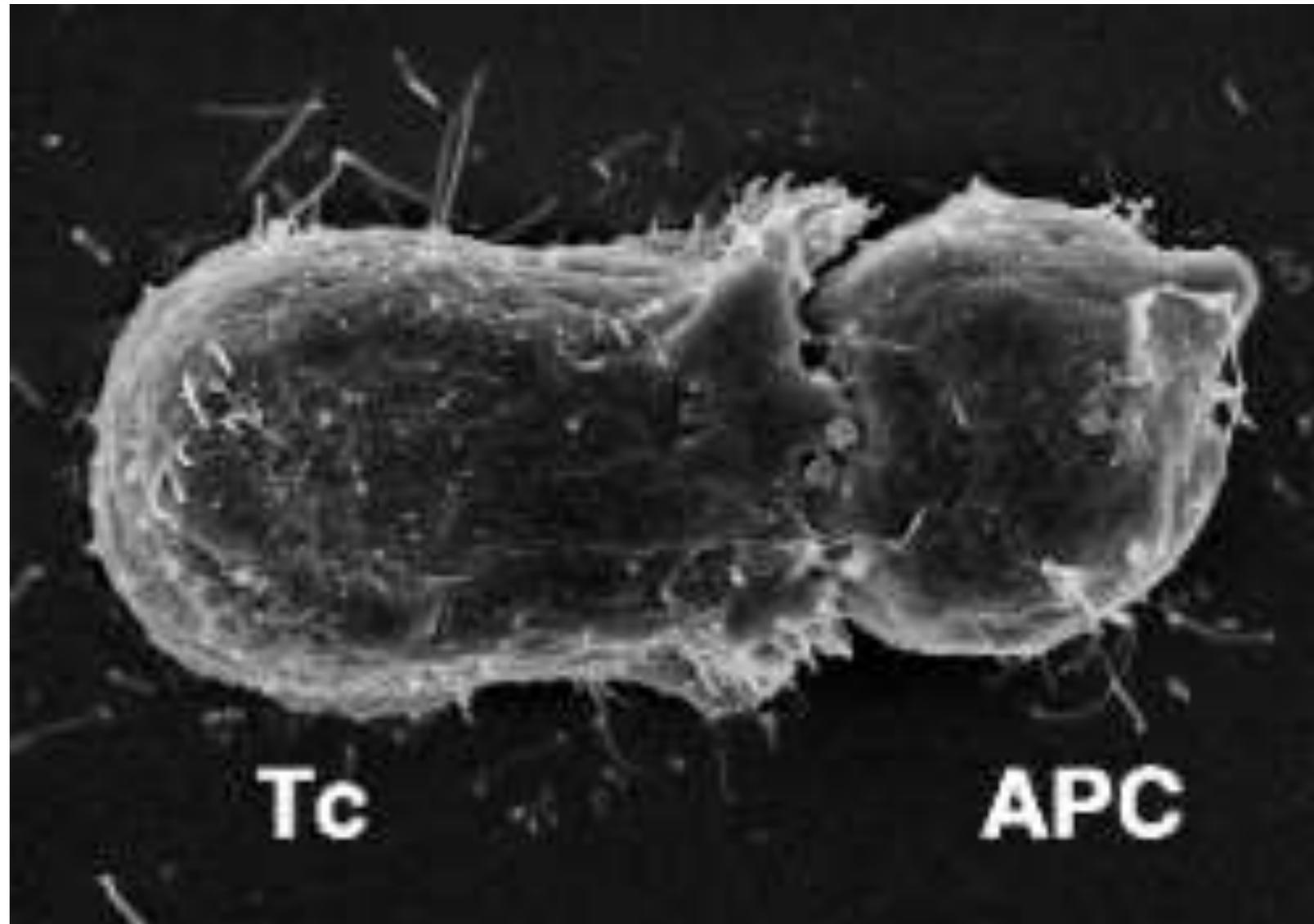
Az immunológiai szinapszis kialakulása



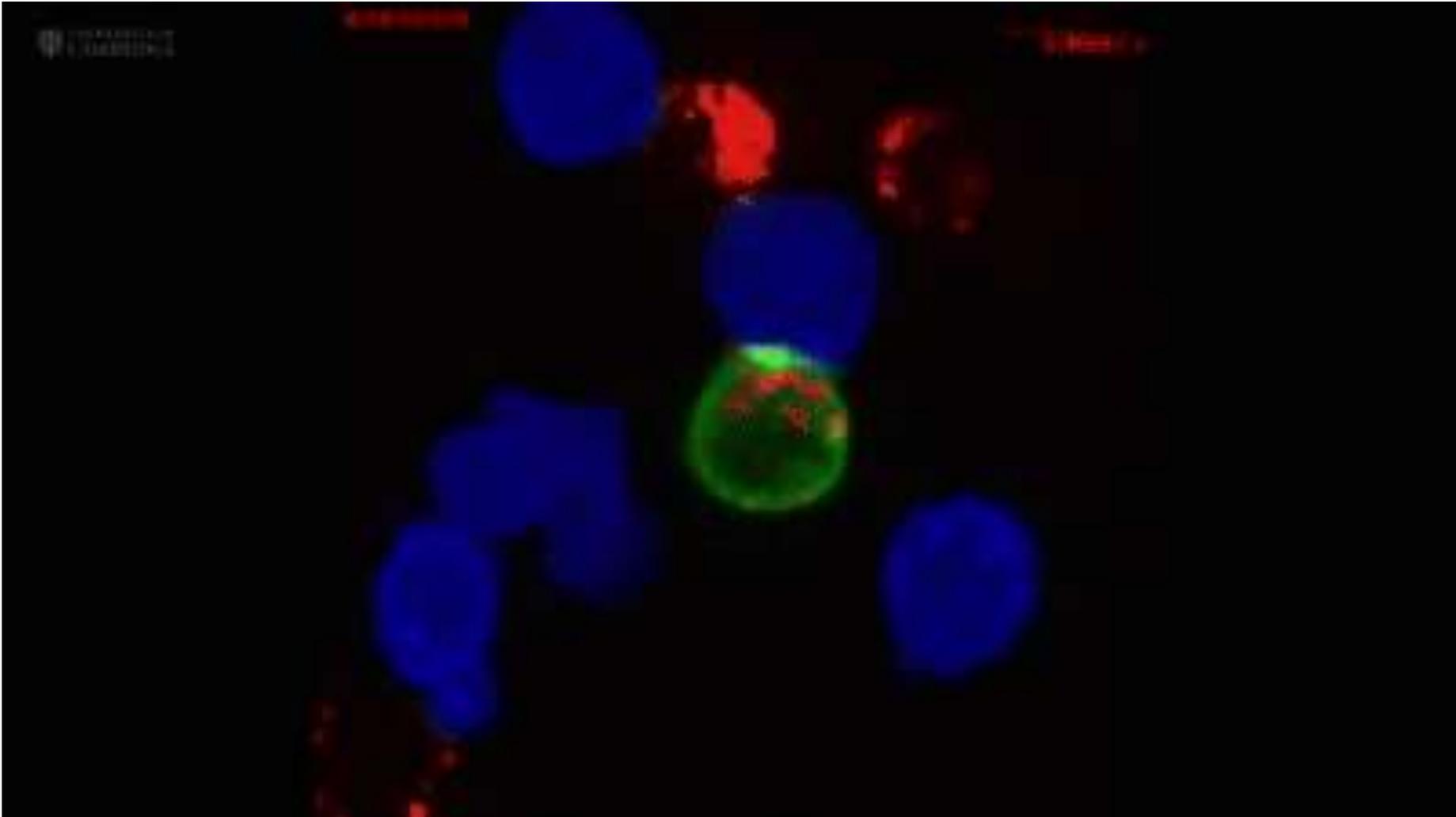
Az immunológiai szinapszis kialakulása



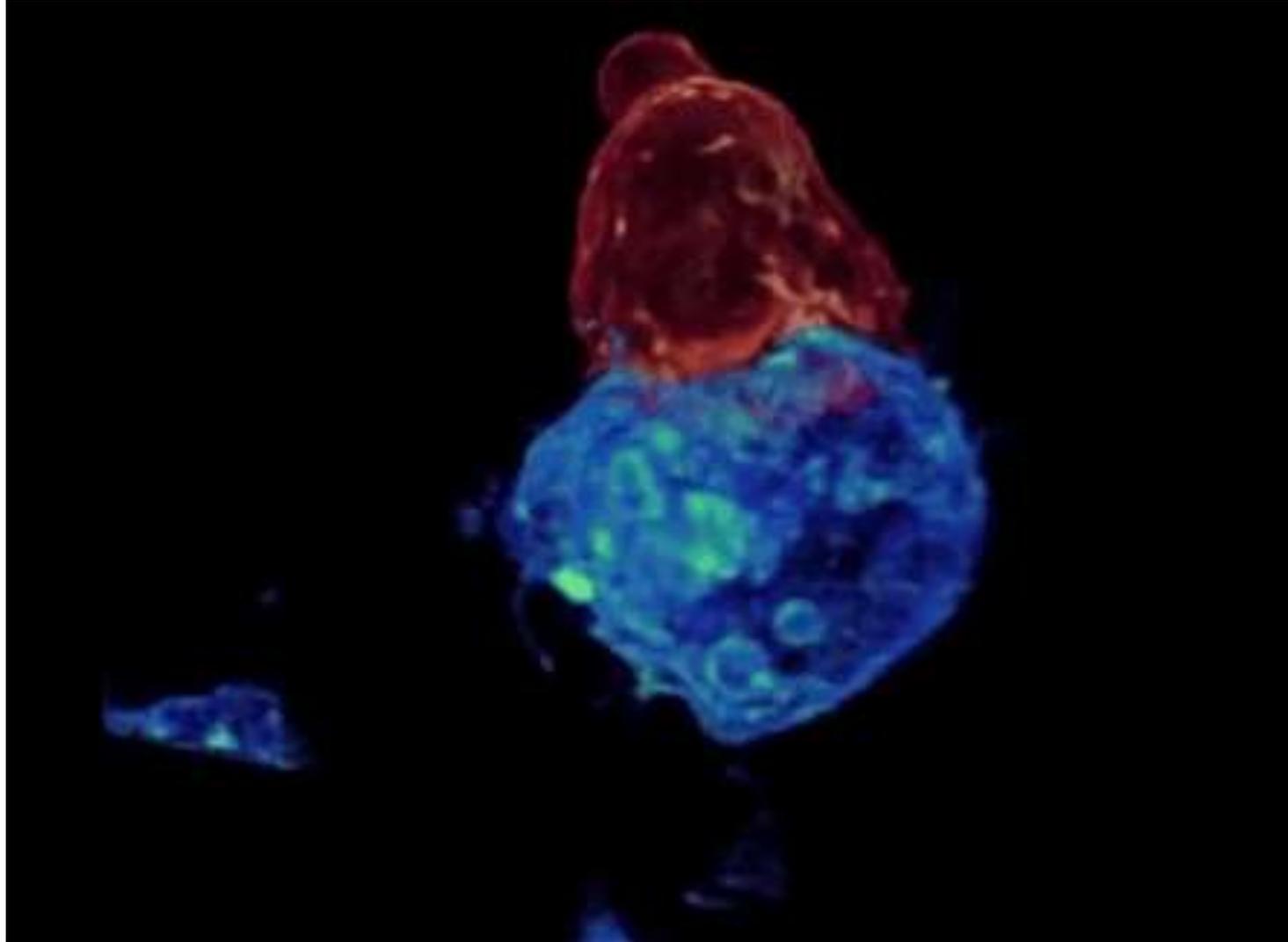
Az immunológiai szinapszis kialakulása

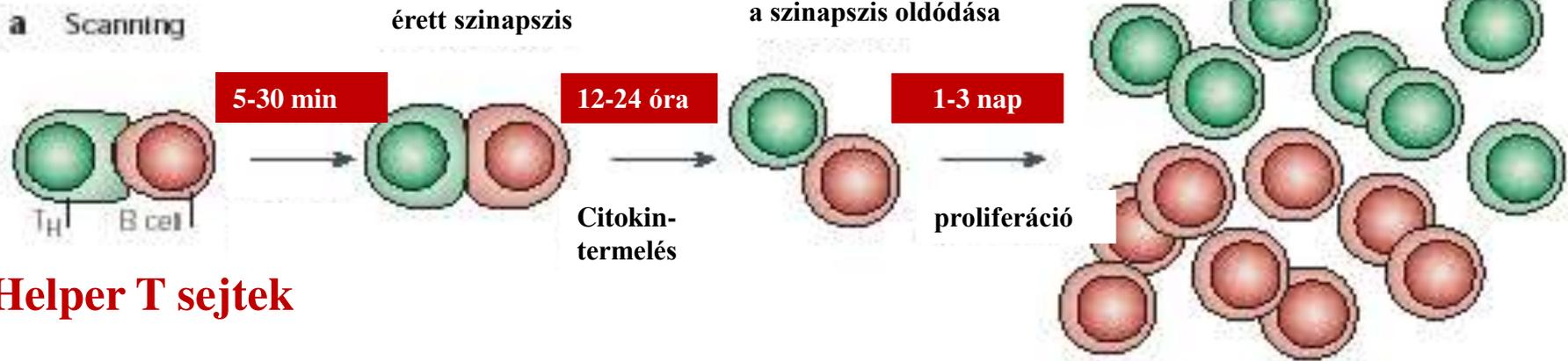


Az immunológiai szinapszis kialakulása

