

Lymphatic organ

• primary lymphoid organ = lymphocyte กำเนิด

- thymus

- red bone marrow

• secondary lymphoid organ = lymphocyte activate & proliferate

- spleen

- lymph node

- tonsil

- MALT (mucosa-associated lymphoid tissue) = Payer's patch & appendix

• thymus

- ทุ่มตัว = ทุ่มตัว แห่ง T-cell production

- after puberty = involution จัดตั้ง ชีวี adipose tissue ↑

- development

- 3rd pharyngeal pouch ชั้น endoderm & mesoderm.

- เริ่มต้น WS แห่งผู้ตัว lymphocyte WG วัน gestation

- histology

- หุ้ม capsule = connective tissue

- incomplete lobules

- หุ้ม blood vessel แห่ง capsule

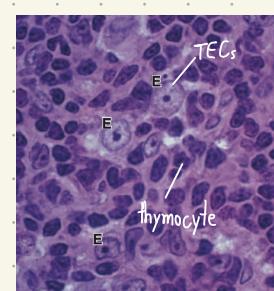
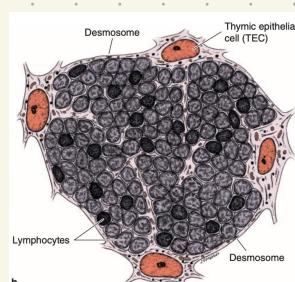
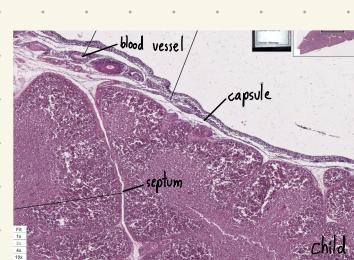
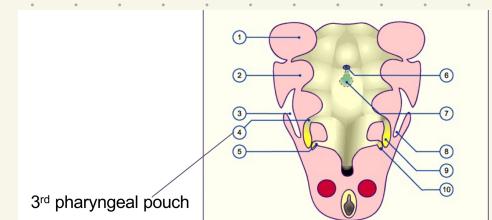
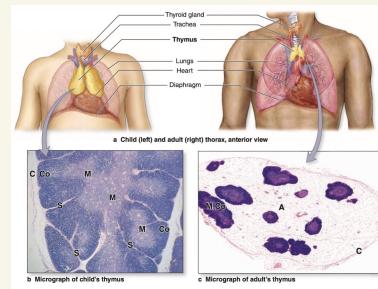
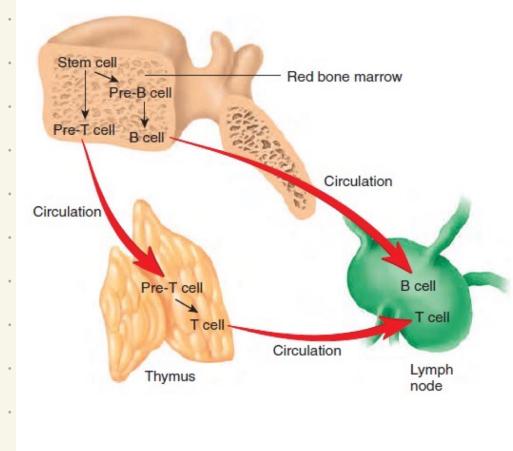
- child : ↑ lymphatic / ↓ adipocyte

- adult : ↓ lymphatic / ↓ adipocyte

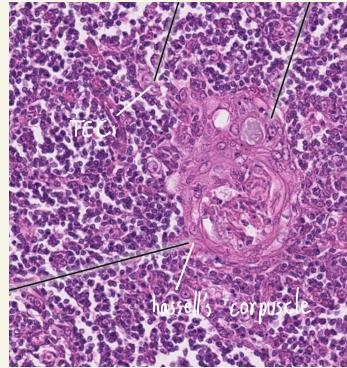
- cortex

- thymocytes = developing T cell

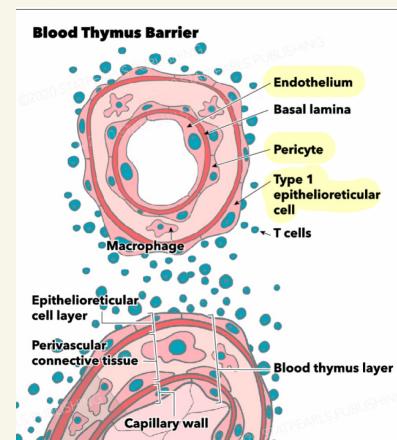
- TECs (thymic epithelial reticular cell) = cell ผู้ดูแล



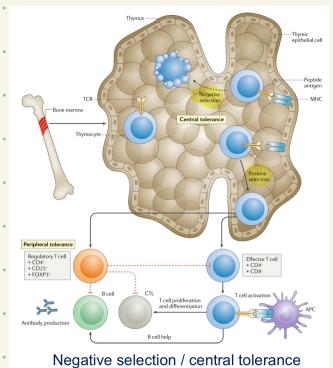
- macrophage
- dendritic cell
- medulla
 - thymocyte : Tonkin cortex
 - hassall's corpuscle
 - សំណើលូប thymus
 - cluster of TECs
 - concentric lamellae
 - keratohyalin granule
 - dendritic cell
- blood thymic-barrier (BTB)



- 血管 vessel នៃ cortex
- ពិន្ទុរួម្រួម antigen នៃក្នុង immature T cell
- structure
 - TECs (thymic epithelial reticular cell)
 - endothelial cell
 - pericyte



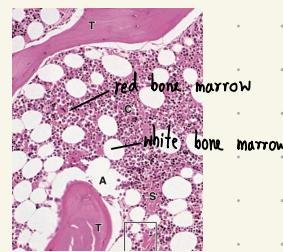
- function
 - development & maturation of T-cell
 - CD4⁺ T cell តែទៅ: CD4⁺/CD8⁺ T cell តែទៅ: CD8⁺
 - negative selection = និរសារនៃពុកអាមេរីក T cell ក្នុងបំបាត់ autoimmunity



- clinical correlation = digeorge syndrome
 - 22q11 microdeletion → 3rd pharyngeal pouch មិនធ្វើឡើ
 - thymic hypoplasia / aplasia = T cell deficiency
 - (មានឯក parathyroid)
 - hypocalcemia, cardiac defect, cleft palate

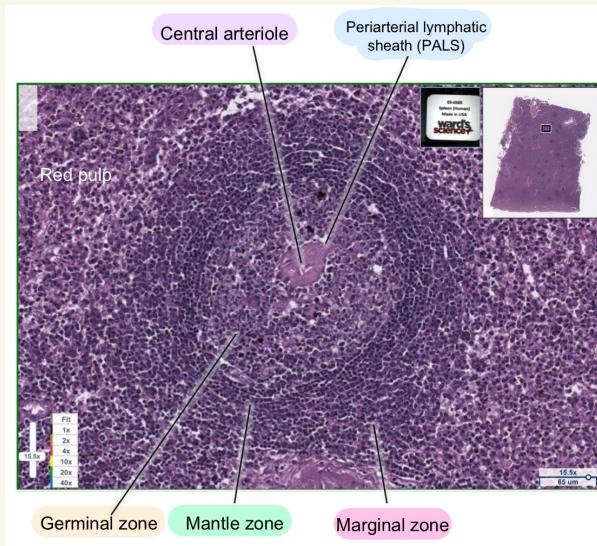
• bone marrow

- yellow bone marrow = adipocyte
- red bone marrow = hematopoiesis



• spleen

- largest lymphoid organ
- structure
 - capsule : connective tissue
 - trabecular artery
 - white pulp
 - central arteriole



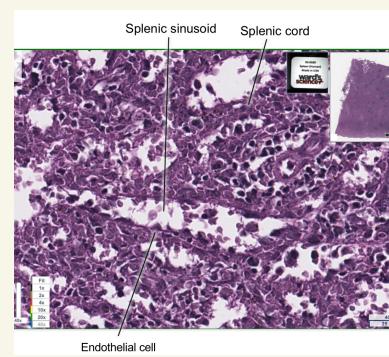
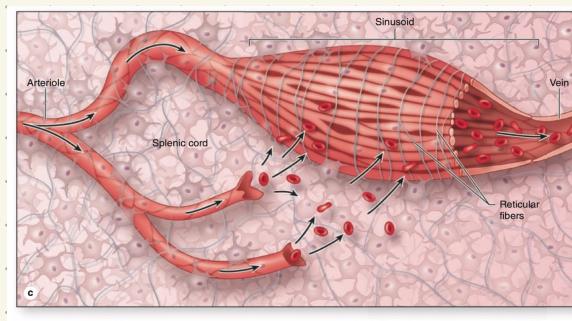
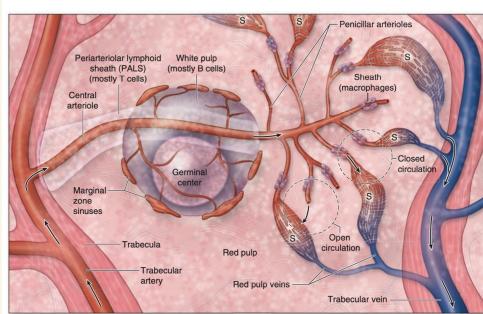
- PALS (periarterial lymphatic sheath) = այլ mature T cell օջախ
- germinal center = այլ activated B cell
- mantle zone = այլ inactivate B cell & macrophage
- marginal zone = այլ inactivate B cell, macrophage & dendritic cell