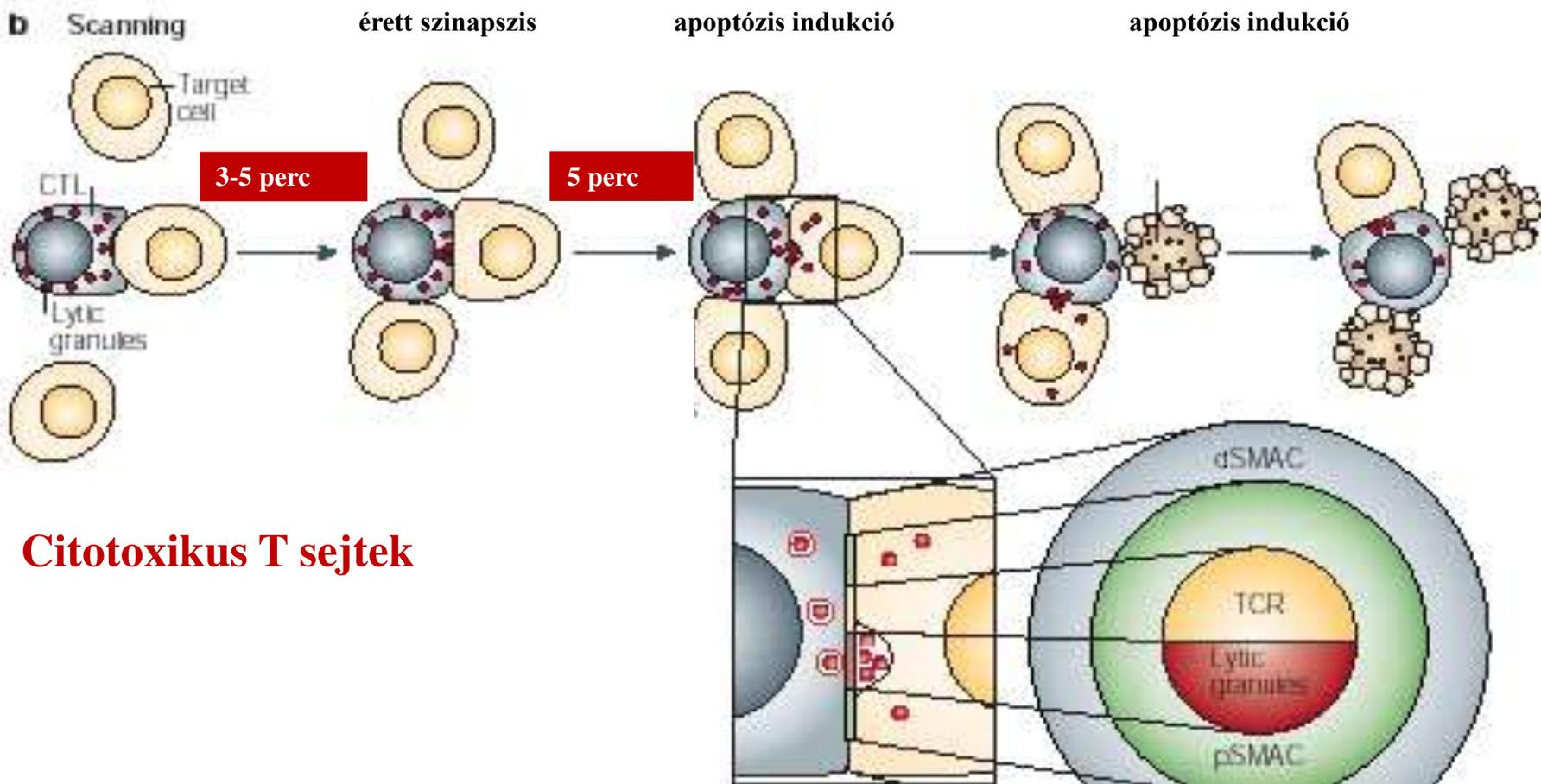


Az immunológiai szinapszis kialakulása



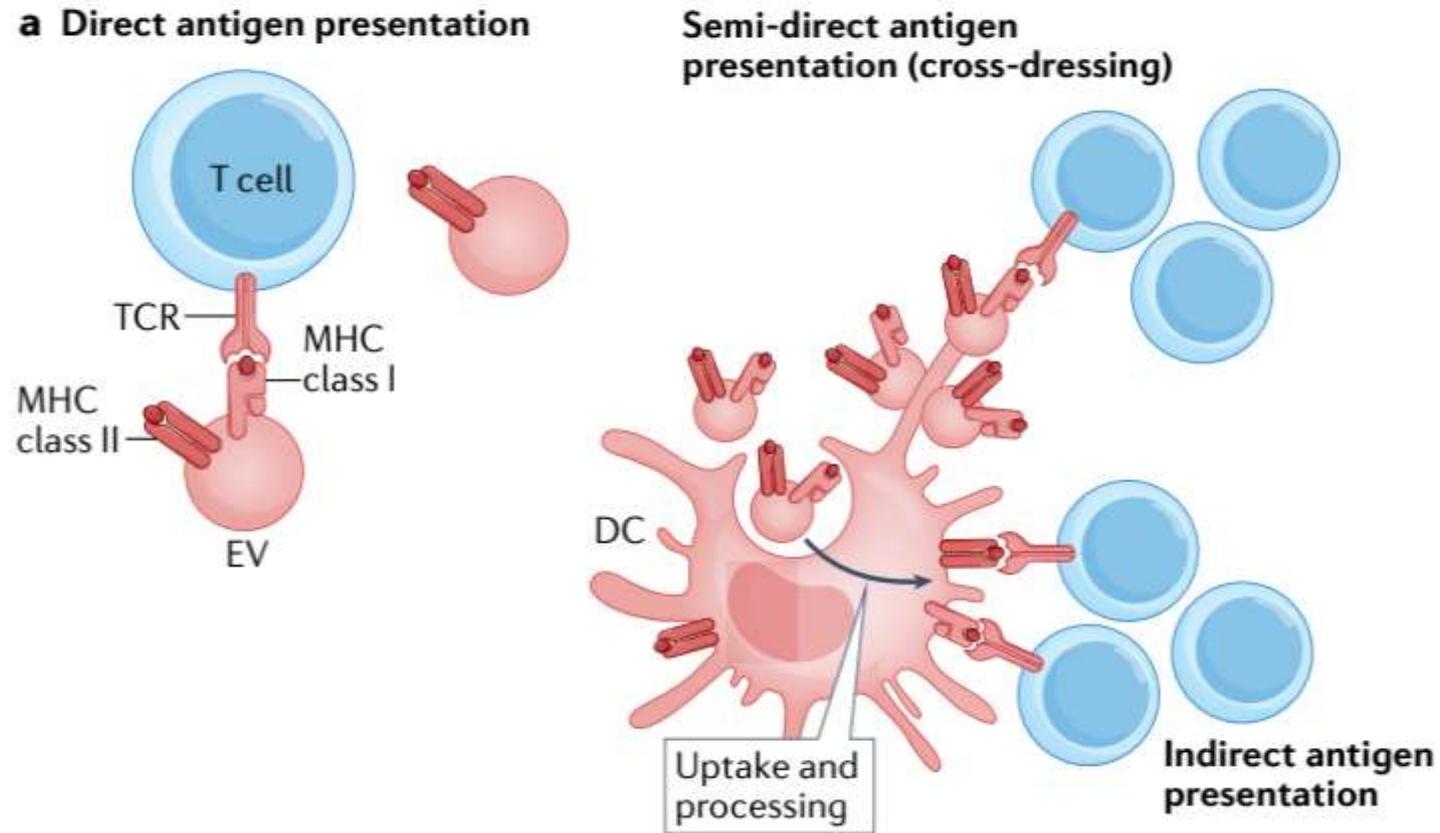


Helper T sejtek

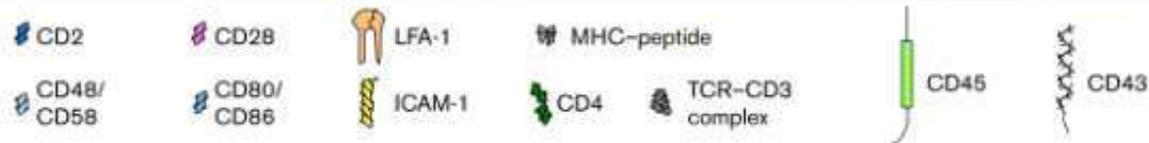
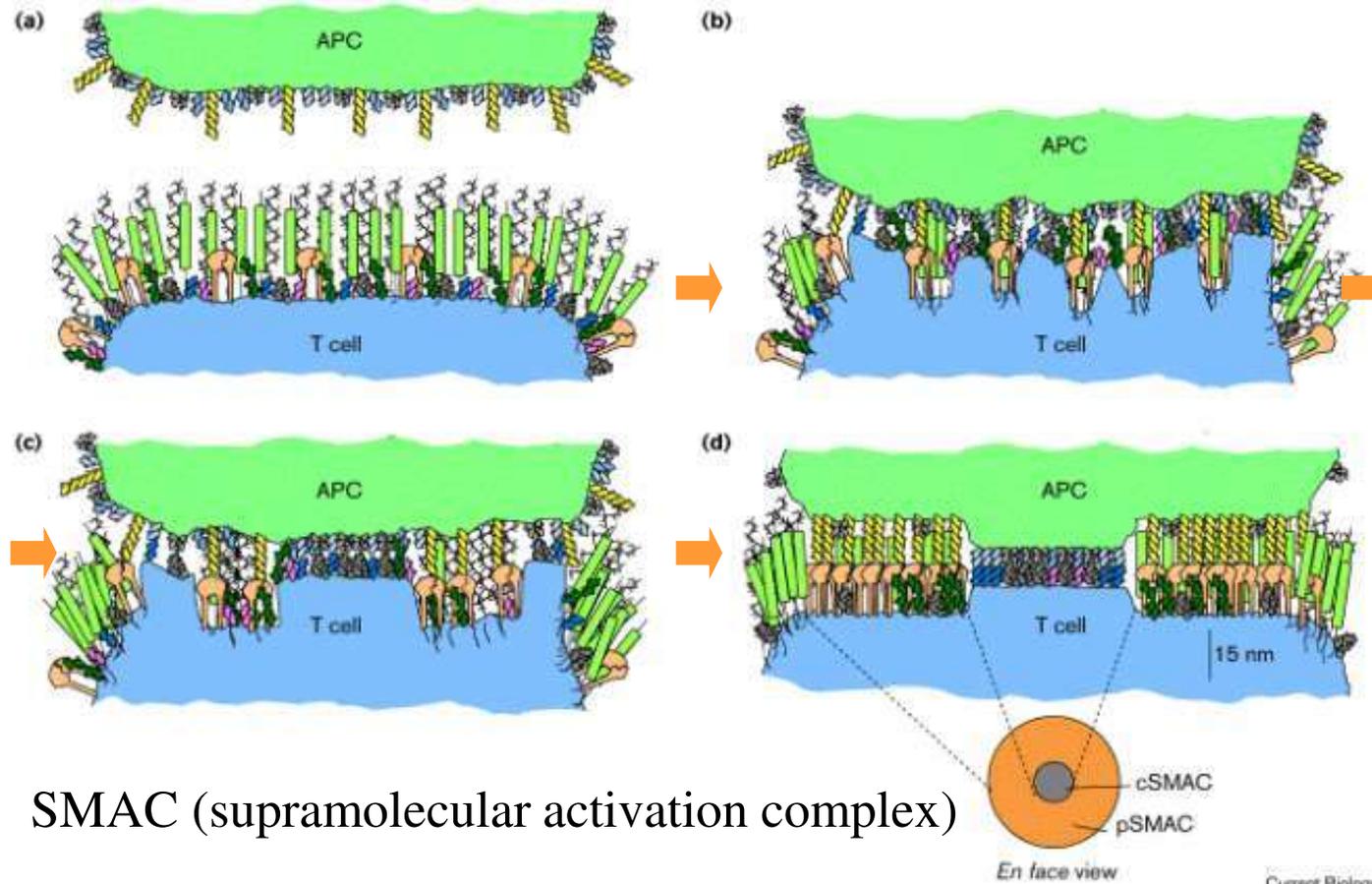


Citotoxikus T sejtek

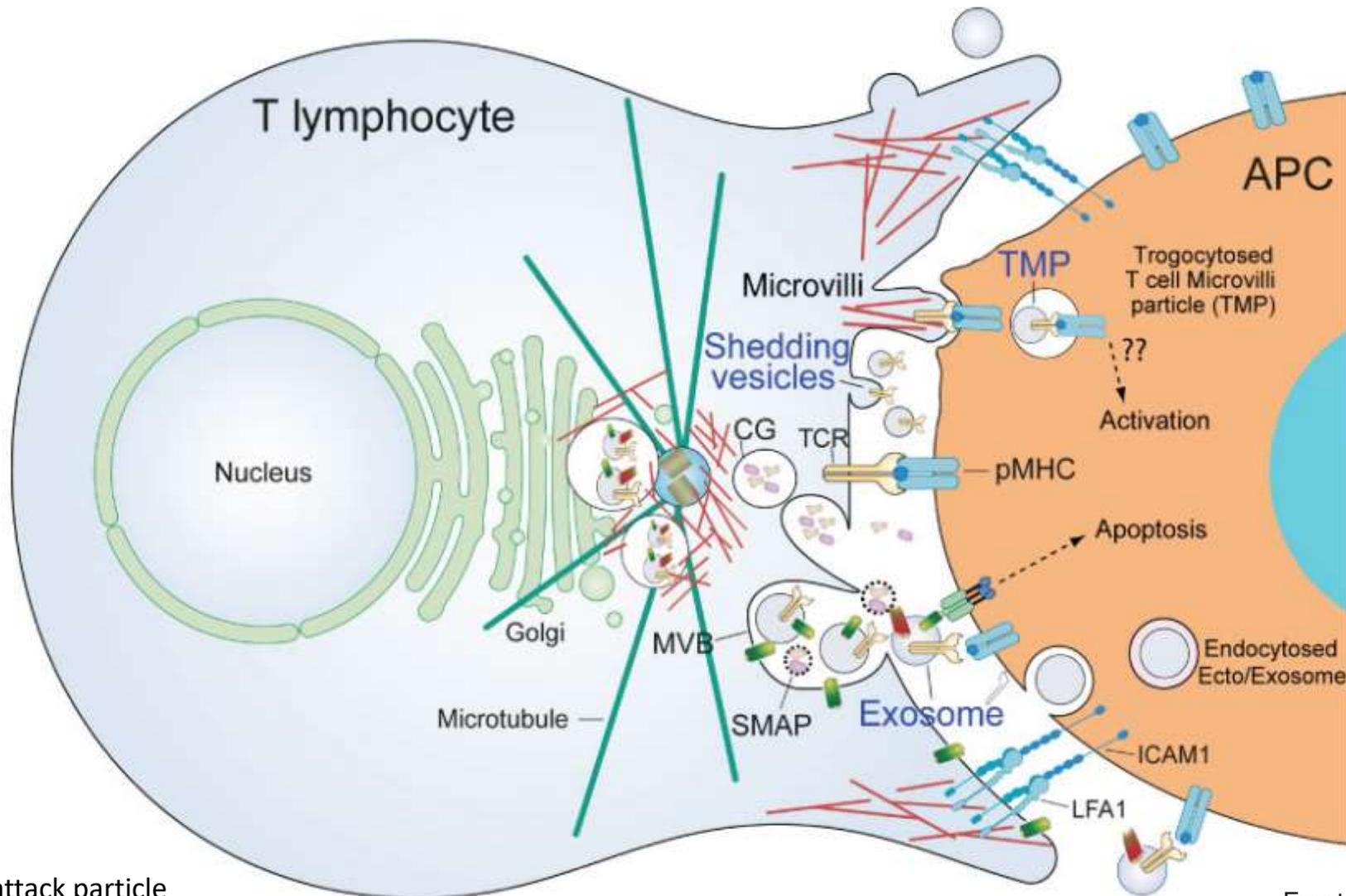
Az extracelluláris vezikulák szerepe az antigén bemutatásban



Az immunológiai szinapszis kialakulása

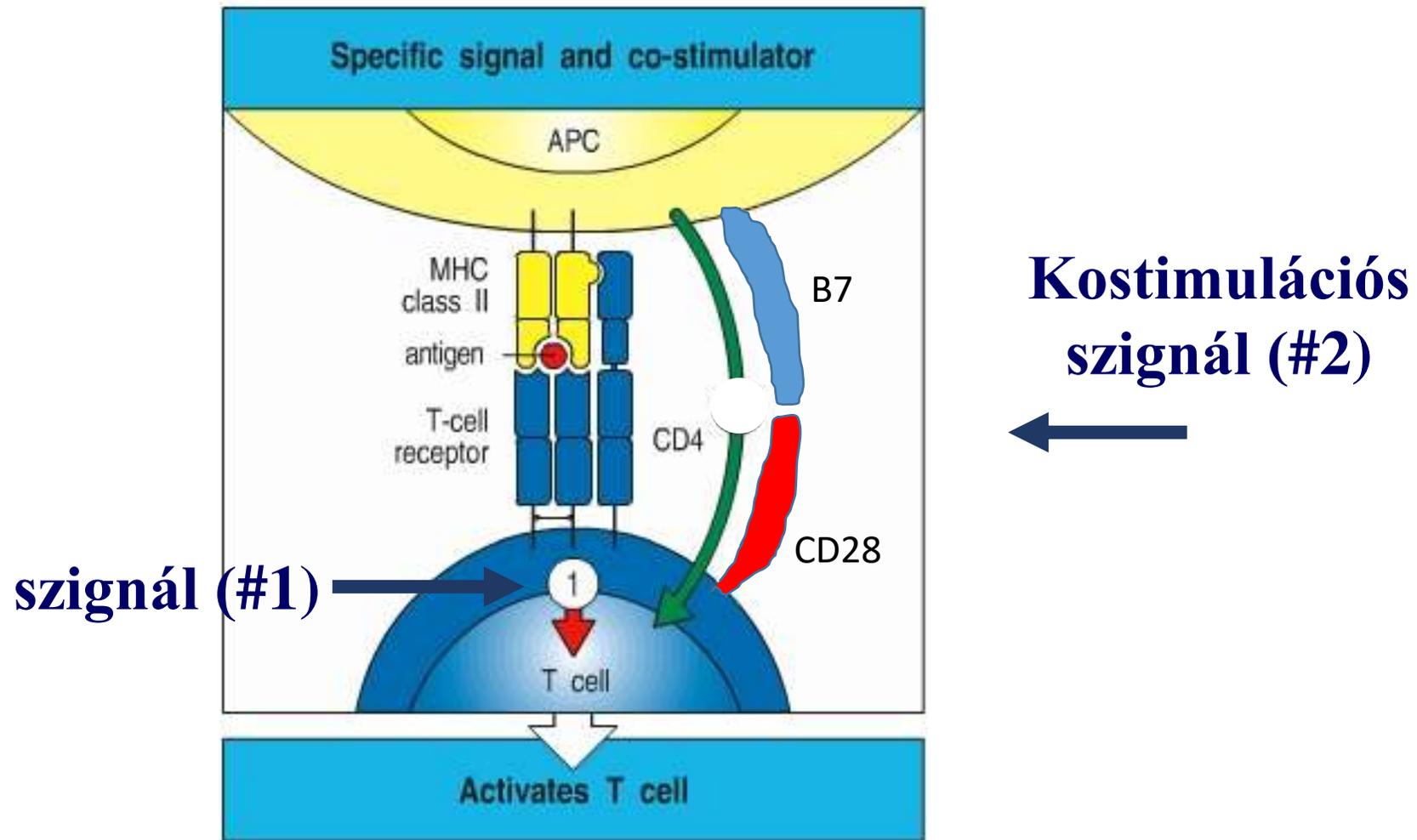


Az immunológiai szinapszis



SMAP=supramolecular attack particle

A T sejt aktivációhoz legalább két szignál kell (#1és #2)



T sejt anergia

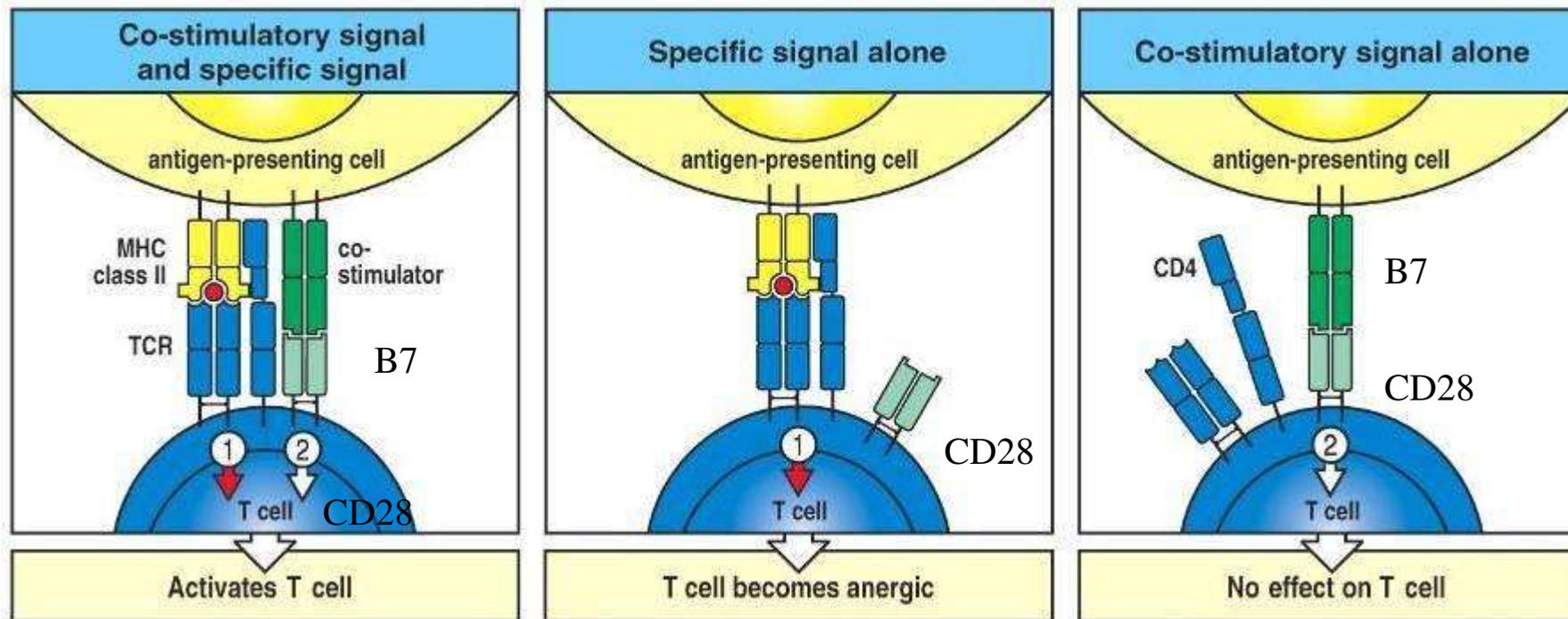
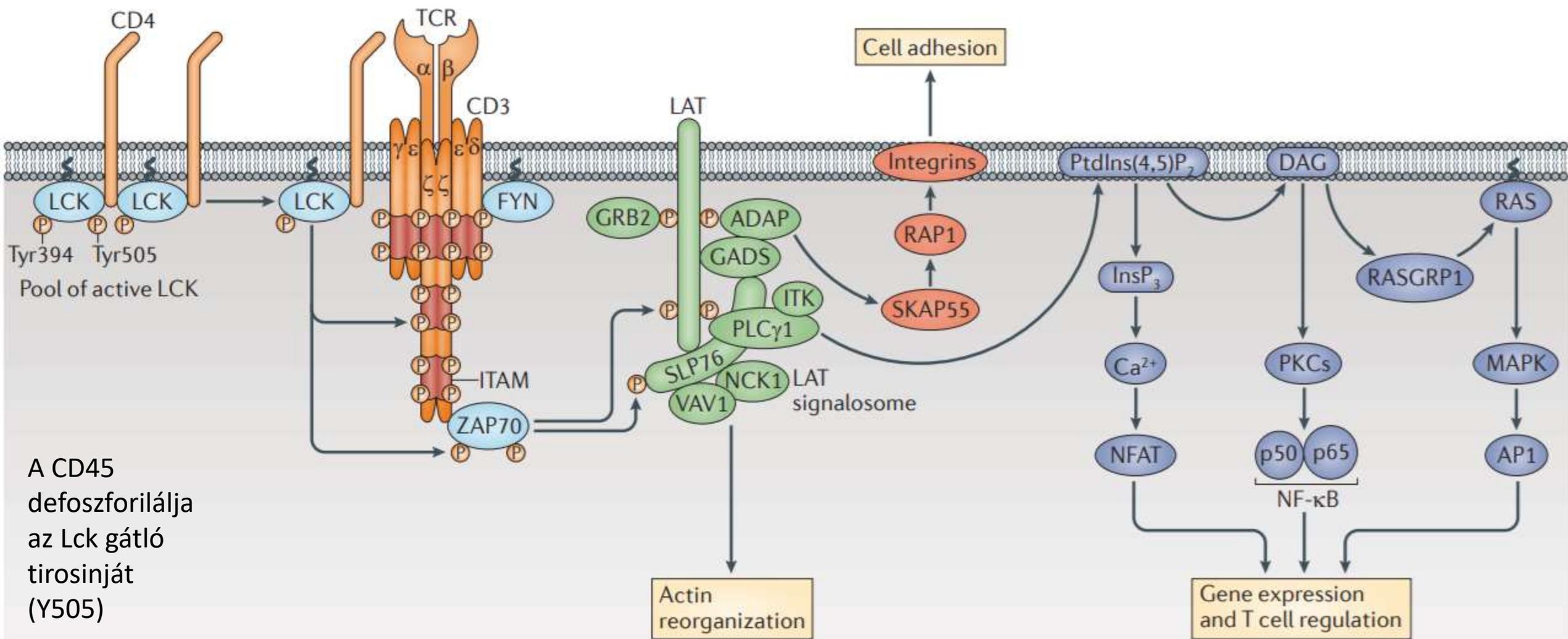
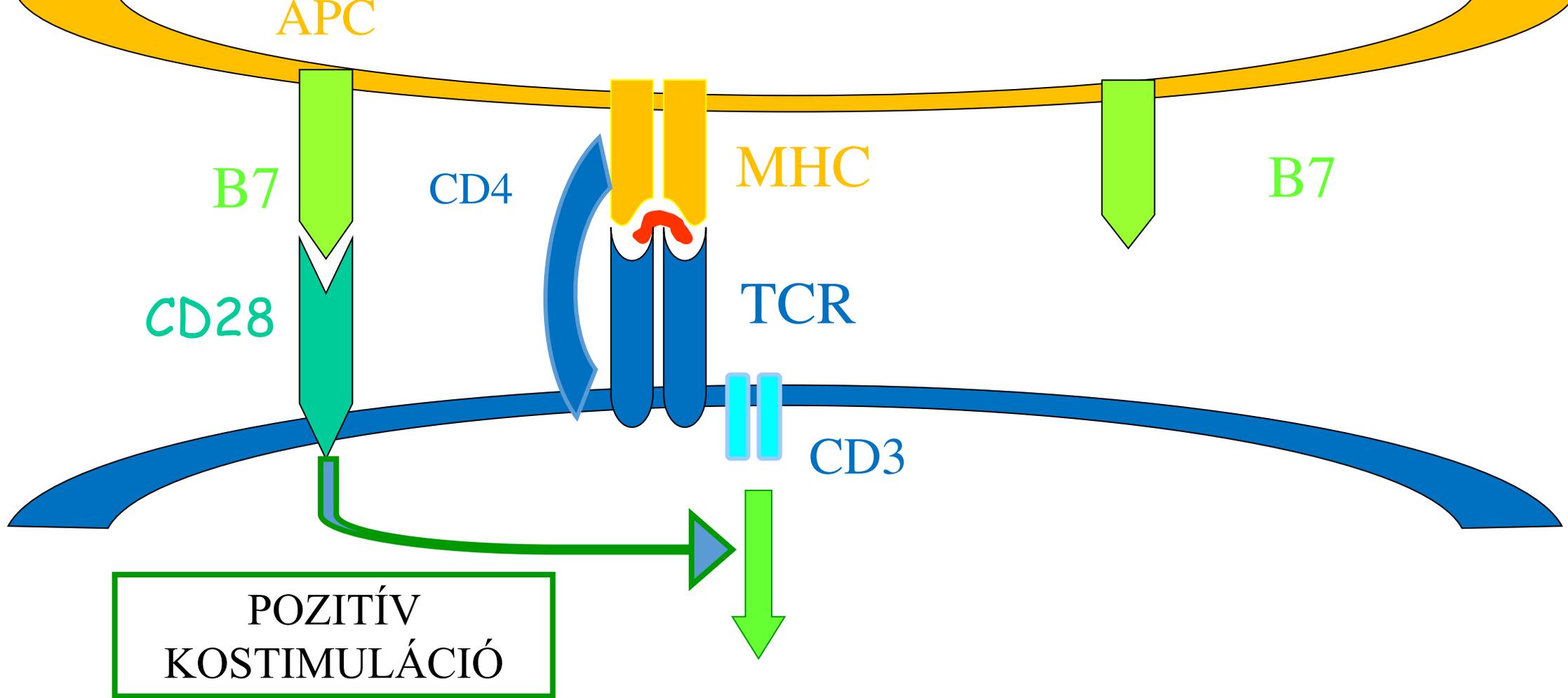