- red pulp
 - splenic cord (billroth's cord)
 - stave cell թաղակածություն
 - splenic sinusoid

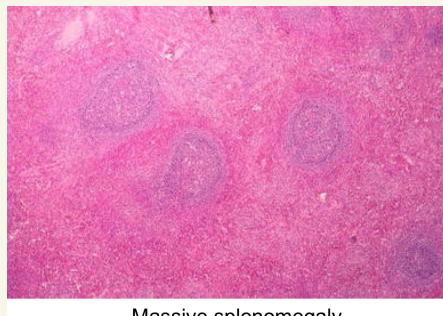
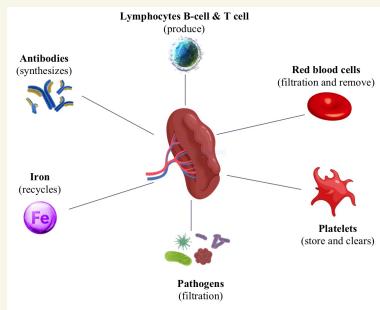


• circulation

- close = trabecular a. > central arteriole > penicillar arteriole > sinusoid > pulp v. > trabecular v.
- open = penicillar arteriole և պայմանագործված անցքերություն sinusoid ← մեծաւություն և ցանցավորություն



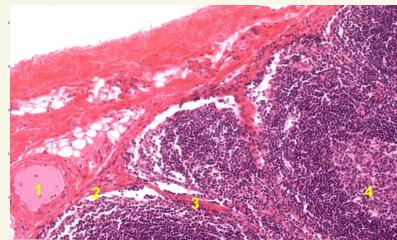
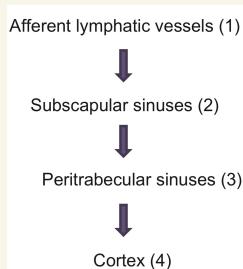
- function



- clinical correlation = splenomegaly

- lymph node

- circulation



- histology

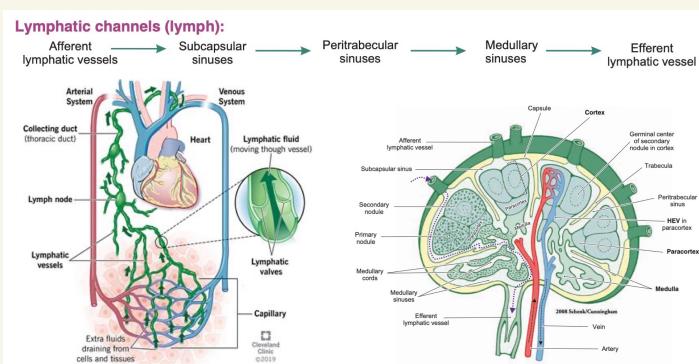
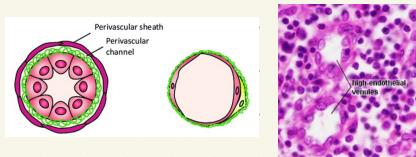
- cortex (B cell zone)

- lymph nodule

- minor proliferation B cell, helper T cell & follicular dendritic cell

- paracortex (T cell zone)

- HEVs (high endothelial venules) = minor lymphocyte egress blood → lymphoid tissue

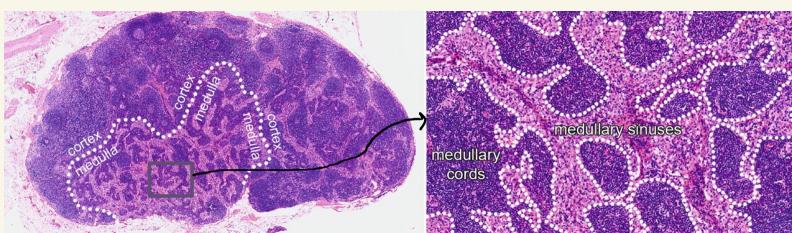


- eosinophilic infiltrate

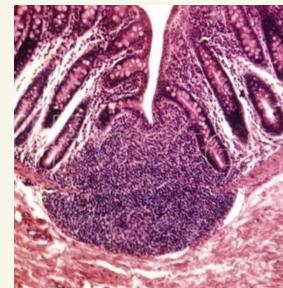
- medulla

- medullary sinus = discontinuous endothelium

- medullary cord = macrophage, B cell & plasma cell



- function
 - នៅក្នុងសាប្តិកសមរុបនៃ lymph
 - multiply activated T & B cell
- clinical correlation = swollen lymph node
 - កំណត់ infection, inflammation & cancer



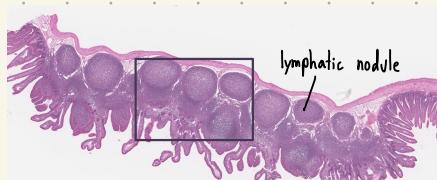
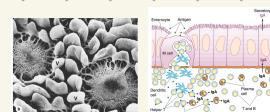
MALT (mucosa-associated lymphoid tissue)

- គោល់នៅ tonsil, peyer's patch & appendix
 - palatin, lingual & pharyngeal
- ឯក lymphoid organ នៃព្រឹងភាគក្រោង
- មួយ B cell មានការងារ

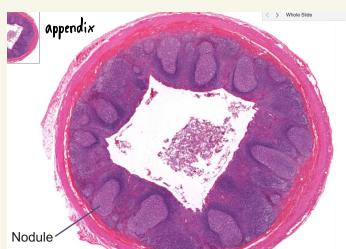


GALT (gut-associated lymphatic tissue) : នៃព្រឹង GI

- peyer's patch
- នៅនៅ ileum
- epithelial : M cell នូវ antigen/antibody ឱ្យចូល
- នូវ lymphocyte & dendritic cell

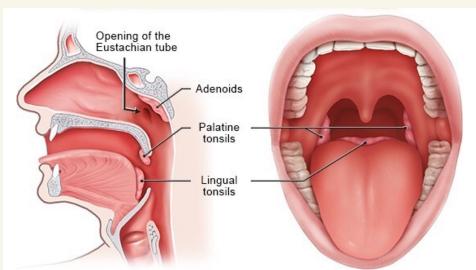


appendix

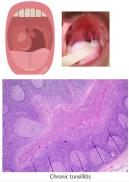


tonsil

- palatine tonsil
 - pharyngeal tonsil (adenoid)
 - lingual tonsil
 - tuber tonsil
- } មួយ cell នូវ: រឿង



- clinical correlation = tonsillitis

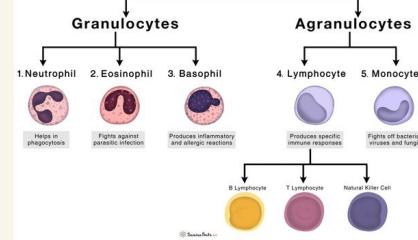


- viral > bacterial infection

WBC



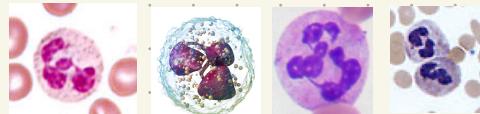
TYPES OF WHITE BLOOD CELLS



• granulocyte

- neutrophil
- eosinophil
- basophil

• neutrophil



- PMNs (polymorphonuclear leukocyte)

• មីនេវែងក្នុង ការេងការងារប៊ិន នៃ bacterial / fungal infection

• រំភឿង់ដែល inflammation នូវត្រូវតាម cytokines colony stimulating factor (CSFs)

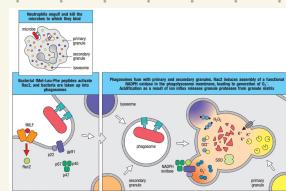
• ផ្តល់ microbe នៃ circulation & extravascular