Figure 6-19 The Immune System, 2/e (© Garland Science 2005)

kostimulációs szignál
hiányában

A TCR-en keresztüli jelátvitel





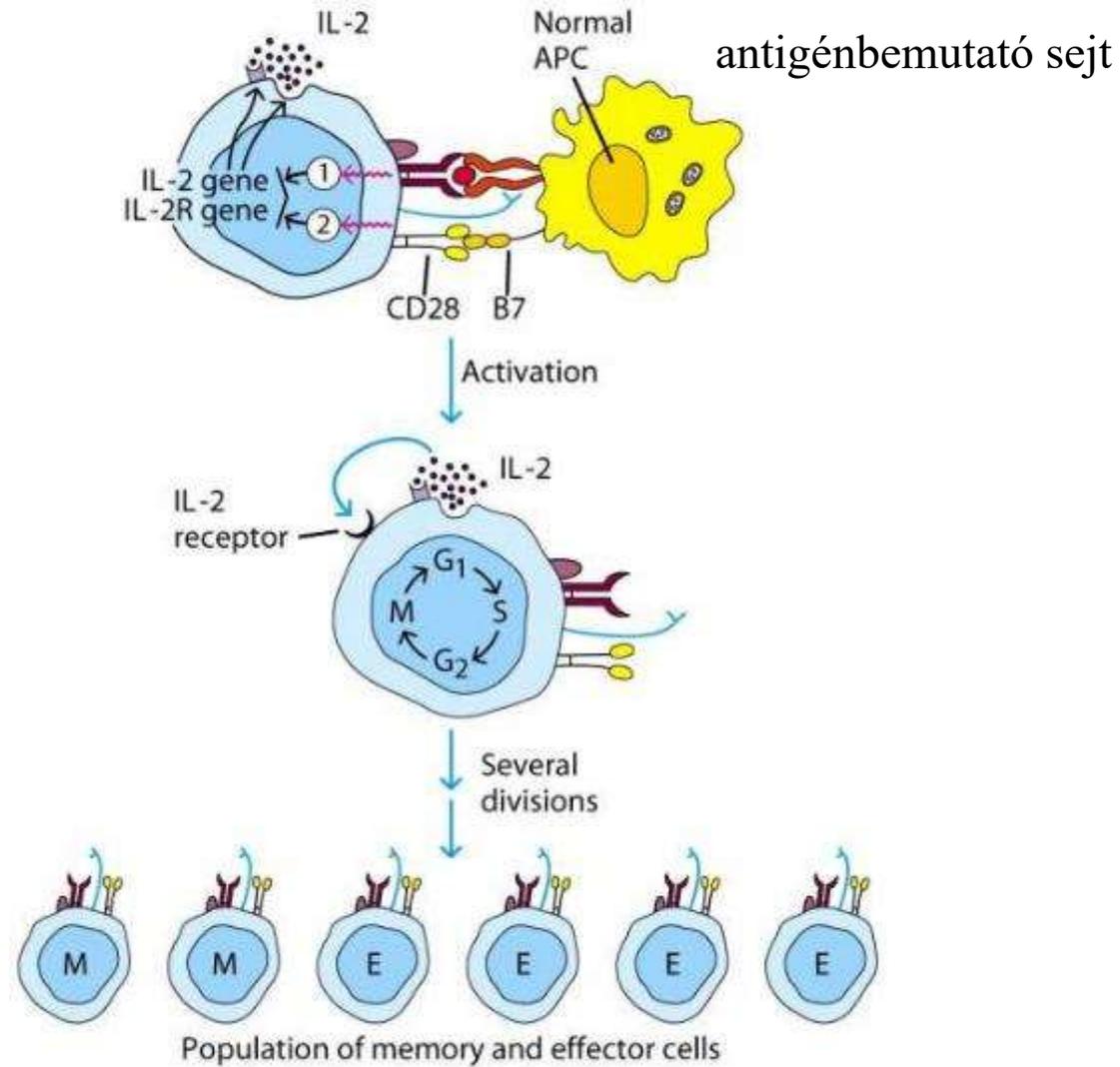
POZITÍV
KOSTIMULÁCIÓ

T sejt

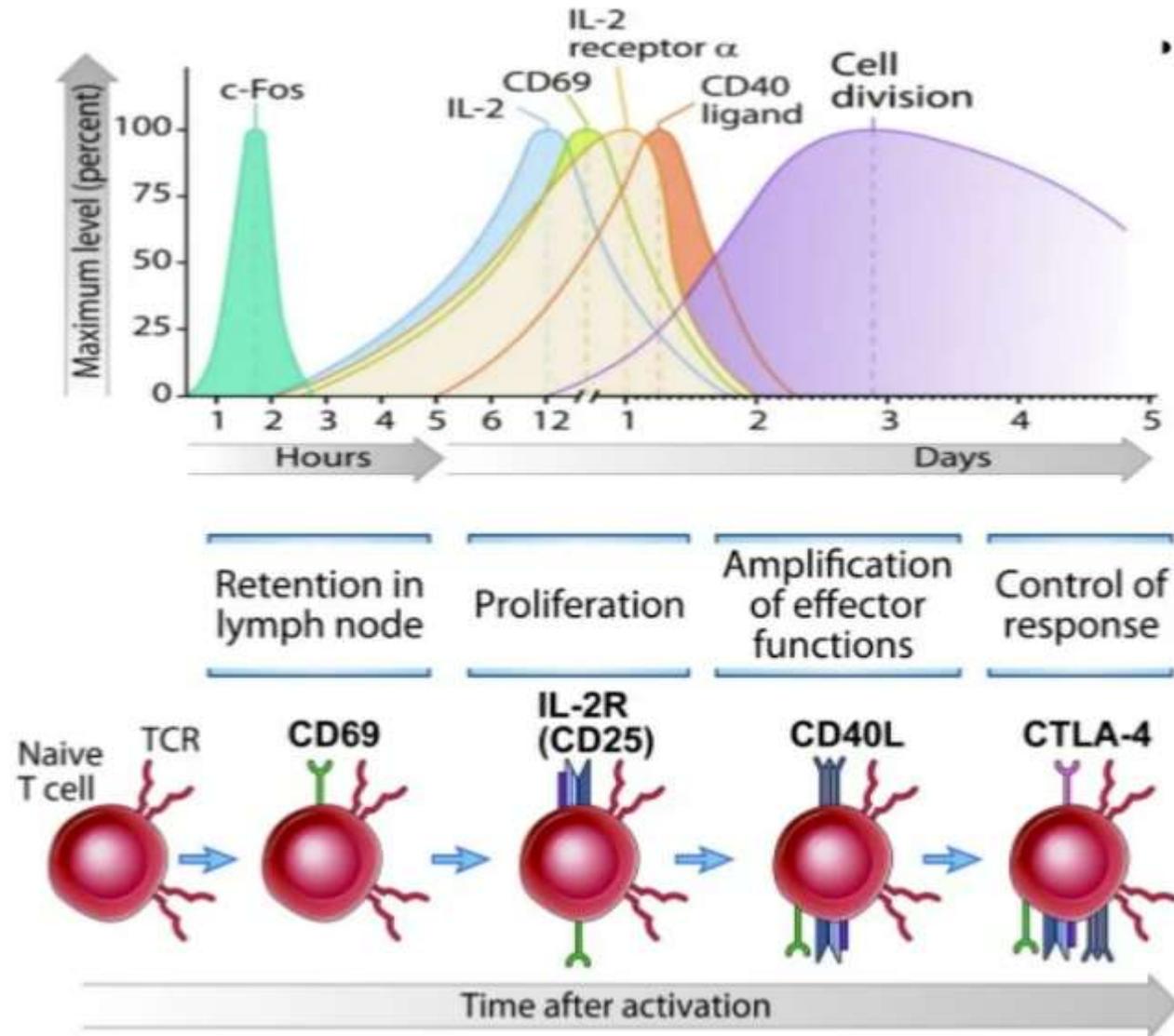


sejtmag
IL-2 mRNS

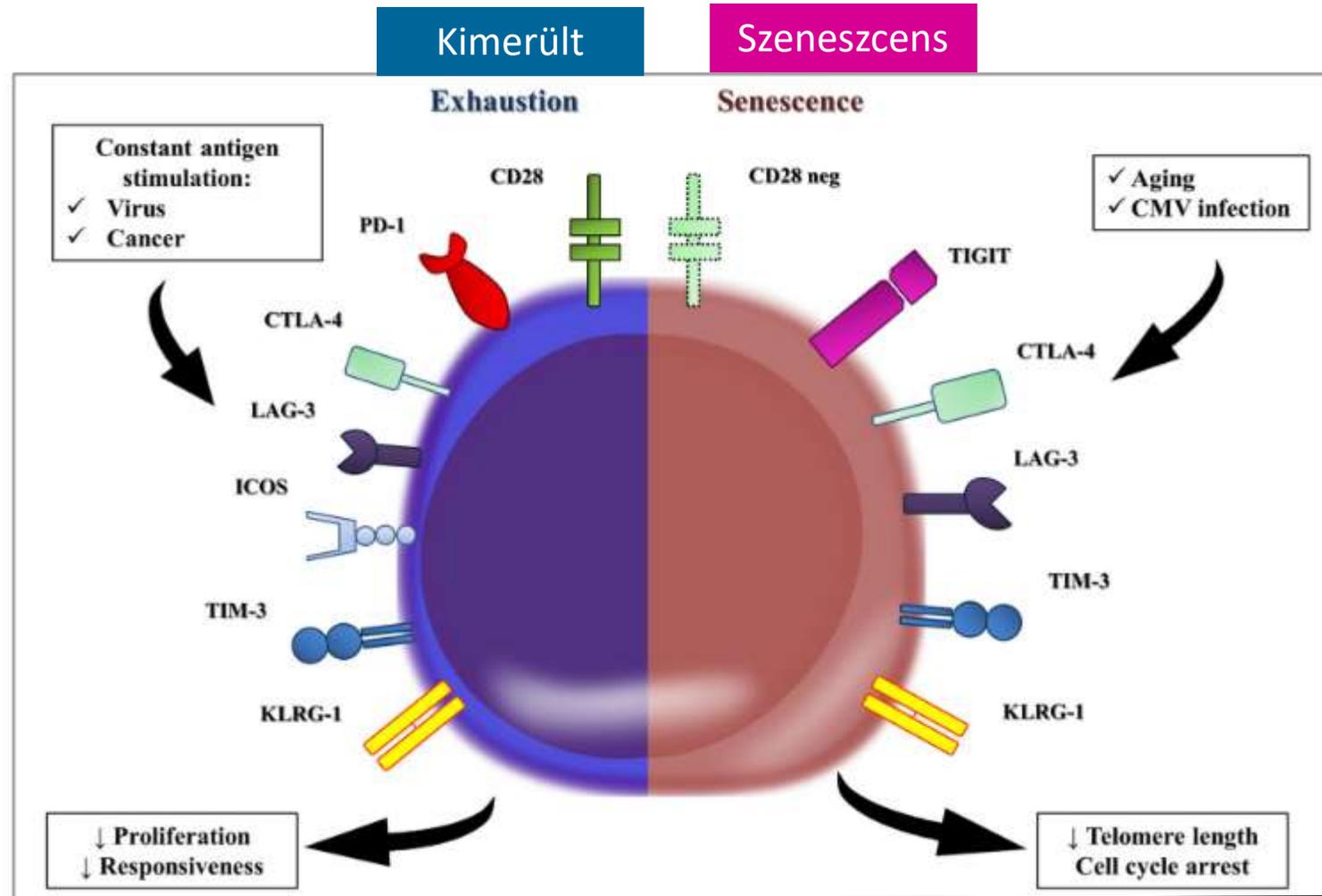
Az IL-2 autokrin T sejt növekedési faktor



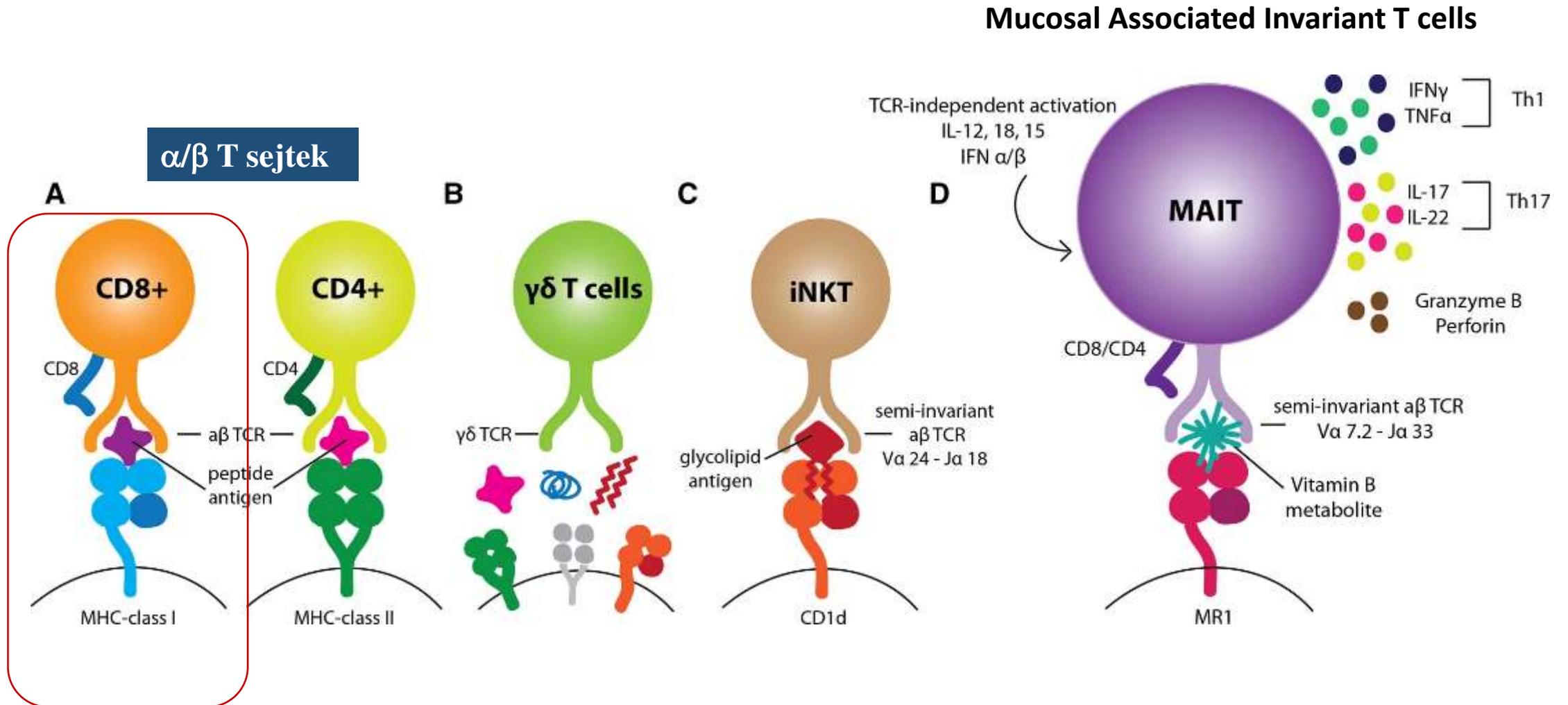
A T sejt aktiváció során bekövetkező génexpressziós változások



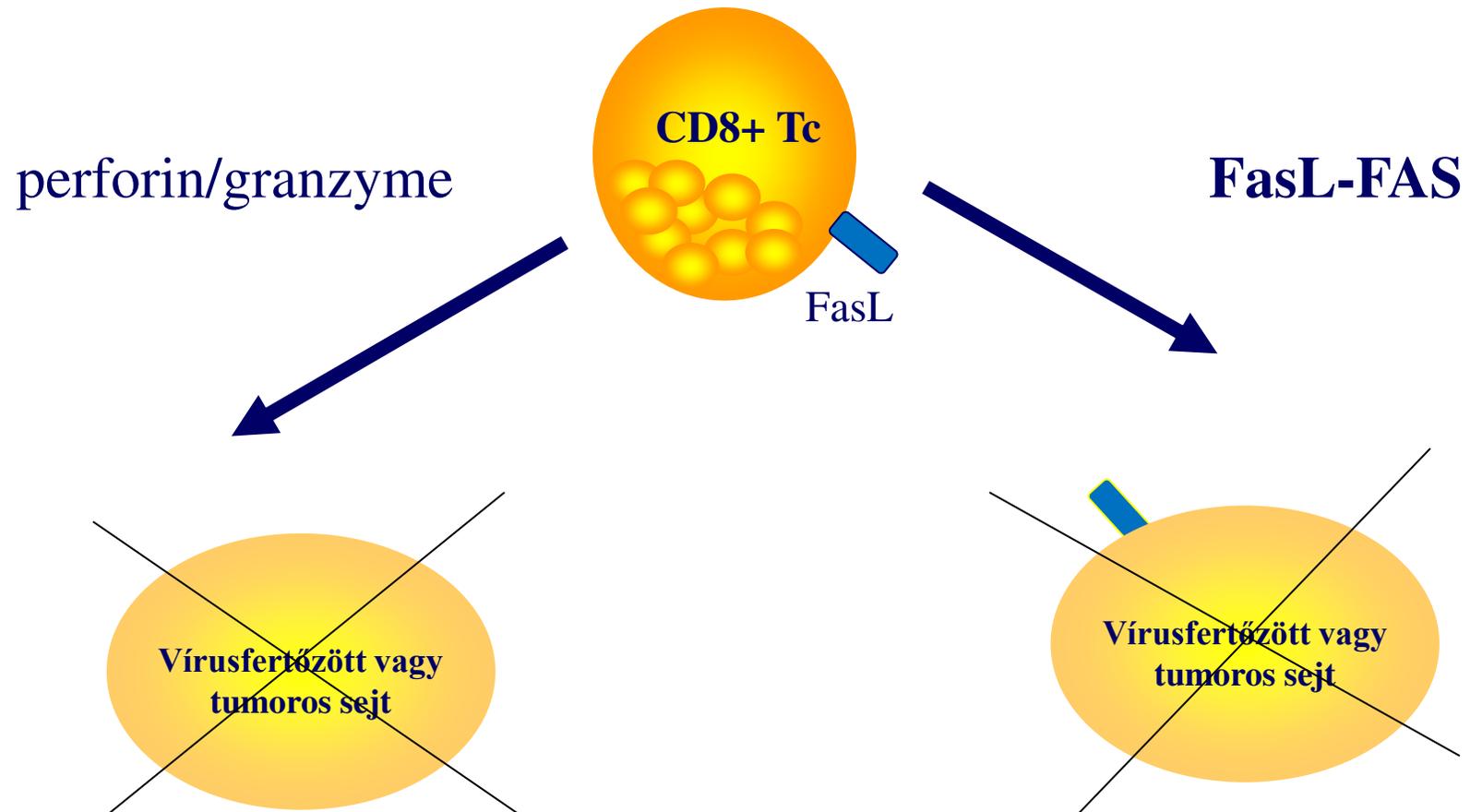
A T limfociták kimerülése és öregedése



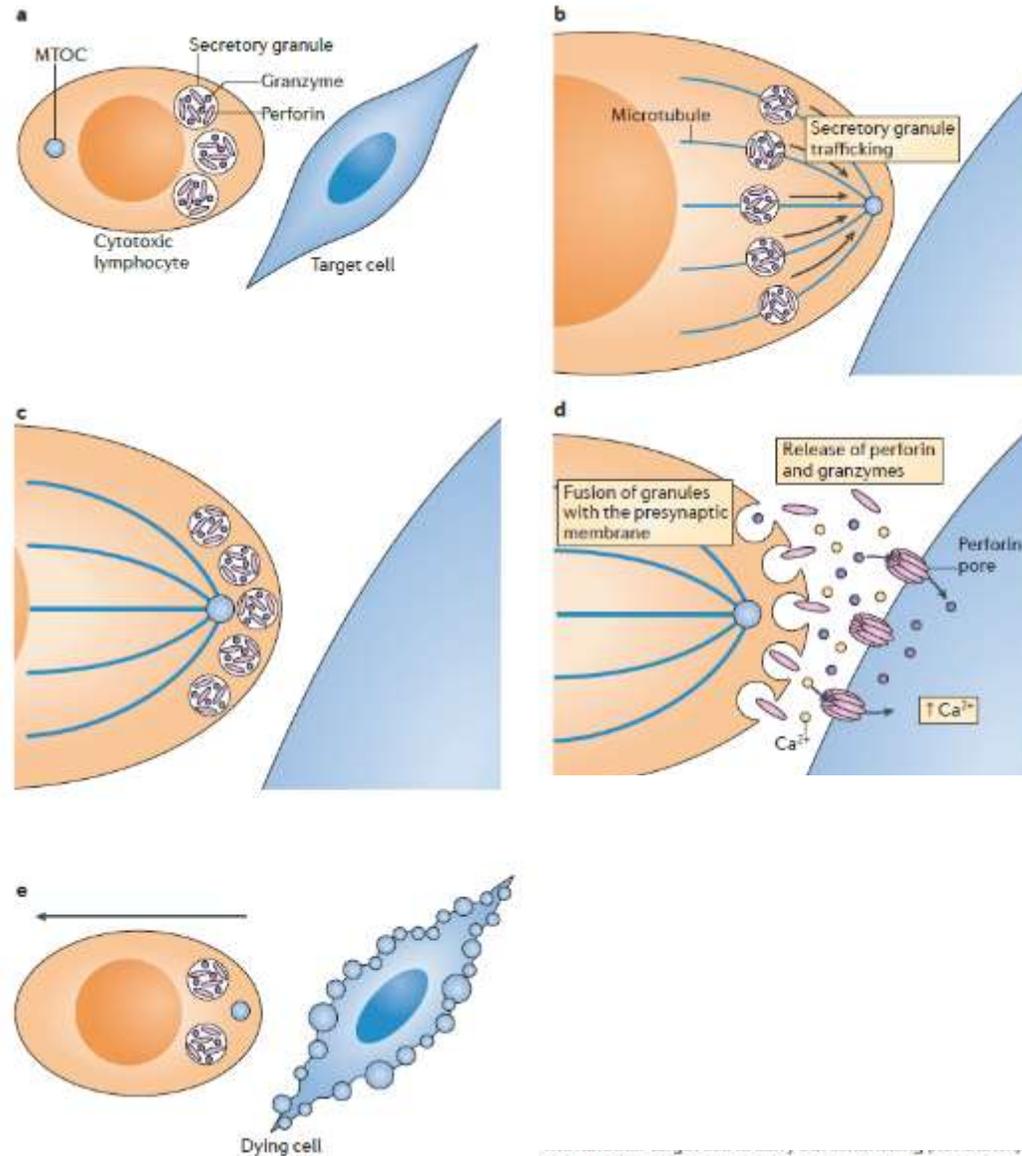
A T sejtek típusai



CD8+ citotoxikus T sejt



Citotoxikus T sejtek



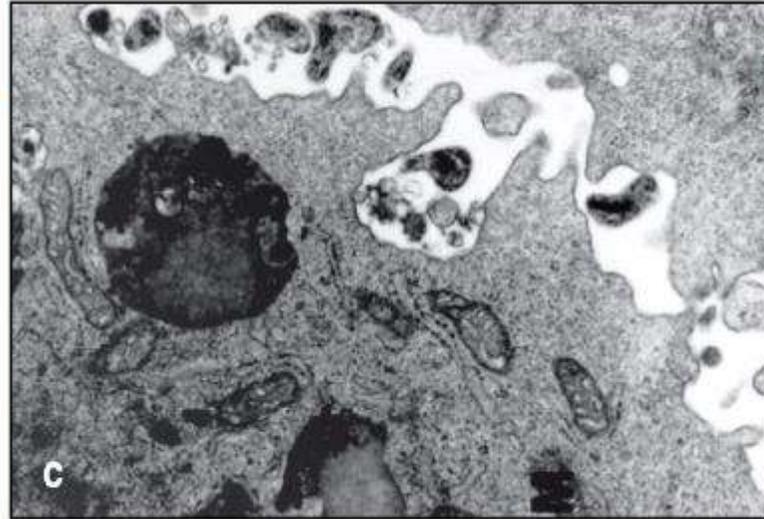
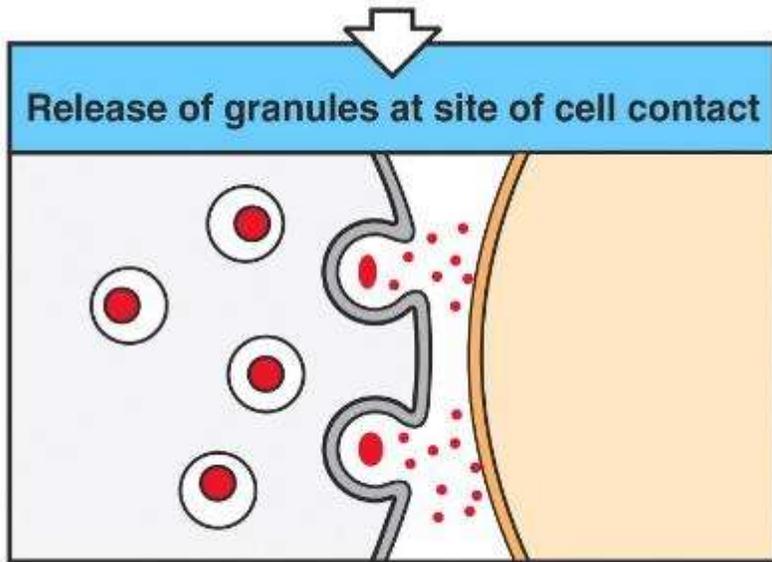


Figure 8-29 part 3 of 3 Immunobiology, 6/e. (© Garland Science 2005)

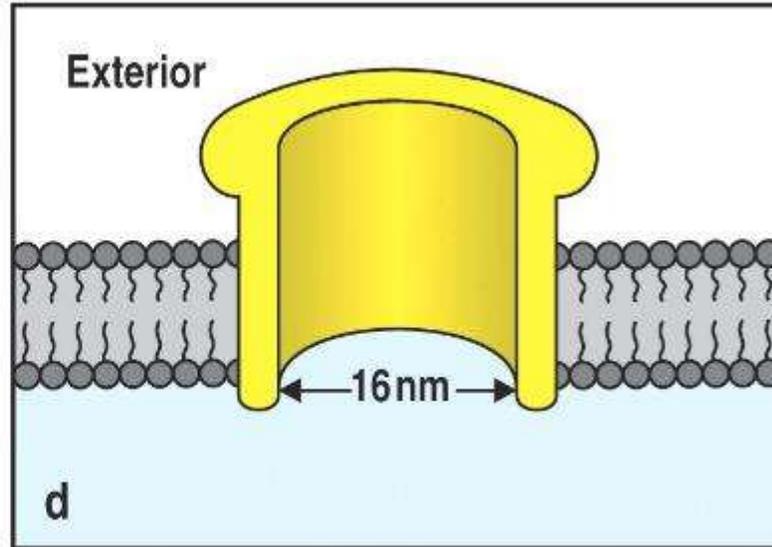
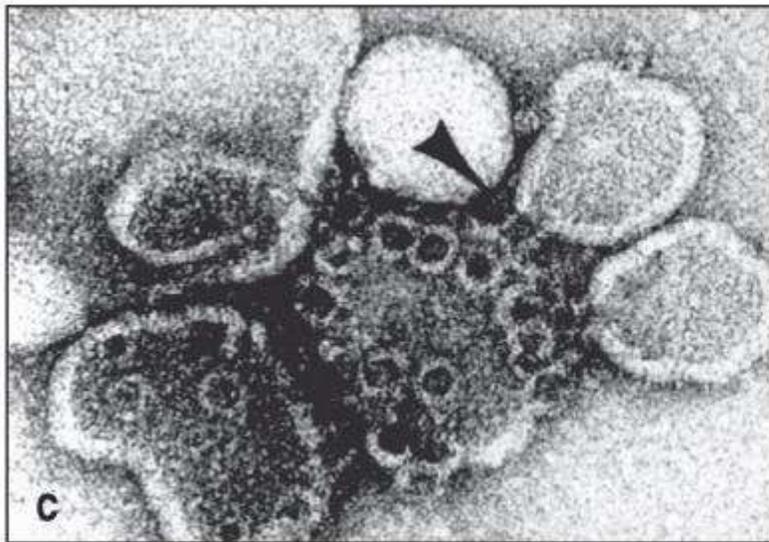
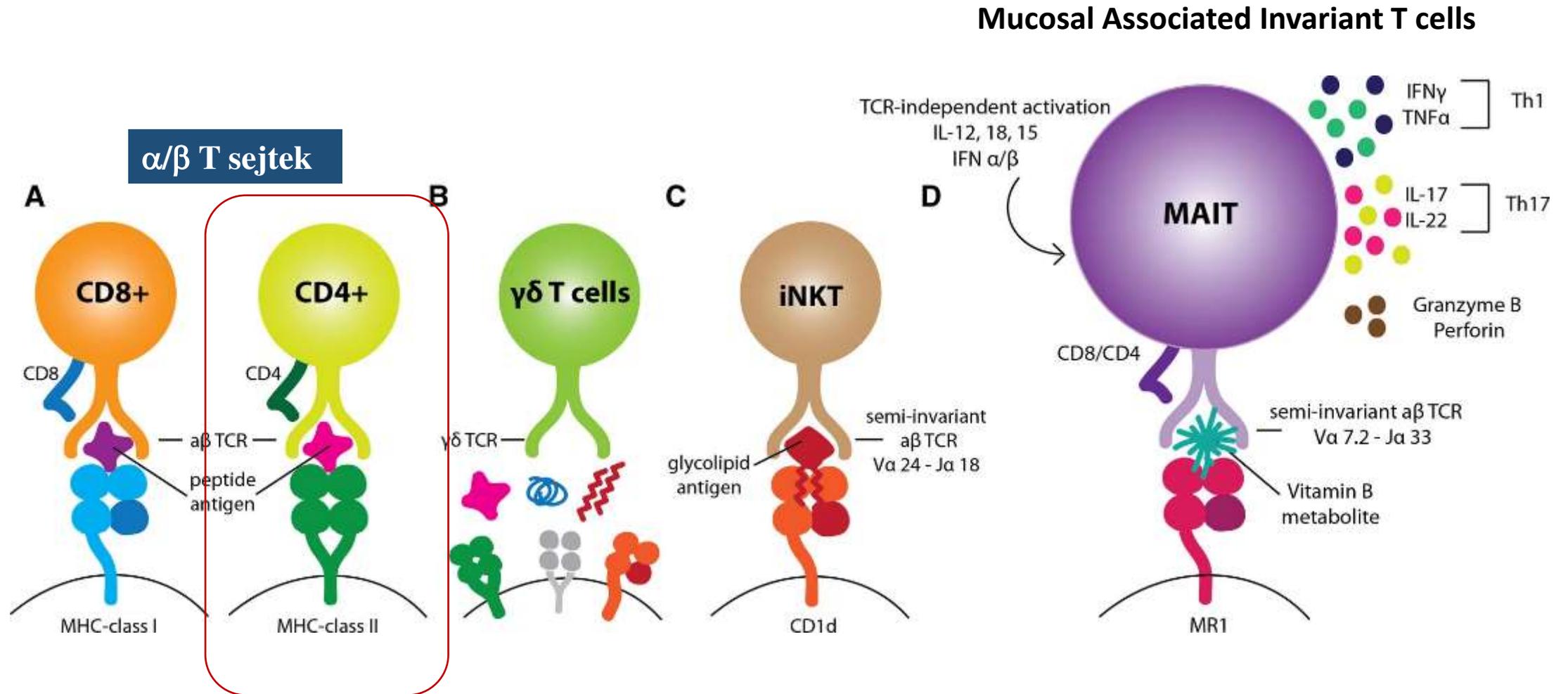


Figure 8-36 part 2 of 2 Immunobiology, 6/e. (© Garland Science 2005)



A T sejtek típusai

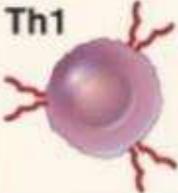
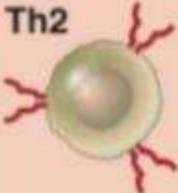
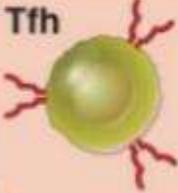
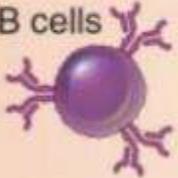