• មីនឹងទីសាច់ នៃ receptor នៃ microbe នូវ opsonize នូវ complement system

• មីនេវែងក្នុងក្រុងសំណង់

• ចែកជាឌីន neutrophil នៃ microbe

• phagocytosis និងផ្ទាល់ ROS



• degranulation = នូវ protease ចោកនៅលើ cell

• NETs = នូវ net កំពុង chromatin & enzyme ឲ្យប្រកាស bacteria

• eosinophil

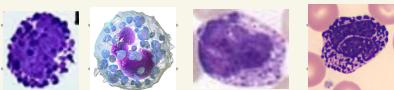


• ចូលចូល GI, thymus, uterus & adipose tissue

• កំណត់កំពុងកុន parasite, helminth & allergen inflammatory disease

• តំបន់ eosin dye នៃការឱ្យ cationic protein

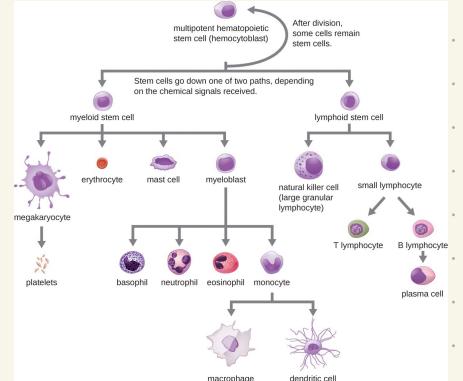
• basophil



• មីនេវែងក្នុង

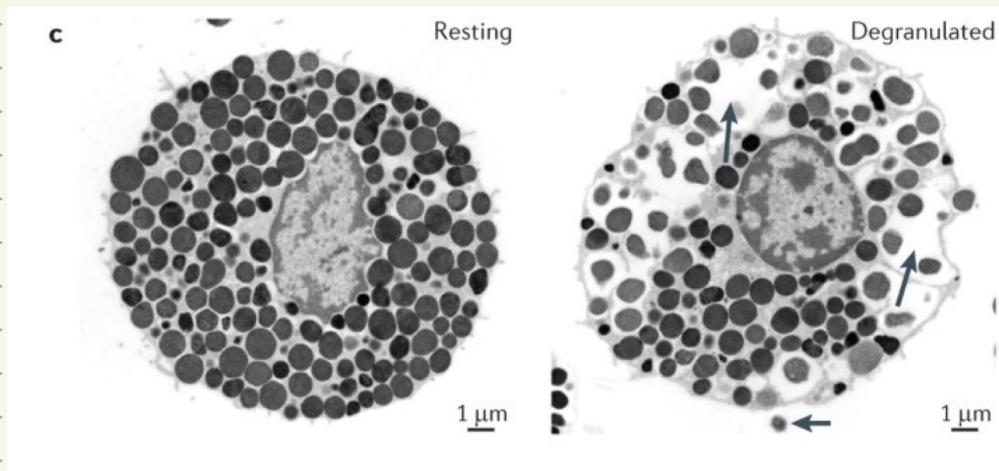
• រំភឿង់នៃការងារប៊ិន inflammation

• គ្រួស activate តាម IgE



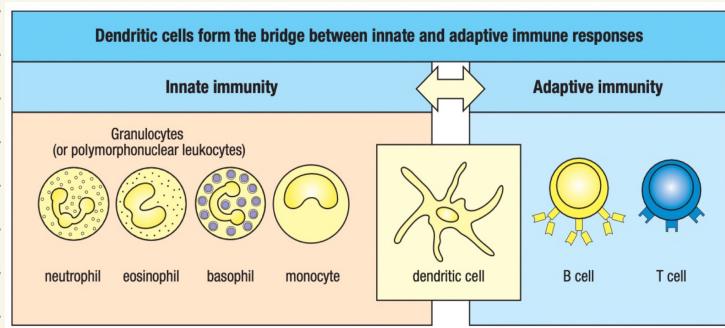
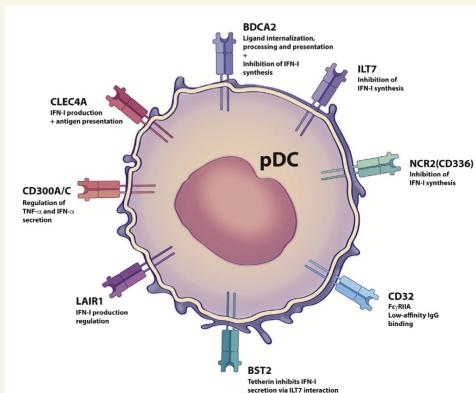
mast cell

- អំពីរង្វែង skin & mucosal
- អានុវត្ត សំខាន់ TLRs, opsonization & antibody (allergy)
- ផ្តល់ granule នៃ
 - histamine
 - proteolytic enz.
 - lipid mediator & cytokine = នូវឯក inflammation
- ប្រើបាយ helminth, snake & insect venom & pathogen
- និរូចិតា allergy

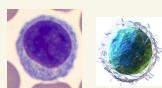


dendritic cell

- អំពីរង្វែង sentinel (ការដាក់) នូវ antigen presentation
- plasmacytoid dendritic cell (pDC)
 - immune response to virus
 - ផ្តល់ type I interferon (IFN-1/α)



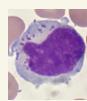
• lymphocyte



- B cell

- T cell

- NK cell



→ granzyme & perforin

- NK cell ด้วยหนังสี cytotoxic granule ทำให้มี programmed cell death

- ควบคุมตัวเอง germline-encoded receptor

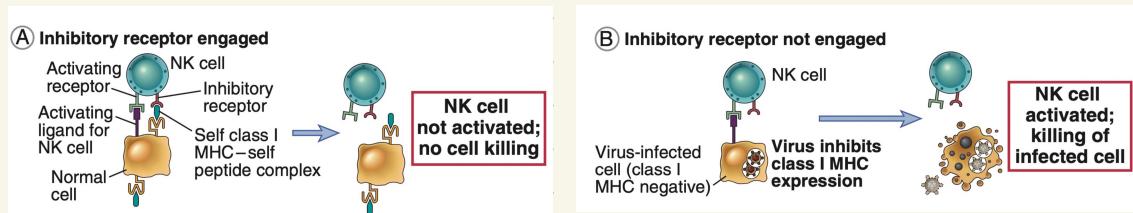
- ตรวจสอบ NK cell

- healthy host cell = มี self class I MHC ที่บังคับ inhibitory receptor ของ NK cell

- infected & abnormal cell

- activating receptor ของ NK cell จับกับ surface molecule ของ cell ผิดปกติ

- ไม่มี self class I MHC หรือ inhibitory receptors ที่บังคับ



- activating receptor = NK62D & CD16

- inhibitory receptor = KIRs, CD94 & lectin subunit

- NK cell & macrophage

- NK cell หลัง IFN-γ หลังจาก macrophage

- macrophage หลัง cytokine หลังจาก NK cell

↳ IL-15, type I IFNs & IL-12

- antibody-dependent cell cytotoxicity (ADCC)

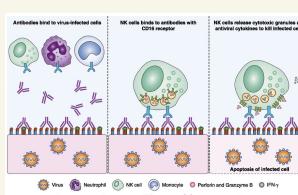
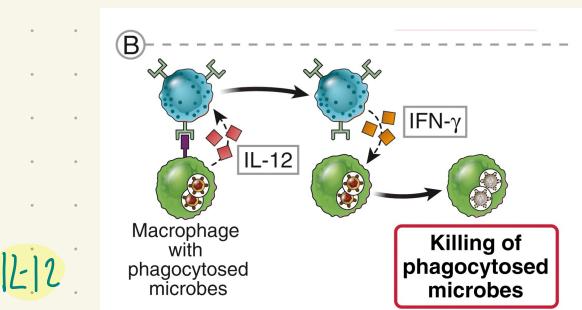
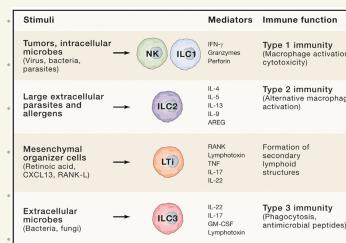
- ผ่าน CD16 & Fc receptor หลังจาก IgG

- ผ่าน NK cell หลังจากรับสัญญาณ CD4 T helper

- ILC1s : Th1

- ILC2s : Th2

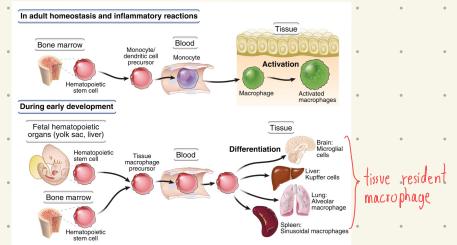
- ILC3s : Th17



monocyte

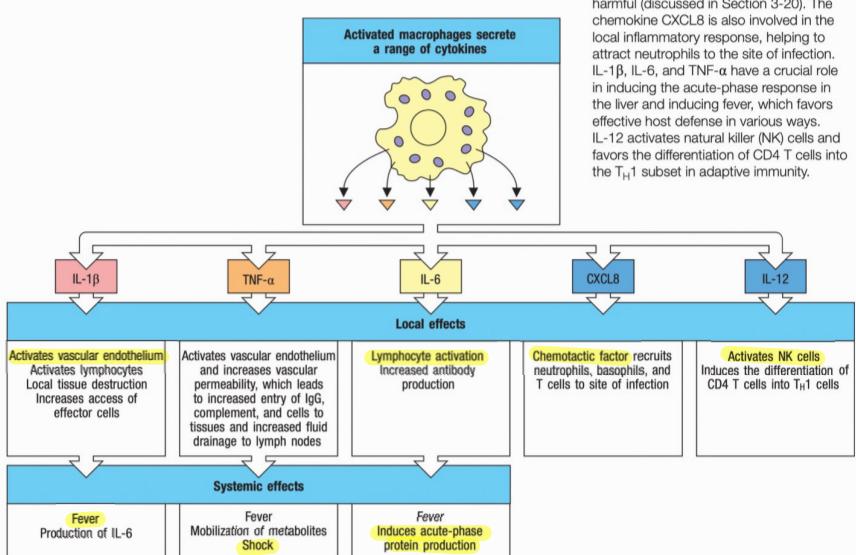
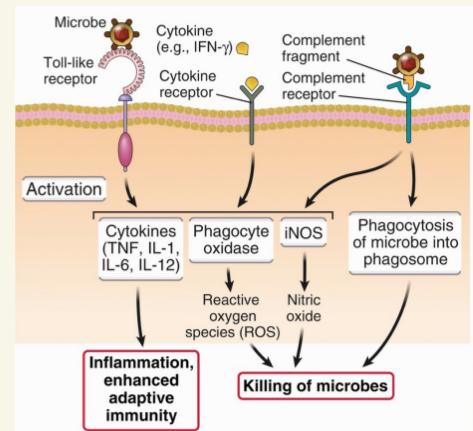