A CD4+ helper T sejtek fő típusai

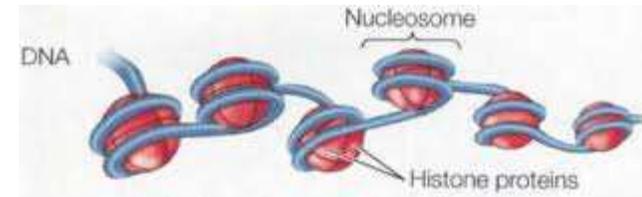
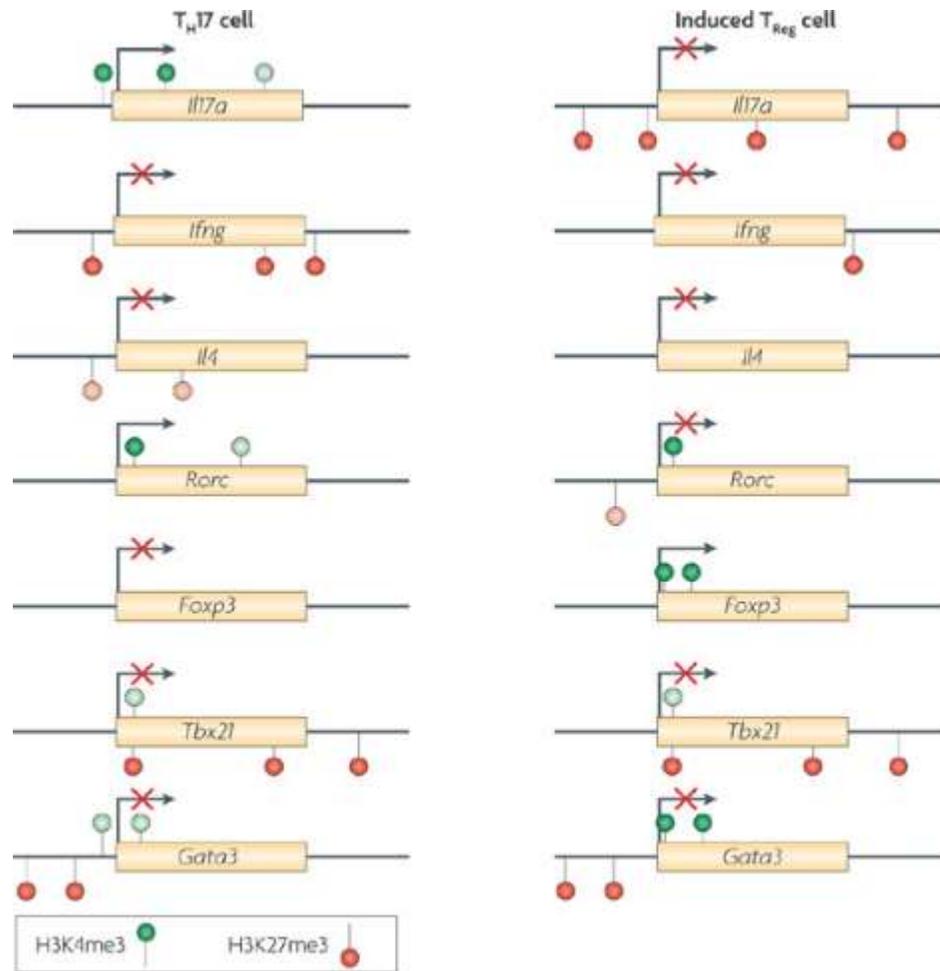
I-es típusú

II-es típusú

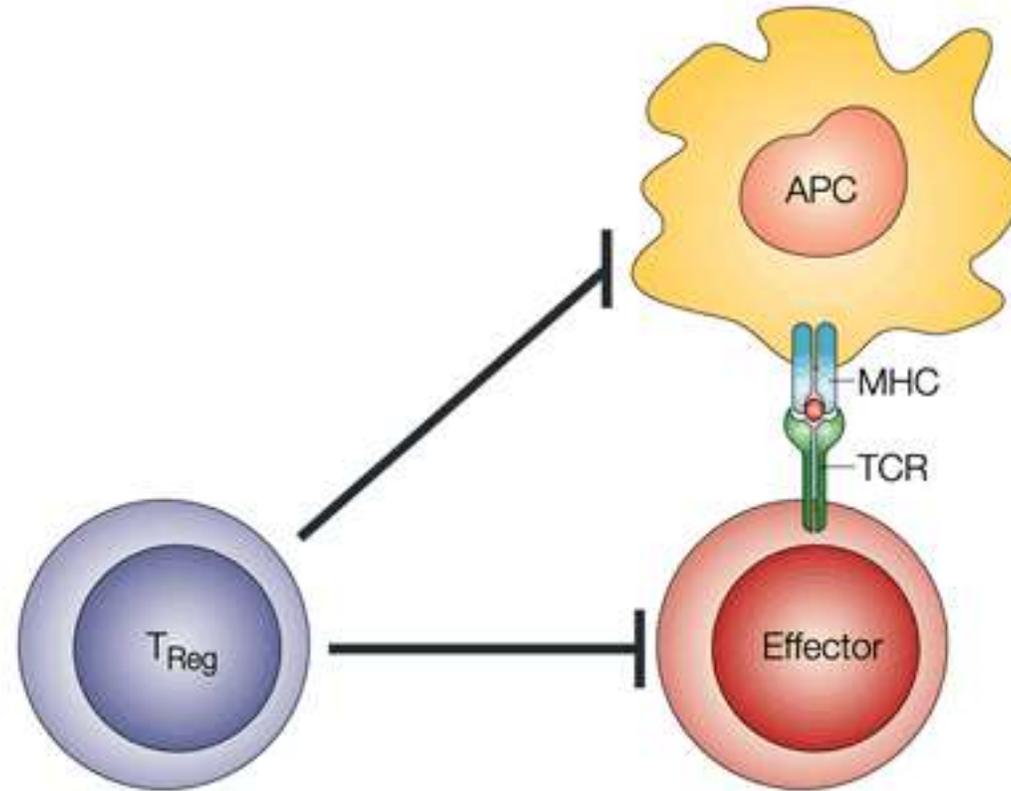
III-as típusú

Effector T cells	Defining cytokines	Principal target cells	Major immune reactions	Host defense	Role in disease
Th1 	IFN- γ	Macrophages 	Macrophage activation	Intracellular pathogens	Autoimmunity; chronic inflammation
Th2 	IL-4 IL-5 IL-13	Eosinophils 	Eosinophil and mast cell activation; alternative macrophage activation	Helminths	Allergy
Th17 	IL-17 IL-22	Neutrophils 	Neutrophil recruitment and activation	Extracellular bacteria and fungi	Autoimmunity; inflammation
Tfh 	IL-21 (and IFN- γ or IL-4)	B cells 	Antibody production	Extracellular pathogens	Autoimmunity (autoantibodies)

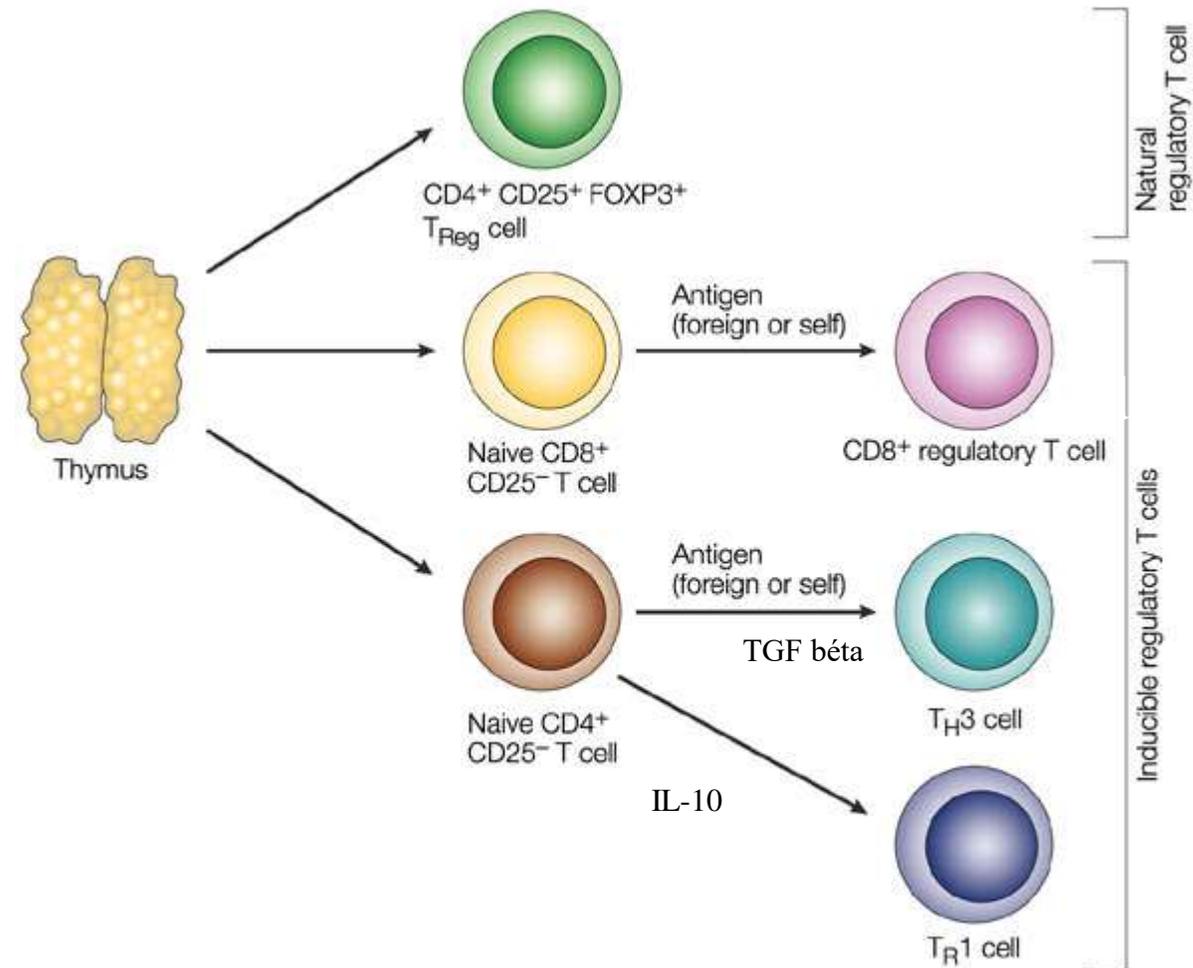
Epigenetikai változások felelősek a T sejt fenotípusok kialakításáért



Reguláló T sejtek

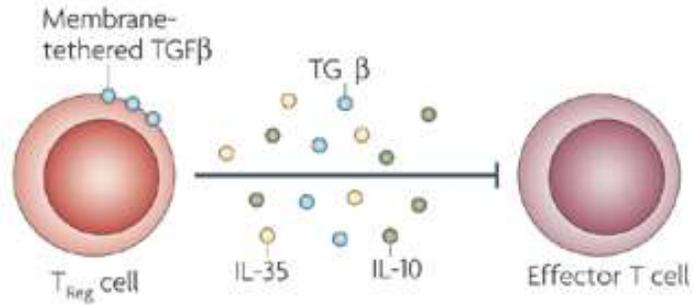


Reguláló T sejtek

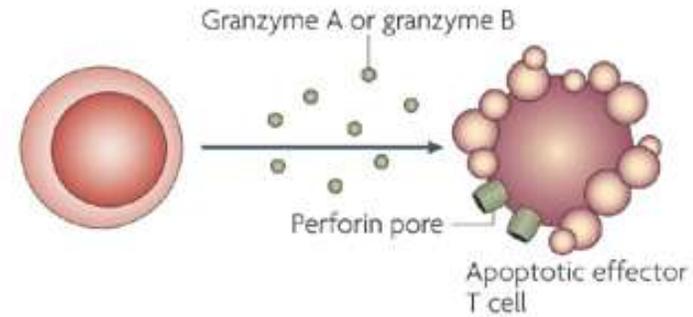


Reguláló T sejtek

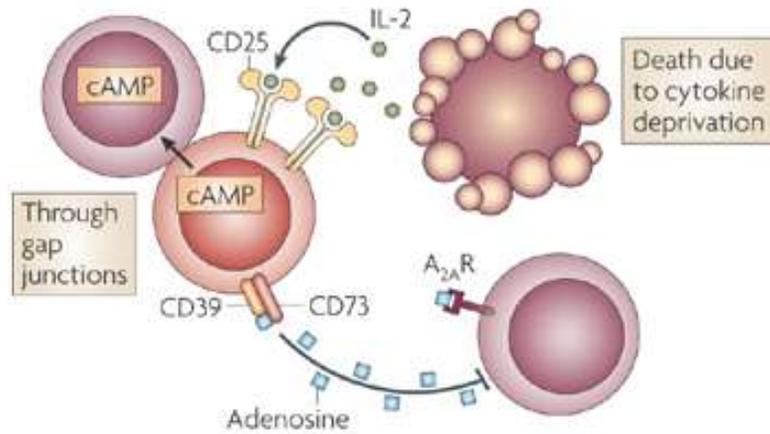
a Inhibitory cytokines



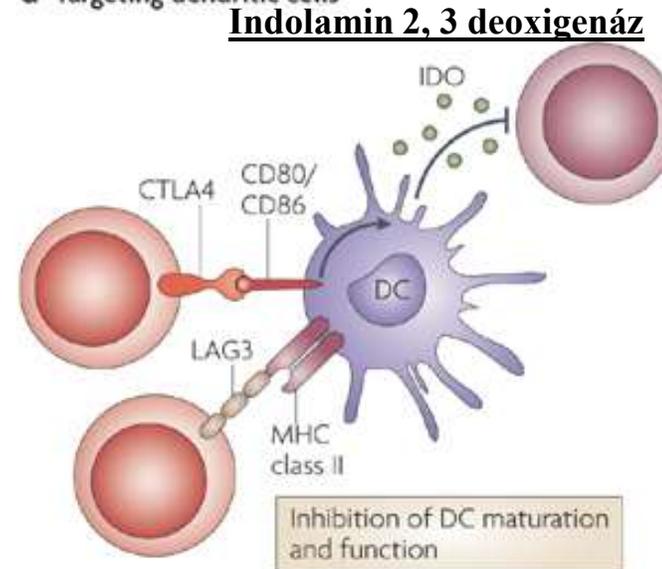
b Cytolysis



c Metabolic disruption

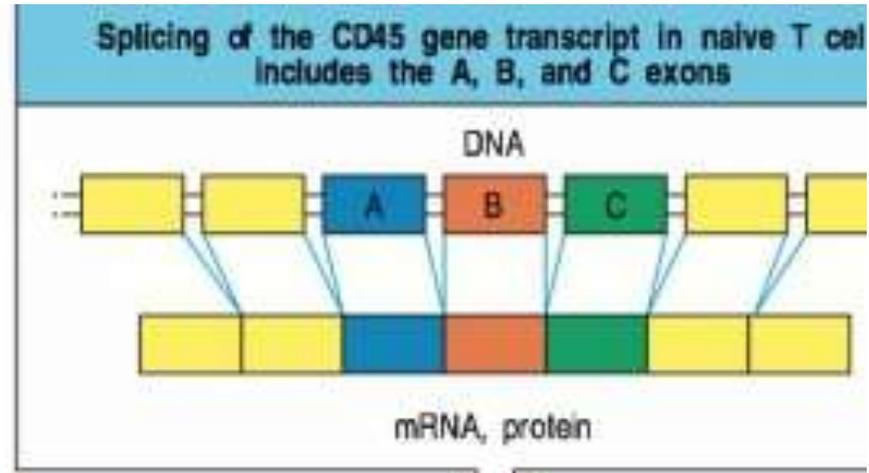
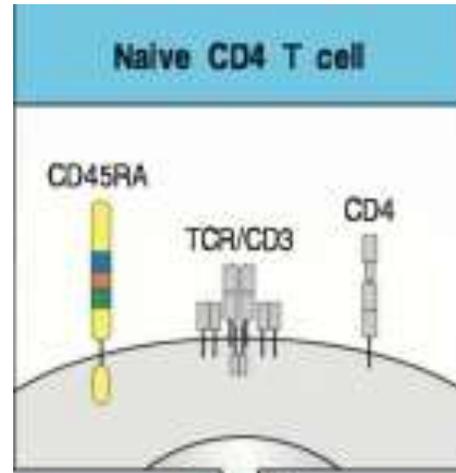