- monocyte օջնելի extravascular tissue ກວຍມີນີ້ macrophage
- ໃໝ່ tissue resident macrophage ໃນງົງທີ່ tissue ແນນການ



ໄຟຈິດສັງເກດ monocyte

Feature	Neutrophils	Macrophages
Origin	HSCs in bone marrow	HSCs in bone marrow (in inflammatory reactions) Many tissue-resident macrophages: stem cells in yolk sac of fetal liver (early in development)
Life span in tissues	1–2 days	Inflammatory macrophages: days or weeks Tissue-resident macrophages: years
Responses to activating stimuli	Rapid, short lived, enzymatic activity	More prolonged, slower, often dependent on gene transcription
Phagocytosis	Rapid ingestion of microbes	Prolonged ability to ingest microbes, apoptotic cells, tissue debris, foreign material
Reactive oxygen species	Rapidly induced by assembly of phagocyte oxidase (respiratory burst) <small>Lysosomal ROS</small>	Less prominent
Nitric oxide	Low levels or none	Induced following transcriptional activation of iNOS → <small>ນຳຄົນ NO</small>
Degranulation	Major response; induced by cytoskeletal rearrangement	Not prominent
Cytokine production	Low levels per cell	Major functional activity, large amounts per cell, requires transcriptional activation of cytokine genes
Extracellular traps	Rapidly induced, by extrusion of nuclear contents	Little
Secretion of lysosomal enzymes	Prominent	Less



harmful (discussed in Section 3-20). The chemokine CXCL8 is also involved in the local inflammatory response, helping to attract neutrophils to the site of infection. IL-1 β , IL-6, and TNF- α have a crucial role in inducing the acute-phase response in the liver and inducing fever, which favors effective host defense in various ways. IL-12 activates natural killer (NK) cells and favors the differentiation of CD4 T cells into the T_H1 subset in adaptive immunity.

ນໍຫັກຂອງ macrophage

classical macrophage activation (M1)

- ຮັດຕັ້ງດ້ວຍ TLRs & IFN- γ

- ກຳລັງ microbe & inflammation

alternative macrophage activation (M2)

- ຜົນຕີ IL-10 & TGF- β

- tissue repair & anti-inflammation

Lymphatic vessel

• សំណង់ស្ថាប់សុខ

- central nervous system
- coats of eyeball
- internal ear
- epidermis
- cartilage & bone
- placenta

• valve

• muscular wall contraction

• histology

• ក្រឡាយតាម

• flattened endothelium

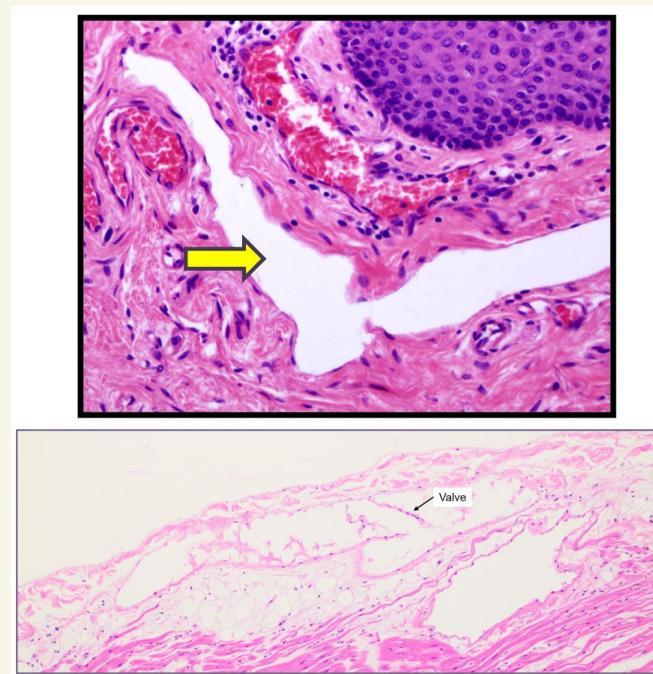
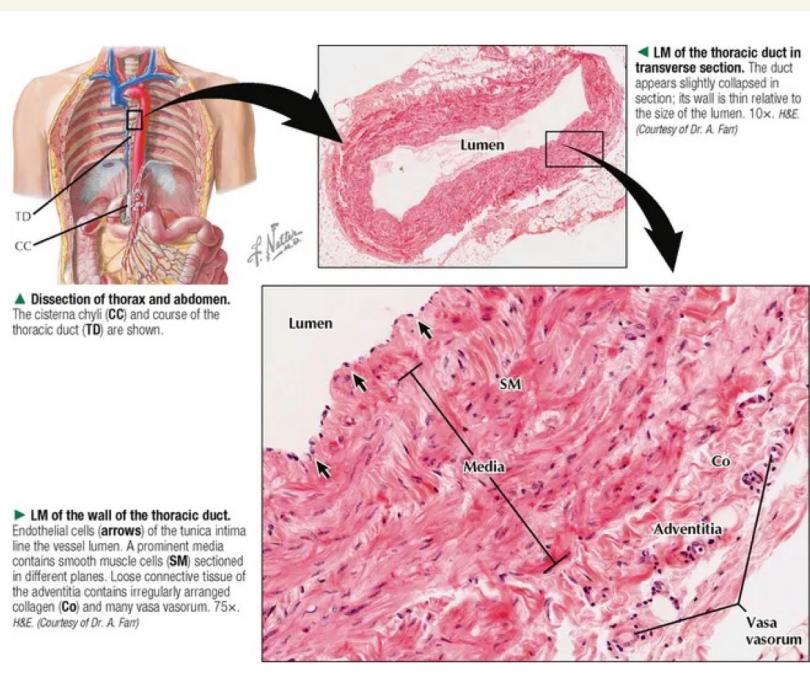
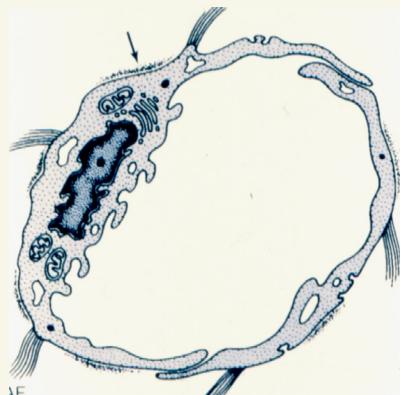
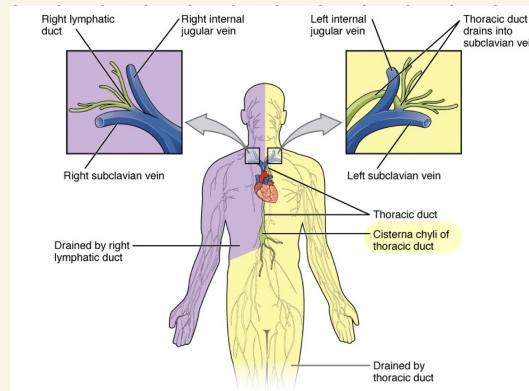
• incomplete basal lamina

• មិនមែន tight junction

• tunica intima = endothelium

• tunica media = smooth muscle → thoracic duct នៃវេស់

• tunica adventitia = connective tissue



Innate immune

• innate immunity

- មួយតែចំណាំ
- receptor មានលាយសំខាន់ នៅក្នុងទី diversity
- receptor នូវ non-clonal
 - ↳ identical receptor on all cell
- germline encoded

• adaptive immunity

- ទាញឃកបាន antigen
- receptor នឹង 2 នំនៅ នៅក្នុង diversity
- receptor នូវ clonal
 - ↳ lymphocyte ត្រូវបានដាក់ទៅមាន receptor ពីរក្នុង
- somatic recombination

• anatomical barrier

- mechanical : movement of mucus & fluid
- chemical : acid, surfactant, enzyme
- microbiological : microbiota កែវជាតិ antimicrobial peptide និង lysozyme

• សំគាល់សំខាន់ complement system (inflammation)

① activate C3 → C3b & C3a

- alternative pathway : microbial surface
- classical pathway : antibody-antigen complex
- lectin pathway : mannose-binding lectin (MBL) ក្បែងក្រុង microbe glycoprotein

② C3a ក្បែងក្រុង inflammation

C3b ក្បែងក្រុងពីរ opsonization & phagocytosis
(ដោយ WBC ការងារបុញ្ញលេញ)

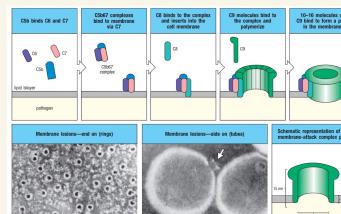
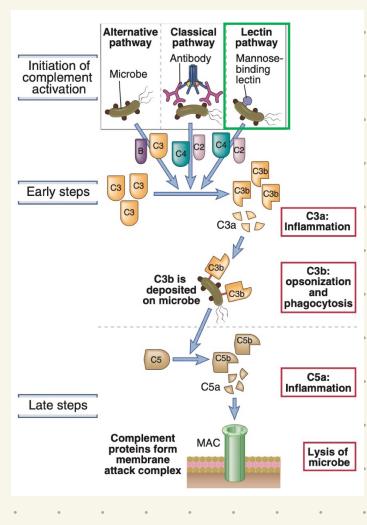
③ C5 → C5b & C5a

④ C5a ក្បែងក្រុង inflammation

C5b + C6 + C7 + C8 + C9 = membrane attack complex (MAC)