d Targeting dendritic cells

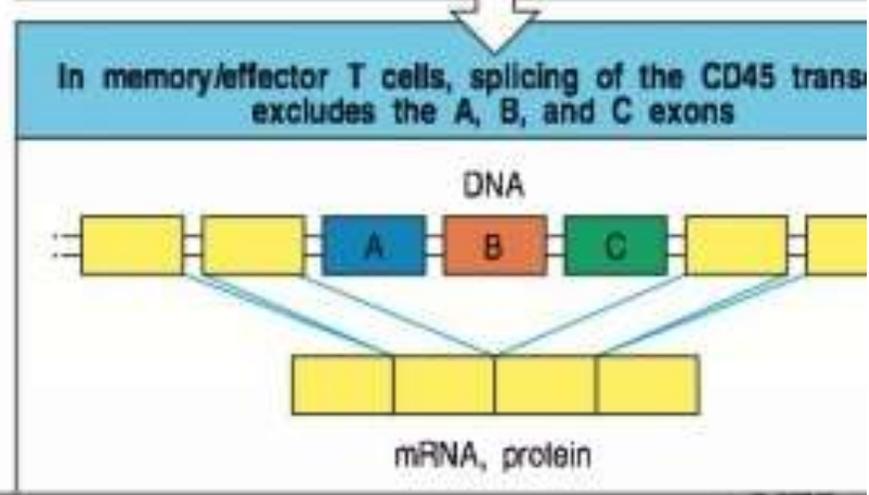
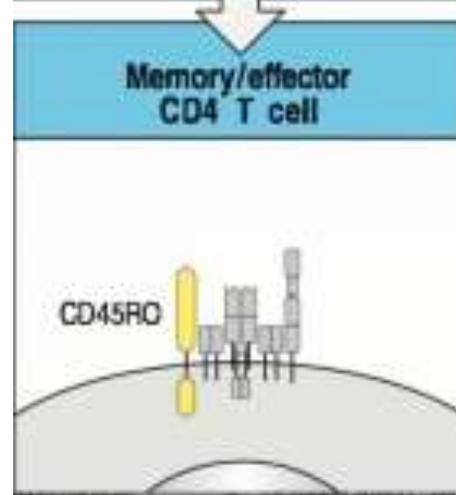


T sejt memória

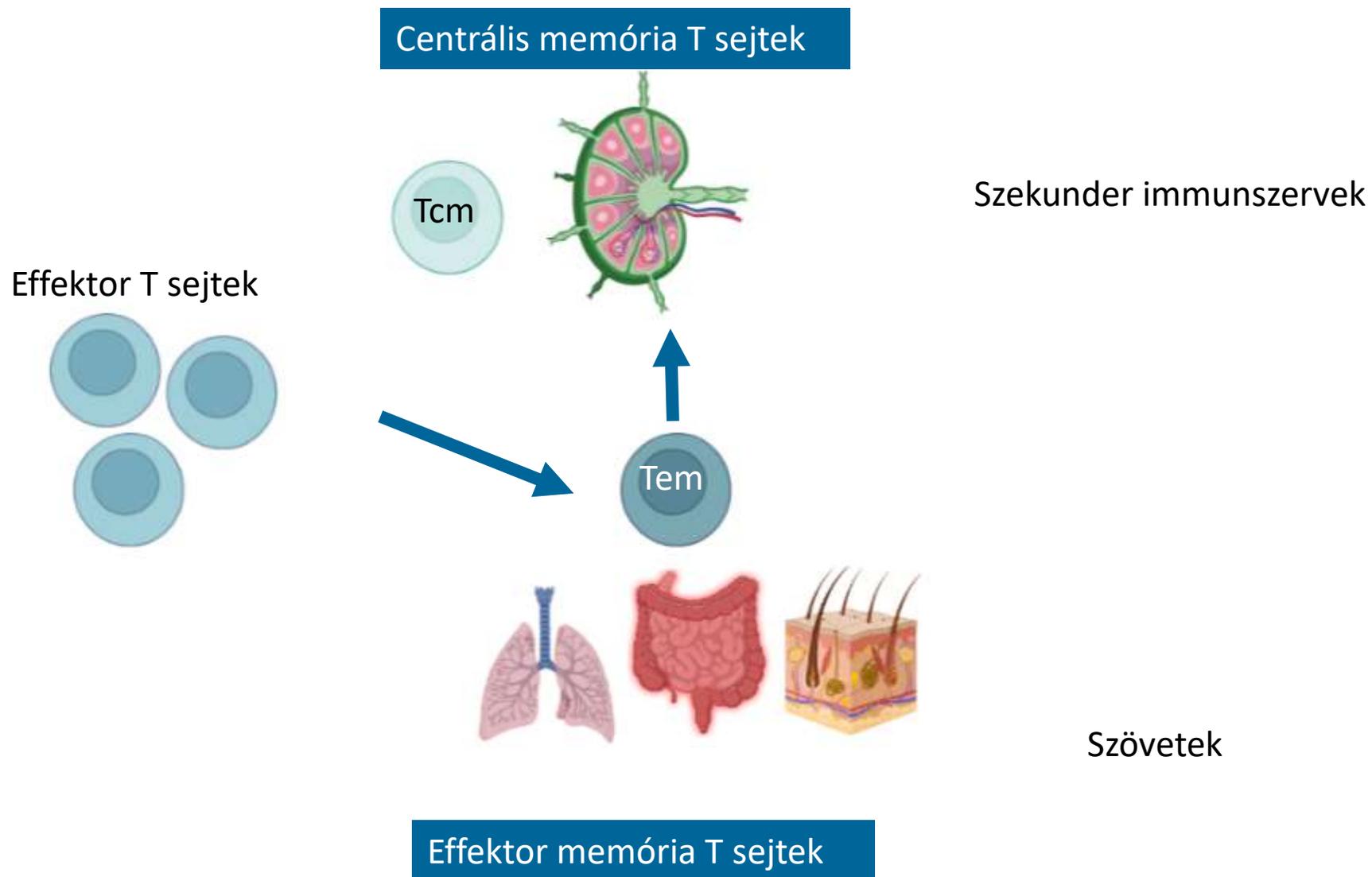
naiv



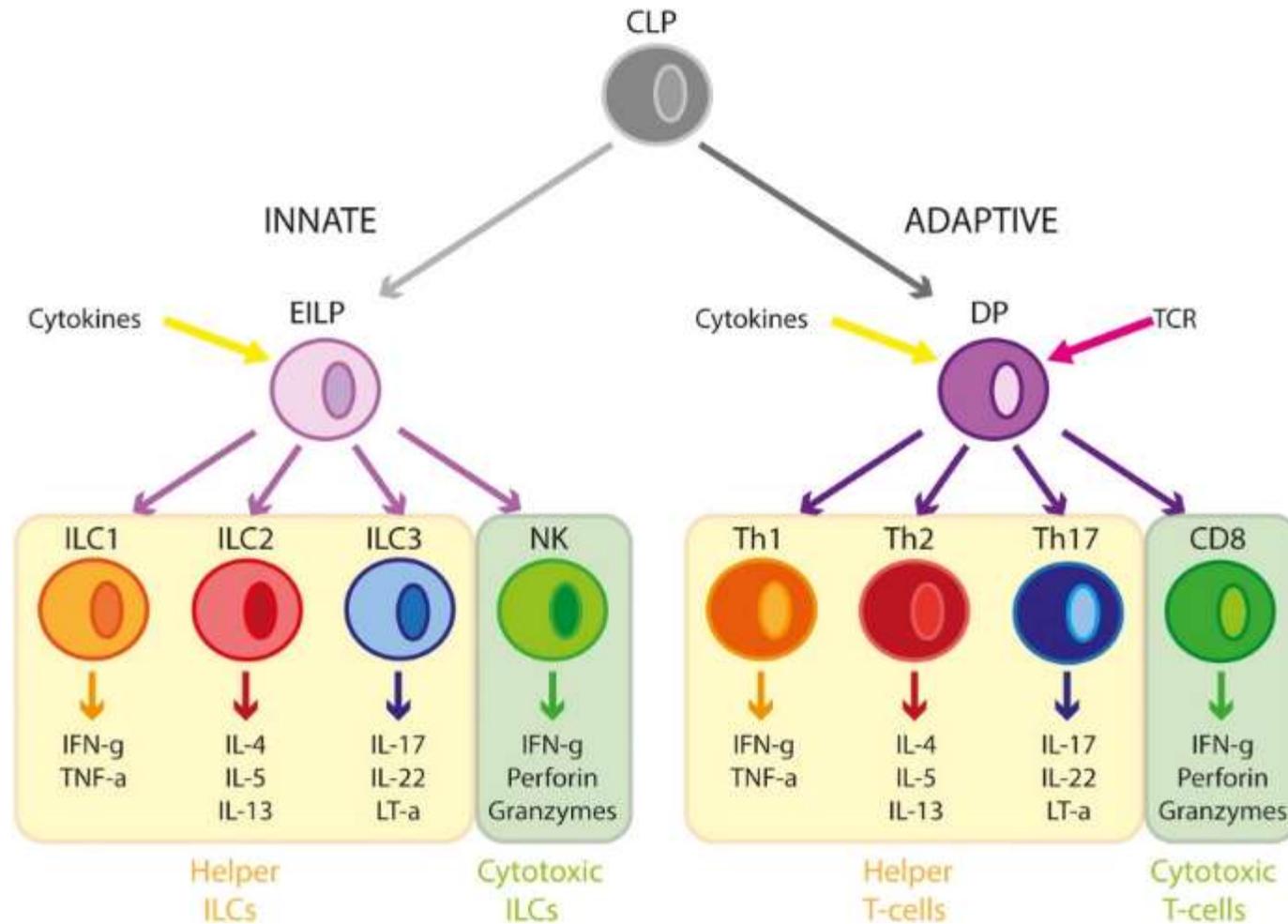
memória



Memória T sejtek



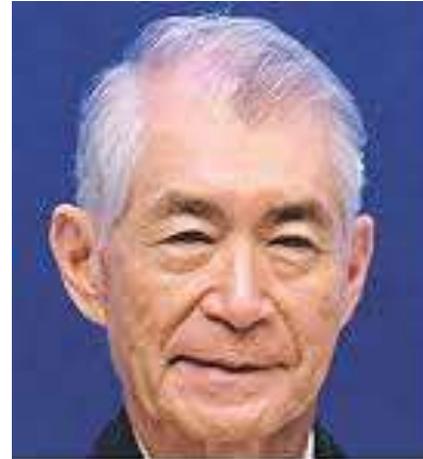
A T helper sejtek az Innate lymphoid sejtekkel együtt védik a szervezetet