⑤ MAC ឃើបុងនៃ microbe ឱ្យនូវ ផលិត

	Skin	Gut	Lungs	Eyes/nose/oral cavity
Mechanical	Epithelial cells joined by tight junctions			
	Longitudinal flow of air or fluid	Longitudinal flow of air or fluid	Movement of mucus by cilia	Tears Nasal cilia
Chemical	Fatty acids	Low pH Enzymes (pepsin)	Pulmonary surfactant	Enzymes in tears and saliva (lysozyme)
	β -defensins Lamellar bodies Cathelicidin	α -defensins (cryptidins) Regill (lecticidins) Cathelicidin	α -defensins Cathelicidin	Histatins β -defensins
Microbiological	Normal microbiota			



• function օս complement system

- opsonization & phagocytosis : C3b
- inflammation : anaphylatoxin (C5a & C3a)
- Cell lysis : MAC
- pathogen-associated molecular pattern (PAMPs) : cell հետք
- danger-associated molecular pattern (DAMPs) : cell թաղանթիութեան

• pattern recognition receptor (PRRs)

- receptor օս innate immune system պարագանեան microbe & damage cell
- լօյնացած բառ cell : membrane / cytosol / endosome

• toll-like receptor (TLRs)

- TLR1 : TLR2 } bacterial lipopeptide (G⁺)
- TLR2 : TLR6 }

- TLR2 : bacterial peptidoglycan (fungi)

- TLR4 : LPS (G⁻)

- TLR5 : bacterial flagellin

- TLR3 : dsRNA

- TLR7 : ssRNA թշու corona

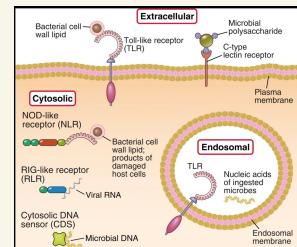
- TLR8 : ssRNA

- TLR9 : CpG DNA (bacteria & herpesvirus)

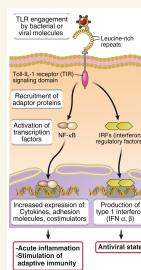
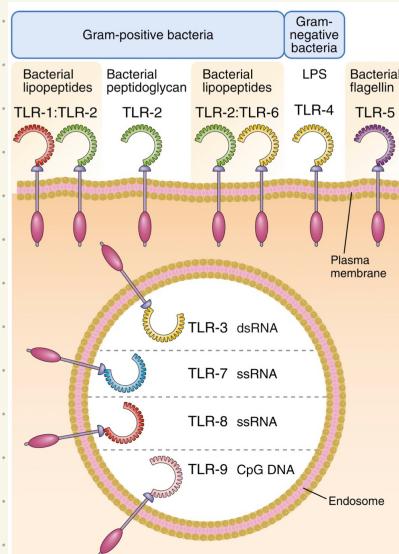
- աջդիր գործառնութեան transcription factor

- nuclear factor κB (NF-κB) : inflammation

- interferon regulatory factor (IRFs) : աջդիր անտիվիրալ cytokine (type I interferon)



Innate immune recognition by mammalian Toll-like receptors		
Toll-like receptor	Ligand	Hematopoietic cellular distribution
TLR-1/TLR-2 heterodimer	Lipopeptides (Gram-positive bacteria), Lipoteichoic acids (Gram-positive bacteria), Zymosan (yeast), β-glucans (bacteria and fungi)	Macrophages, dendritic cells, mast cells, eosinophils, basophils
TLR-2/TLR-6 heterodimer		
TLR-3	Double-stranded RNA (virus)	Macrophages, dendritic cells, intestinal epithelium
TLR-4 (plus MD-2 and CD14)	LPS (Gram-negative bacteria), Lipopeptides (Gram-positive bacteria)	Macrophages, dendritic cells, mast cells, eosinophils
TLR-5	Flagellin (bacteria)	Intestinal epithelium, macrophages, dendritic cells
TLR-7	Single-stranded RNA (virus)	Plasmacytoid dendritic cells, macrophages, eosinophils, B cells
TLR-8	Single-stranded RNA (virus)	Macrophages, neutrophils
TLR-9	DNA with unmethylated CpG (bacteria and herpesviruses)	Plasmacytoid dendritic cells, eosinophils, B cells, basophils
TLR-10 (human only)	Unknown	Plasmacytoid dendritic cells, eosinophils, B cells, basophils



- NOD-like receptor (NLRs)

- ស្ថិតិៗ DAMPs & PAMPs នៃប៊ូន cytosol → ការបញ្ចប់ peptidoglycan នៃ bacterial cell wall
- ឧប្បជ្ជ NOD1, NOD2 & NLRP-3
- សែវង់សម្រេច: activate NF- κ B transcription factor
- NOD2 នៅលី intestinal paneth cell

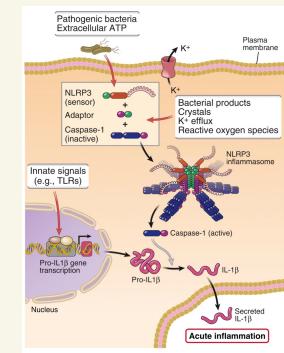
- NLRP-3 នៅក្នុង

① រួមកិប adaptor & caspase-1 : NLRP-3 inflammasome

② caspase-1 តែងតាំង activate

③ caspase-1 ឲ្យតែ pro-IL 1 β \rightarrow IL-1 β

④ IL-1 ក្នុង inflammation \rightarrow fever



- RIG-like receptor (RLRs)

• ស្ថិតិៗ dsRNA ផែវសេរីប៉ុណ្ណោះដែលរាយសំនួល antiviral type I IFNs

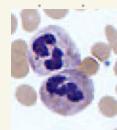
• ឈកតា dsRNA ក្នុងតាមពេកយកកំបកតិះ & មែន 5' triphosphate moiety

- cytosolic DNA sensor (CDSS)

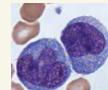
• ស្ថិតិៗ dsDNA ផែវសេរីប៉ុណ្ណោះដែលសំនួល type I IFN និង autophagy

- cell នៃ innate immune

- neutrophil (polymorphonuclear leukocyte - PMNs)



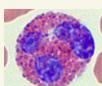
- monocyte / macrophage



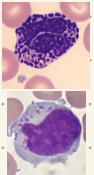
- dendritic cell

- mast cell

- eosinophil



- basophil



- NK cell



• cytokines

• proinflammatory

- TNF (tumor necrosis factor)

- IL-1 (interleukin-1)

- IL-6 (interleukin-6)

• anti-inflammatory

- IL-10 (interleukin-10)

- TGF- β

• NK cell & virus

- IL-12 (interleukin-12)

- IFN- γ (interferon- γ)

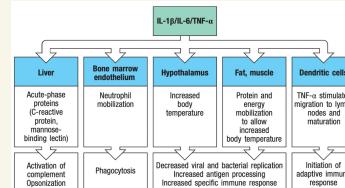
- type I IFNs (IFN- α , IFN- β)

- IL-15 (interleukin-15)

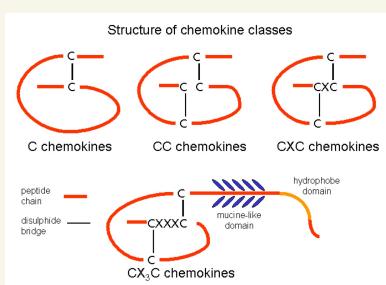
- IL-18 (interleukin-18)

- chemokines = receptor ∇ G-protein coupled & muscarinic

- CXCL8 = neutrophil ∇



Cytokine	Principal cell source(s)	Principal cellular targets and biologic effects
Tumor necrosis factor (TNF)	Macrophages, T cells	Endothelial cells: activation (inflammation, coagulation) Neutrophils: activation Hypothalamus: fever Liver: synthesis of acute-phase proteins Muscle, fat: catabolism (cachexia) Many cell types: apoptosis
Interleukin-1 (IL-1)	Macrophages, endothelial cells, some epithelial cells	Endothelial cells: activation (inflammation, coagulation) Hypothalamus: fever Liver: synthesis of acute phase proteins T cells: Th17 differentiation
Chemokines	Macrophages, dendritic cells, endothelial cells, T lymphocytes, fibroblasts, platelets	Leukocytes: increased integrin affinity, chemotaxis, activation
Interleukin-12 (IL-12)	Dendritic cells, macrophages	NK cells and T cells: IFN-γ production, increased cytotoxic activity T cells: Th1 differentiation
Interferon-γ (IFN-γ)	NK cells, T lymphocytes	Activation of macrophages Stimulation of some antibody responses
Type I IFNs (IFN-α, IFN-β)	IFN-α: Dendritic cells, macrophages IFN-β: Fibroblasts	All cells: antiviral state, increased class I MHC expression NK cells: activation
Interleukin-10 (IL-10)	Macrophages, dendritic cells, T cells	Macrophages, dendritic cells: inhibition of IL-12 production, reduced expression of costimulators and class II MHC molecules
Interleukin-6 (IL-6)	Macrophages, endothelial cells, T cells	Liver: synthesis of acute-phase proteins B cells: proliferation of antibody-producing cells
Interleukin-15 (IL-15)	Macrophages, others	NK cells: proliferation T cells: proliferation
Interleukin-18 (IL-18)	Macrophages	NK cells and T cells: IFN-γ synthesis
TGF-β	Many cell types	Inhibition of inflammation T cells: differentiation of Th17, regulatory T cells



▪ វិនាទនៃសម្រាប់ innate immune

① inflammation

- mast cell & macrophage ផលិត histamine, TNF & prostaglandin

② recruitment

① rolling

- TNF & IL-1 ងាយក្នុង endothelial cell រួចរាល់ selectin & integrin ligand
- នឹង neutrophil ទេរាងក្នុង

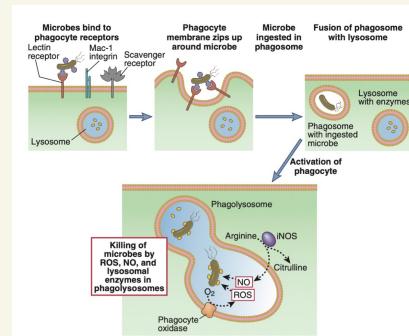
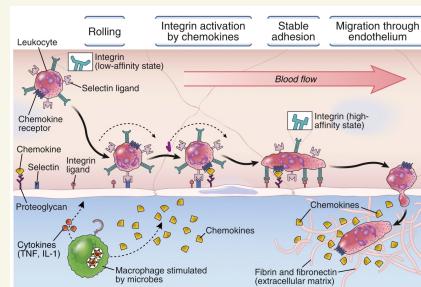
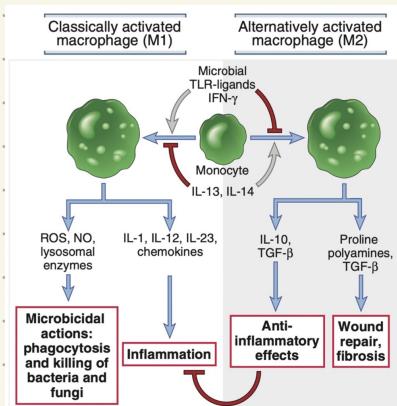
② firm adhesion

③ exavasation

④ phagocytosis

- phagosome រំរាត lysosome = phagolysosome

⑤ tissue repair



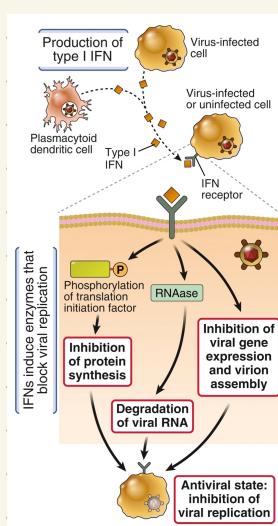
• antiviral

- dendritic cell ផ្គត់ផ្គង់ type I interferon (IFN- α , IFN- β)

▪ inhibit viral protein translation

▪ ↑ viral RNA degradation

▪ inhibit virus gene expression & assembly



• evasion of innate immune

Mechanism of immune evasion	Organism (example)	Mechanism
Resistance to phagocytosis	Pneumococci	Capsular polysaccharide inhibits phagocytosis
Resistance to reactive oxygen intermediates in phagocytes	Staphylococci	Production of catalase, which breaks down reactive oxygen intermediates
Resistance to complement activation (alternative pathway)	<i>Neisseria meningitidis</i>	Sialic acid expression inhibits C3 and C5 convertases
Resistance to antimicrobial peptide antibiotics	Streptococci	M protein blocks C3 binding to organism, and C3b binding to complement receptors
	<i>Pseudomonas</i>	Synthesis of modified LPS that resists action of anti-bacterial peptides

Inflammation

- վար խօս ուղարկություն

• acute inflammation

- vasodilation ← histamine

- ↑ vascular permeability

• exudate = fluid + protein + cell զոլովի interstitial space

- emigration of WBC = հետաքայլություն leukocyte recruitment

- lymphatic response

• ↑ flow = թափառացած լեռու շարժում

- inflammation of lymphatic system

• lymphangitis = lymphatic vessel

• lymphadenitis = lymph node

- mediator

• histamine = vasodilation ← anti-histamine

• eicosanoid (prostaglandin, leukotriene) = vasodilation, vascular permeability, վար, վարություն

• cytokine & chemokine

• platelet-activating factor

• complement

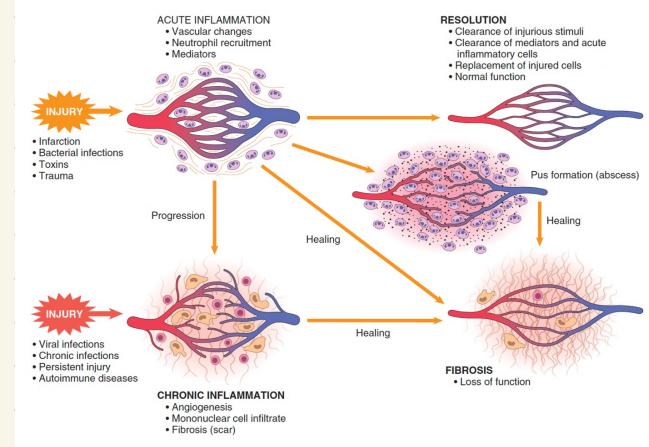
• kinin = վար լիվ դեմք vascular permeability

- morphology

• serous = effusion → blister

• fibrinous = fibrin accumulation → fibrosis

• purulent (suppurative) / abscess = cell-rich (neutrophil, macrophage & debris)



Mediator	Source	Action
Histamine	Mast cells, basophils, platelets	Vasodilation, increased vascular permeability, endothelial activation
Prostaglandins	Mast cells, leukocytes	Vasodilation, pain, fever
Leukotrienes	Mast cells, leukocytes	Increased vascular permeability, chemotaxis, leukocyte adhesion, and activation
Cytokines (TNF, IL-1, IL-6)	Macrophages, endothelial cells, mast cells	Local: endothelial activation (expression of adhesion molecules). Systemic: fever, metabolic abnormalities, hypotension (shock)
Chemokines	Leukocytes, activated macrophages	Chemotaxis, leukocyte activation
Platelet-activating factor	Leukocytes, mast cells	Vasodilation, increased vascular permeability, leukocyte adhesion, chemotaxis, degranulation, oxidative burst
Complement	Plasma (produced in liver)	Leukocyte chemotaxis and activation, direct target killing (membrane attack complex), vasodilation (mast cell stimulation)
Kinins	Plasma (produced in liver)	Increased vascular permeability, smooth muscle contraction, vasodilation, pain

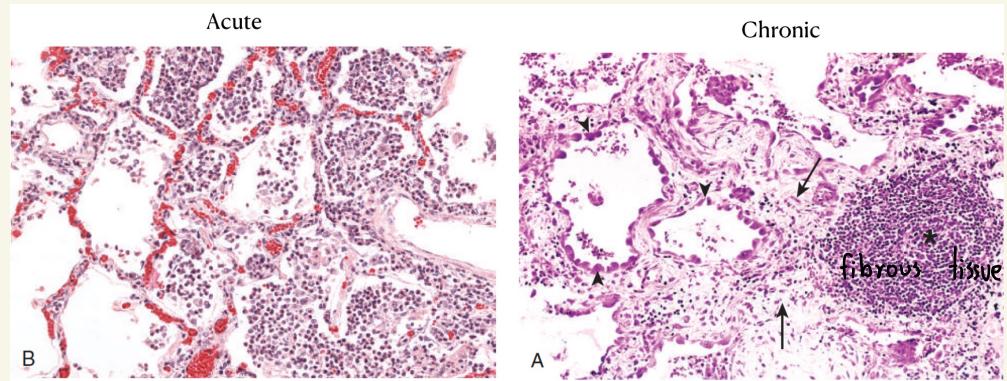
NSAIDs

I

• chronic inflammation

• cause

- inflammation រាយក្រិះ
- hypersensitivity
- ការកុំពោន់ពាក្យសង្គម



• morphology

- ជំនួយ mononuclear cell : lymphocyte & macrophage
- tissue destruction
- attempt at healing : fibrosis

• mediator

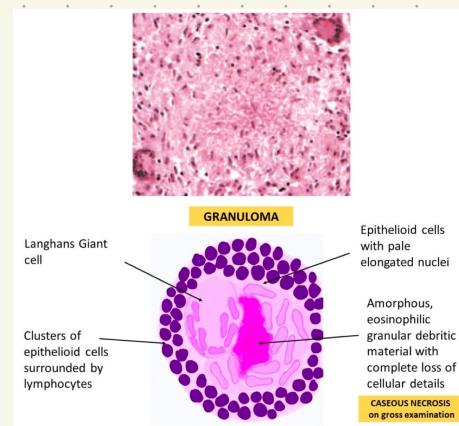
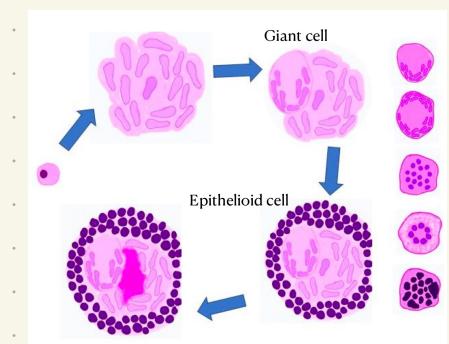
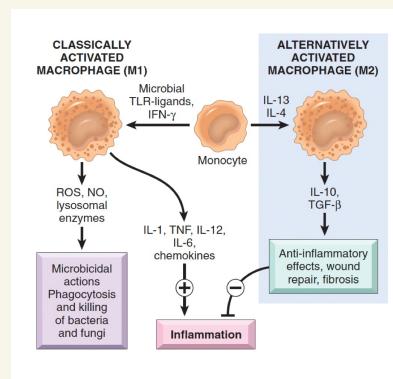
• macrophage