Nobel díj az immune checkpoint blokádnak felfedezéséért

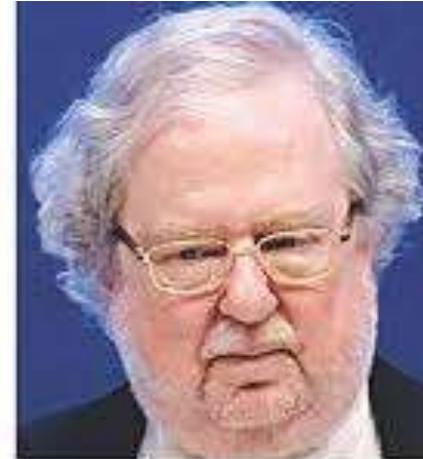


2018



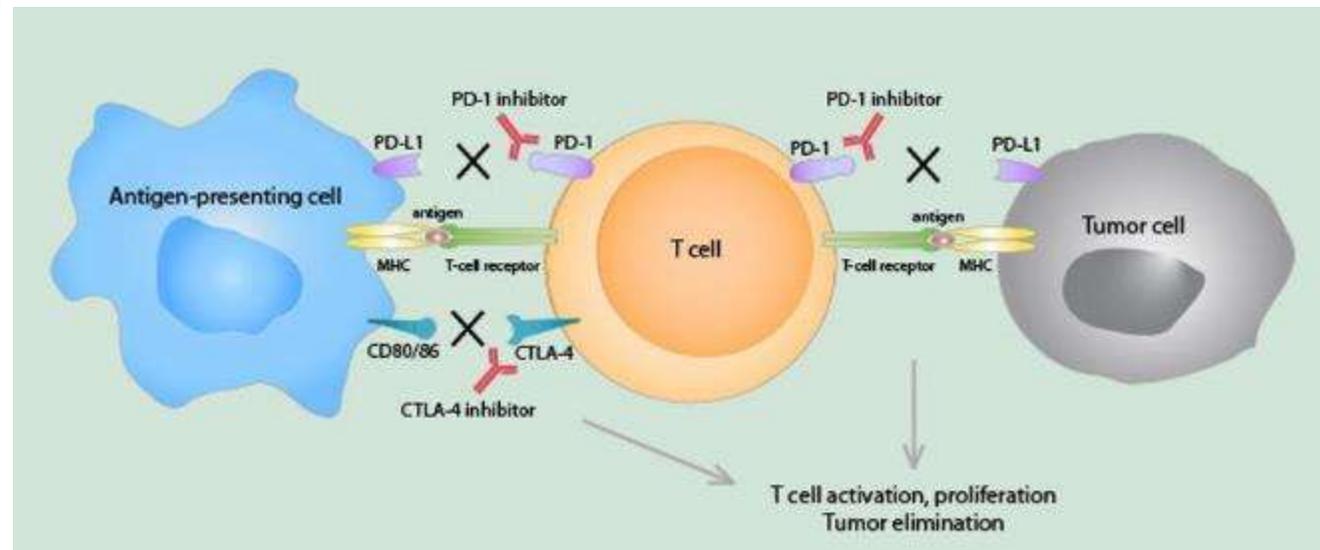
Tasuku Honjo

PD1

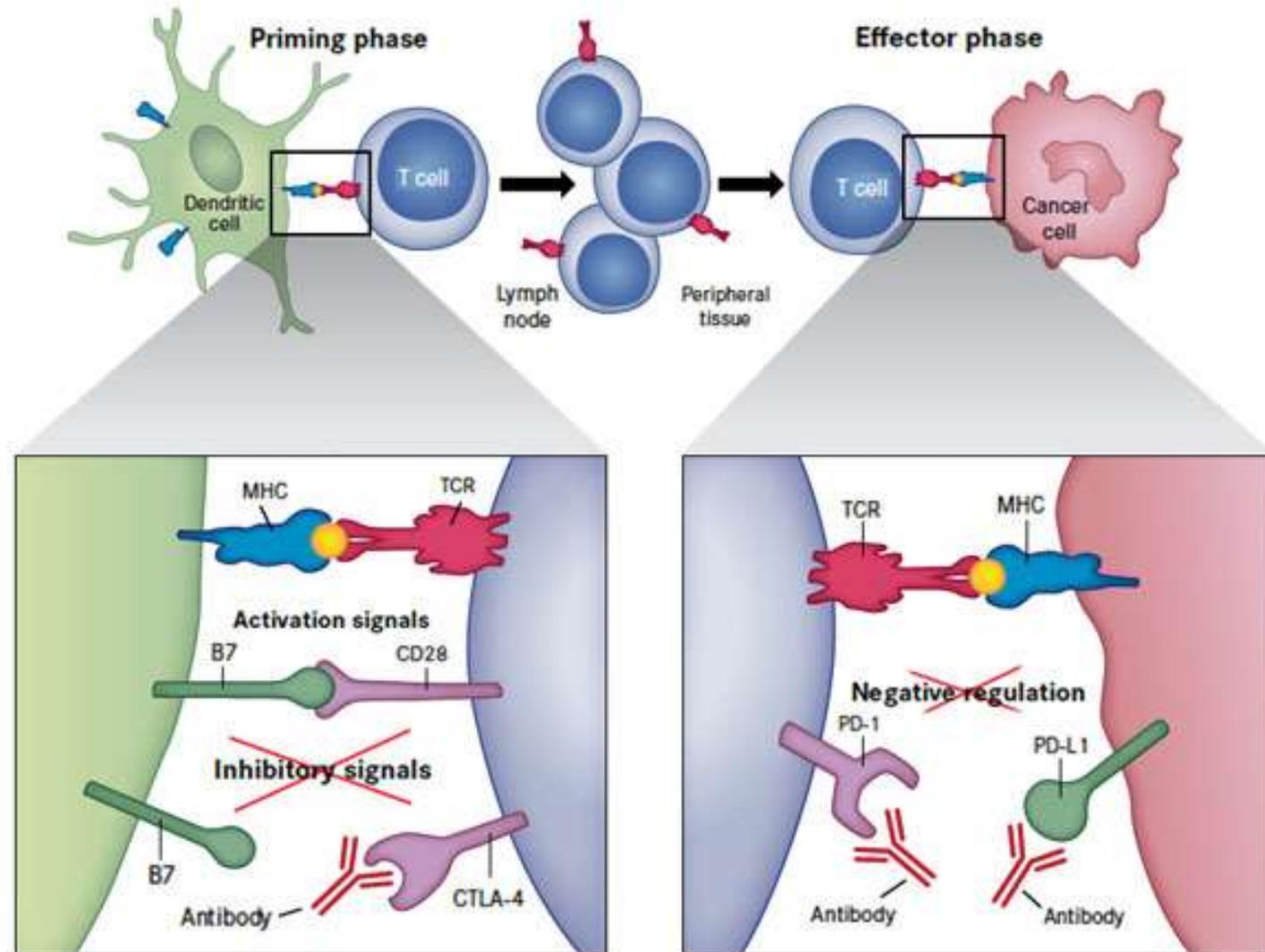


James Allison

CTLA-4



Checkpoint blokád



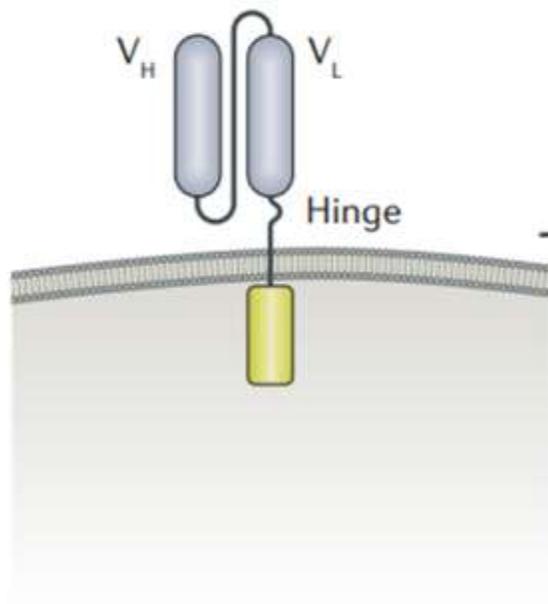
CAR T sejtek

“antitesttel-módosított” T sejtek

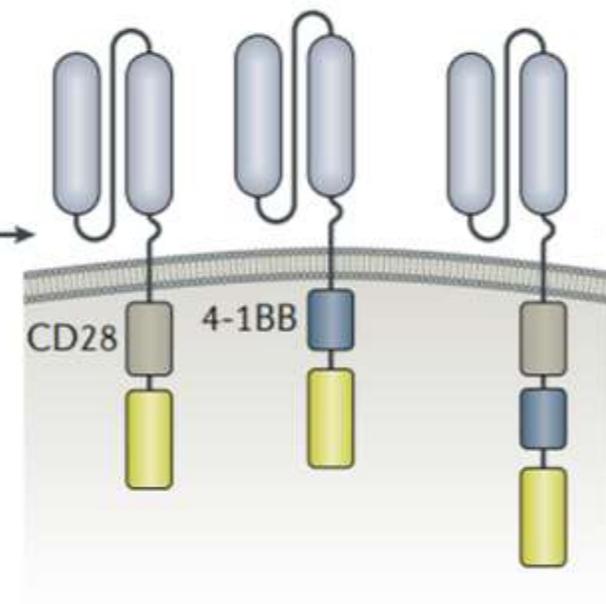


scFv: single chain variable fragment

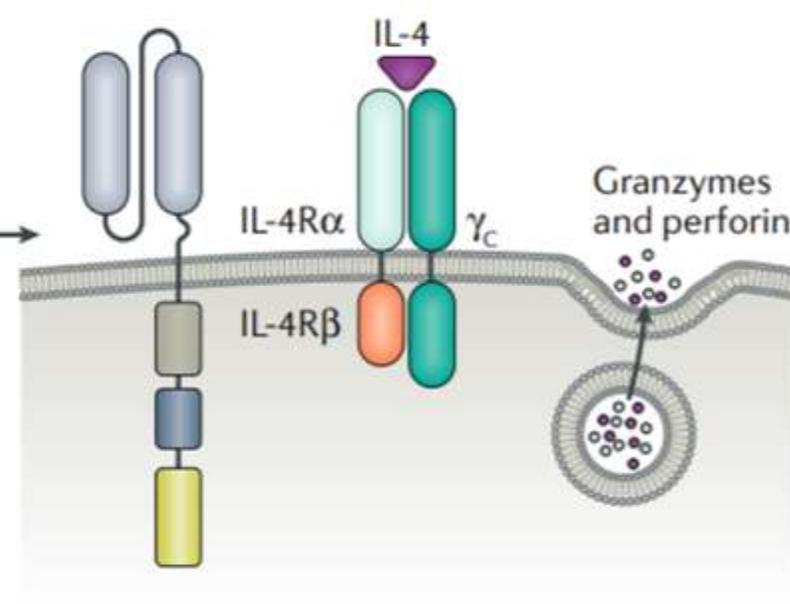
c First-generation CAR



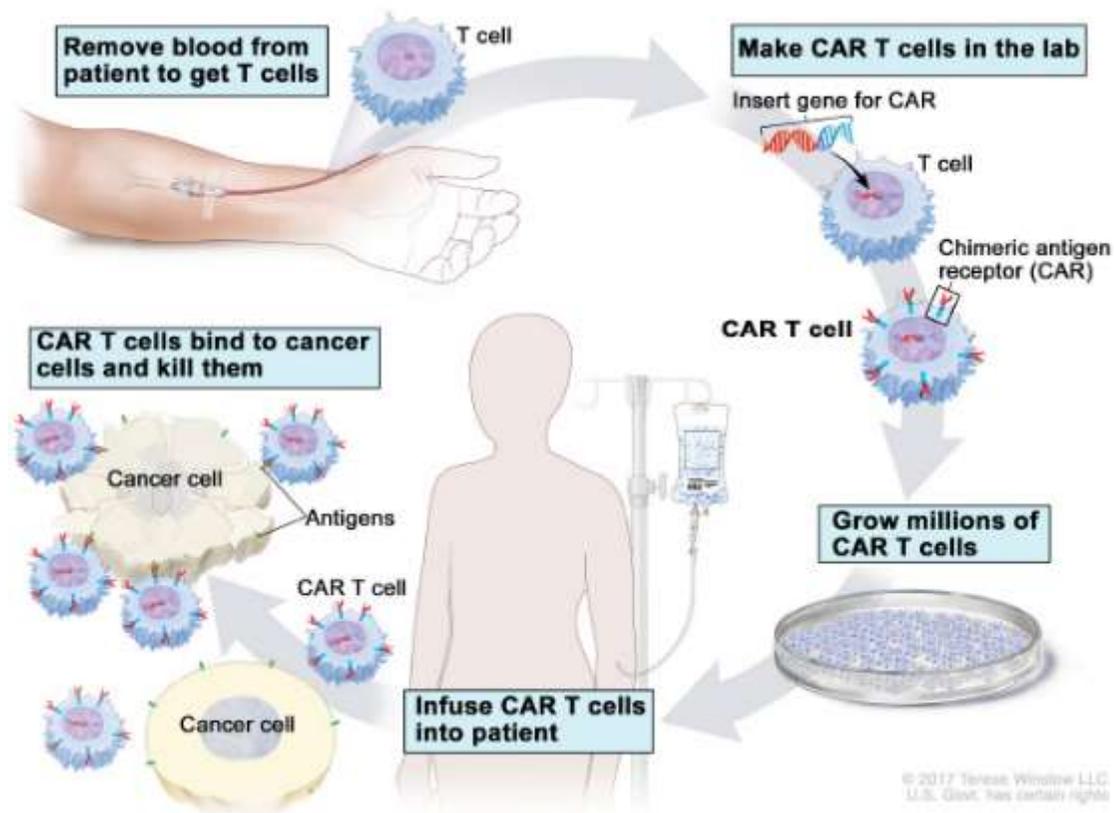
Second- and third-generation CARs



Fourth-generation CAR

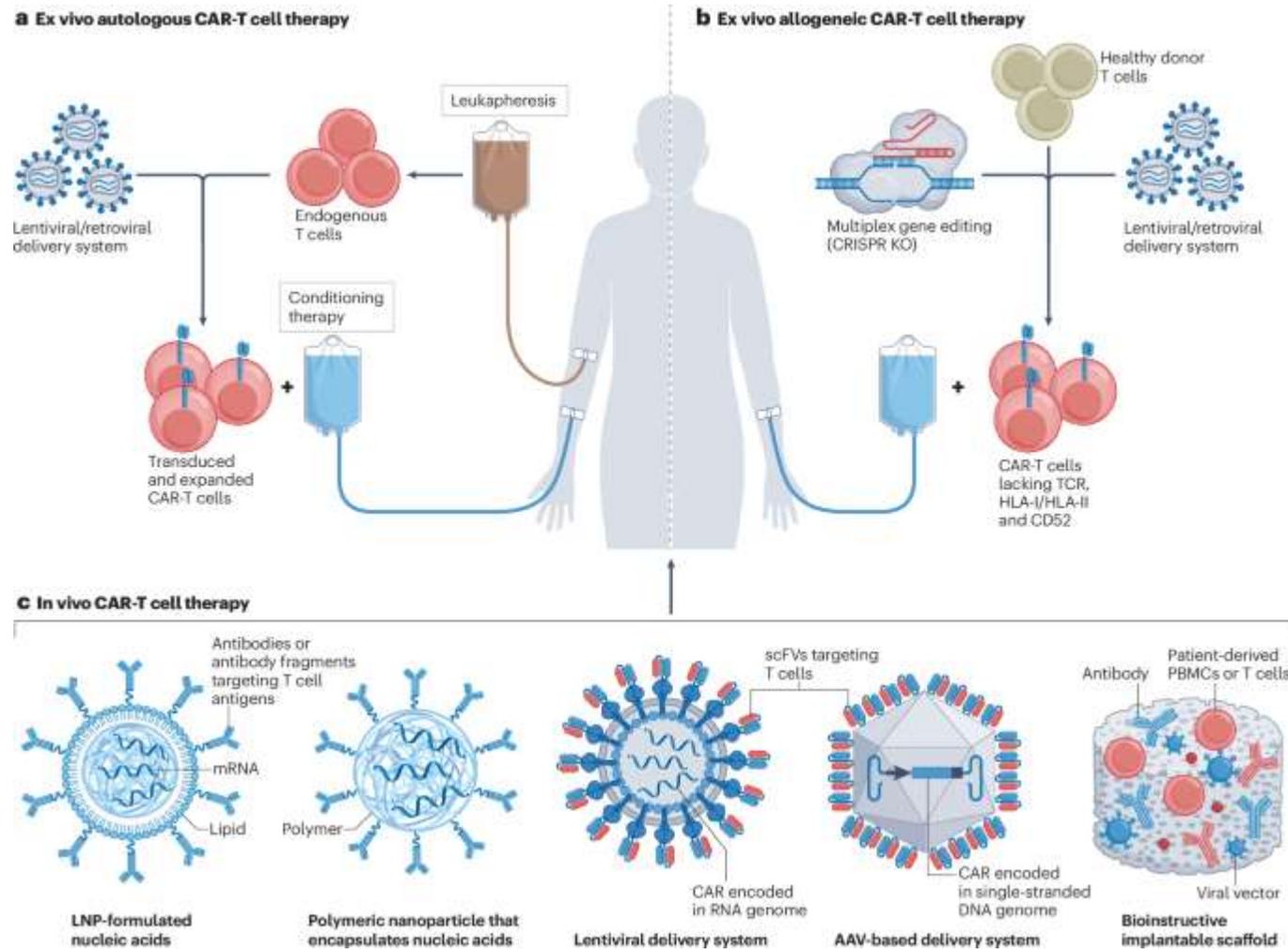


CAR (chimeric antigen receptor) T sejtek)



2017-ben történt engedélyezése óta a CAR T-sejt terápiát > 30 000 hematológiai malignitásban szenvedő beteg esetében alkalmazták már az USA-ban

CAR (chimeric antigen receptor) T sejtek)



Köszönöm a figyelmüket!