- M1 : នូវក្តុំ inflammation
- M2 : ឃុំឱ្យ inflammation

• lymphocyte

• granulomatous formation

- epithelioid cell & multinucleated giant cell = macrophage
- នាម macrophage & T cell នឹងត្រួតពិនិត្យ ឬ
- ឈរីនុទំ TB, leprosy, sarcoidosis & talc
- caseous necrosis = cell សេរីនា granuloma និងយក



• systemic effect of inflammation

- TNF, IL1 & IL6 ឲ្យក្នុំសម្រេច នៅក្បែង COX : PGE2 កំនែ fever
- IL1 & IL6 ឲ្យក្នុំ liver នូវ CRP : opsonization / pro-inflammatory response
- fibrinogen : រុញក្រុង RBC សម្រេច
- TNF, IL1 & IL6 ឲ្យក្នុំ bone marrow : WBC↑ (shift to the left)

• sepsis

- เกิด inflammation ห้องน้ำมี immunosuppression WBC ถูกใช้งานจนหมด

• tissue repair

- fibrosis = collagen

- keloid = scar spread beyond wound

- hypertrophic scar = scar ใหญ่กว่าปกติ

- angiogenesis

① vasodilation

② pericyte แยกตัวออก

③ migration von endothelial cell = อาณัติ VEGF

④ proliferation von endothelial cell

⑤ ร่างกายสร้าง capillary tube

⑥ ร่องรอย periendothelial cell

- ฟังหาย scar = matrix metalloproteinases (MMPs)

• collagenase = ย่อย collagen

• gelatinase = ย่อย fibronectin & amorphous collagen

• stromelysin = ย่อย proteoglycan, laminin, fibronectin & amorphous collagen

• tissue inhibitor of metalloproteinase (TIMPs) = อายุชั้ง MMPs

• balance MMPs & TIMPs จัดการขนาดของ scar

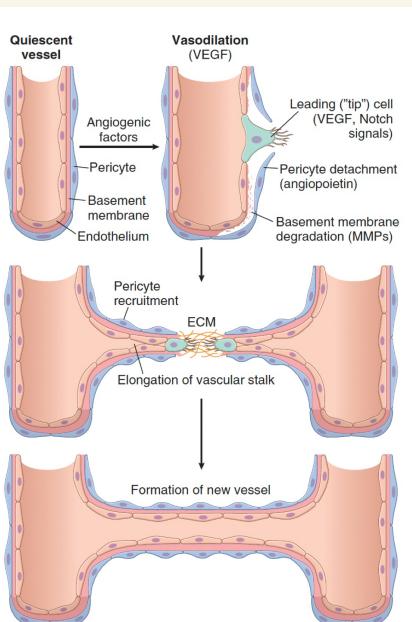
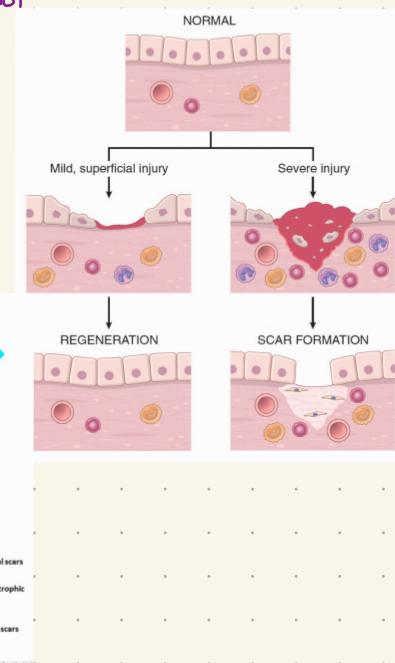
• ปัจจัยที่ส่งผลต่อ tissue repair

Local

- Infection
- Foreign body
- Poor perfusion → เส้นเลือดไม่ดี
- Trauma
- Cancer
- Hyperthermia

Systemic

- Collagen disorder
- Aging
- Diabetes
- Nutritional status
- Alcoholism
- Liver diseases
- Steroid



Cytokine

▪ แบบประสาททางสันดาลของมนุษย์

- autocrine = ส่งสารต่อไปในเซลล์เดียวกัน
- paracrine = เซลล์ส่งสารไปยังเซลล์อื่นๆ ในบริเวณเดียวกัน
- endocrine = เซลล์ส่งสารไปยังอวัยวะอื่นๆ
- แบบออกซิเจน S กับ M
 - interleukin
 - tumor necrosis factors (TNFs)
 - interferons (IFNs)
 - type I = IFN α , IFN β
 - type II = IFN γ
 - colony stimulating factor (CSFs)
 - transforming growth factor (TGFs)

▪ IFN α , IFN β

- ผู้ติดเชื้อ : virally infected cell
- กำจัดเชื้อ : viral replication

▪ IL1 β , IL6, TNF α

- ผู้ติดเชื้อ
- macrophage & DC
- B & T cell (IL6)
- กำจัดเชื้อ
- ร.ต.ก. leukocyte migration
- fever (brain)
- acute phase reactant (liver)

▪ main function

- pro-inflammation
 - = IL1-2-6-12-16-18-23, TNF, IFN

▪ parasitic/allergy

- = IL4-5-13

▪ regulatory

- = IL10, TGF β

▪ differentiation

- = GM-CSF, M-CSF, IL7

▪ chemotactic

- = IL17, IL8

(LT α)

▪ TNF α , TNF β , LT β

- ทำให้เส้นเลือดง่าย : endothelial permeability

▪ IFN γ

- ผู้ติดเชื้อ : CD4

- กำจัดเชื้อ : ร.ต.ก. macrophage & CD4

▪ IL2

- ผู้ติดเชื้อ : CD4

- กำจัดเชื้อ : ร.ต.ก. CD4, CD8 & B cell

• IL12

- ผู้ต่อต้าน : macrophage & DC

• ห้ามตัวที่

• สร้าง NK cell

• 促进 CD4 → Th1

• IL4, IL5, IL13

- ผู้ต่อต้าน : eosinophil

• ห้ามตัวที่ : 促进 CD4 → Th2 ทำให้สร้าง mast cell, eosinophil, basophil

• IL10, TGF β

- ผู้ต่อต้าน : Treg

• ห้ามตัวที่ : 促进 T cell → Treg

• GM-CSF, M-CSF, IL7

- ผู้ต่อต้าน : bone marrow stromal cell

• ห้ามตัวที่

• สร้างเม็ดเลือดขาว monocyte & granulocyte : GM-CSF & M-CSF

• สร้างเม็ดเลือดขาว B cell, T cell & NK cell : IL7

• IL17 (chemokine)

- ผู้ต่อต้าน : Th17

• ห้ามตัวที่ : ร้าย neutrophil

• IL6, IL23, TGF β

• ห้ามตัวที่ : 促进 CD4 → Th17

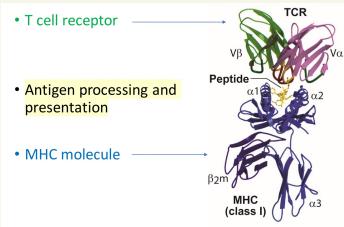
• IL8 (chemokine - CXCL8)

- ผู้ต่อต้าน : neutrophil, fibroblast & macrophage

• ห้ามตัวที่ : ร้าย WBC

Antigen presentation

T cell



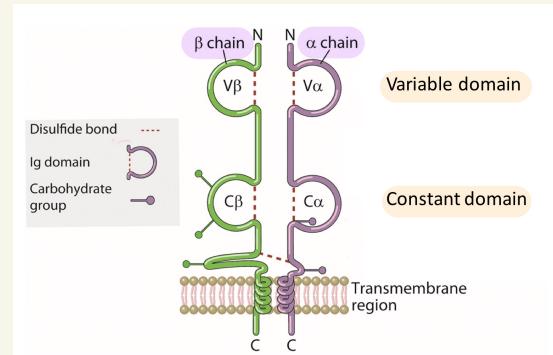
T cell receptor (TCR)

- ស្រែរបៀវត្សេវ TCR α & TCR β

• ព័ត៌មានលើកដែលត្រូវដឹងទៅគឺ variable & constant domain

↳ hypervariable/complementary-determining region (CDRs)

• CDRs = សារធៀតវា peptide-MHC complex



major histocompatibility complex (MHC)

- លុយចិត្ត 2 ស្រែរបៀវត្សេវ

• class I = CD8 $^+$ T cell និង cell ក្នុង

• class II = CD4 $^+$ T cell និង dendritic cell, macrophage & B cell

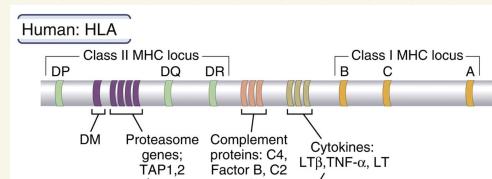
• លុយចិត្ត chromosome 6 = human leukocyte antigen (HLA)

• class I = HLA-A, -B & -C

• class II = HLA-DP, -DQ & -DR

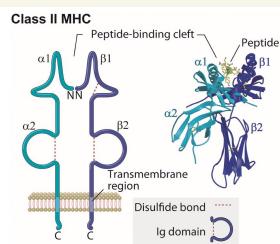
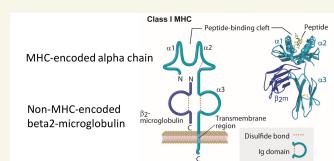
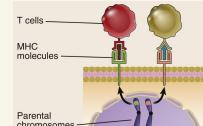
• មី poly morphic = ព័ត៌មានមិនអនុញ្ញាត ព័ត៌មានគួរពនូវ microbe និងកុំភោជន៍

• co-dominant = ផ្លូវការ gene ចំណាំដែល និង



• class I MHC = ខ្លួន α ឬ β ឬ γ ឱ្យកុំប្រើ peptide ឱ្យតែង

• class II MHC = ខ្លួន α ឬ β ឬ γ ឱ្យកុំប្រើ peptide ឱ្យរួម



• អំពីការបង្កើត cytokine

- class I : interferon (α, β, γ)

- class II : IFN- γ & IL-4

• HLA in transplantation

- HLA នៃយុវជន cell ក្នុង

- នូវ immunodominant alloreactive \rightarrow graft rejection

• HLA in pharmacogenomic

- ផ្សេងៗទិន្នន័យ

- HLA-B*5701 and abacavir (antiretroviral drug)
- HLA-B*5801 and allopurinol (gout, hyperuricemia)
- HLA-B*1502 and carbamazepine (epilepsy, nerve pain)

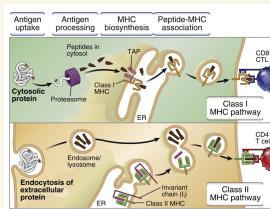
• peptide (antigen)

- TCR ត្រួតពេងដែលរួចរាល់ MHC-peptide complex ដែលត្រូវតីឡើ

- MHC ត្រួតពេងដែលត្រូវតីឡើ សម្រាប់ peptide ឱ្យខ្សោយនាំទៅ : broad specificity of peptide binding

• antigen processing

- Class I MHC

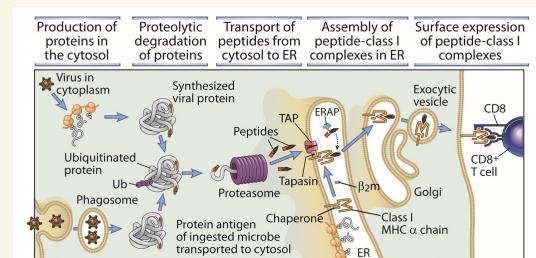


① endogenous antigen នឹងក្នុង cytosol នៃ APC កំណត់

- ស្អែកនៃ Virus

- injected into cytosol by bacteria

- ពាយឃាតុក្នុង vesicle នៃក្រុមហ៊ុន cytosol

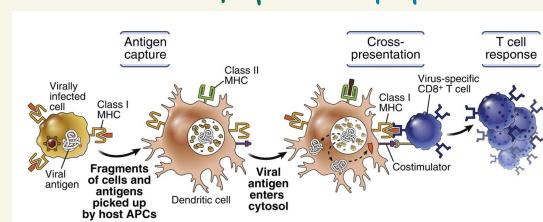


② proteasome ផ្សេងៗ peptide \rightarrow antigen ទៅក្នុងក្នុង ER គ្នាក់បាន Ub គ្នា ពេលបានយូរ

③ TAP ផ្សេងៗ peptide នៃ cytosol \rightarrow ER

④ Class I MHC ក្នុងក្នុង ER គ្នាក់បាន peptide - MHC complex

⑤ ក្នុងក្នុង cell surface



• cross-presentation

- dendritic cell phagocytosis antigen នឹងក្នុង antigen នឹង vesicle \rightarrow cytosol

- class I MHC នឹង

• Class II MHC

① APC សារព័ត៌មាន នៅក្នុង endosome

② endosome នៅក្នុង lysosome

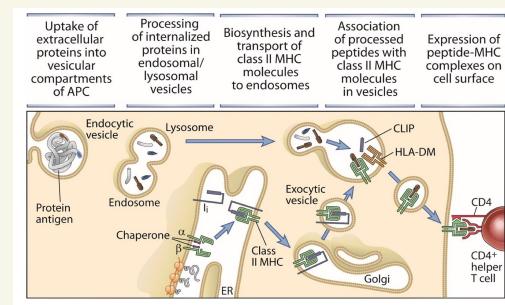
③ Class II MHC នៅក្នុង ER

④ invariant chain (li) នៅក្នុង cleft នៃ MHC ធ្វើឱ្យបានលើក

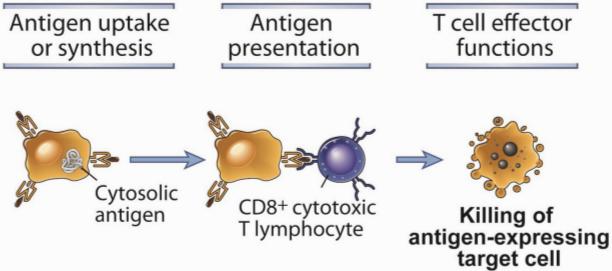
⑤ MHC នៅក្នុង endosome នៅលើ lysosome តាំងនូវរៀង li ដូចនេះនៅក្នុង CLIP នៃ cleft

⑥ HLA-DM និង CLIP នៃ៖ peptide និង

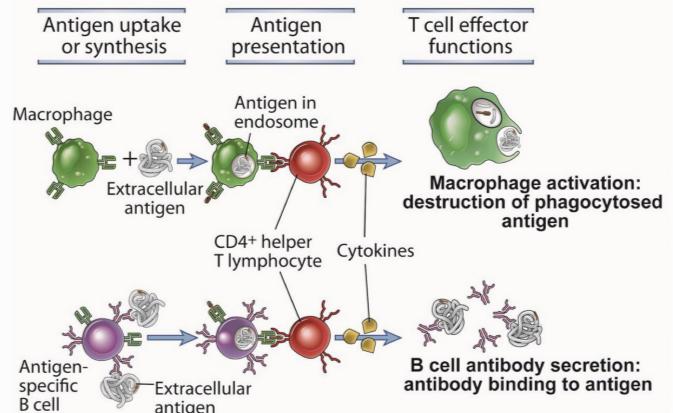
⑦ នៅលើ cell surface



Class I MHC-associated presentation of cytosolic antigen to cytotoxic T lymphocytes



Class II MHC-associated presentation of extracellular antigen to helper T cells

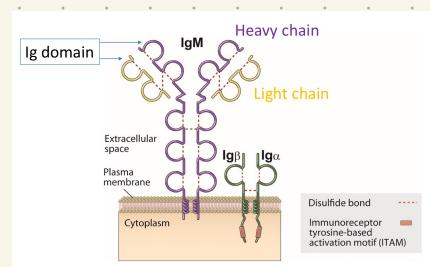


Feature	Class I MHC pathway	Class II MHC Pathway
Composition of stable peptide-MHC complex	Polymorphic α chain of MHC, $\beta 2$ -microglobulin, peptide 	Polymorphic α and β chains of MHC, peptide
Cells that express that MHC	All nucleated cells	Dendritic cells, mononuclear phagocytes, B lymphocytes; endothelial cells, thymic epithelium
Responsive T cells	CD8+ T cells 	CD4+ T cells
Source of protein antigens	Cytosolic proteins (mostly synthesized in the cell; may enter cytosol from phagosomes)	Endosomal/lysosomal proteins (mostly internalized from extracellular environment)
Enzymes responsible for peptide generation	Protease components of cytosolic proteasome	Endosomal and lysosomal proteases (e.g., cathepsins)
Site of peptide loading of MHC	Endoplasmic reticulum	Late endosomes and lysosomes
Molecules involved in transport of peptides and loading of MHC molecules	TAP	Invariant chain, DM



B cell

- B cell receptor (BCR) = immunoglobulin (Ig) - antibody (identical)
- ประกอบด้วย 2 light chain & 2 heavy chain รูปแบบ Y shape



- light chain = 1 variable region (V_L) & 1 constant region (C_L)
- heavy chain = 1 variable region (V_H) & 3-4 constant region ($C_H 1, 2, 3, 4$)

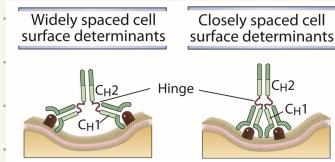
- variable region (Fab region) = จดจำ antigen
- hypervariable region (complementarity-determining region - CDRs)

• อยู่ที่ปลายของ variable region มี 3 CDRs ต่อ 1 สาย

• ประกอบด้วย heavy & light chain

• 3 CDRs of light chain + 3 CDRs of heavy chain = antigen-binding surface

- constant region (Fc region) = effector mechanism of Ab



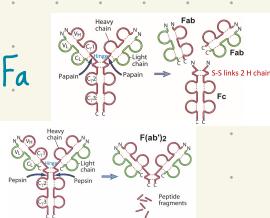
• opsonization.

• ช่วยให้เซลล์ Ab

- hinge region : ชุดเชื่อมระหว่าง Fab & Fc region

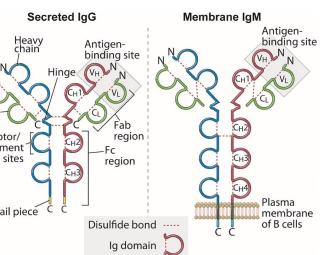
• papain : ตัด hinge region ให้เป็น 2 Fab + 1 Fa

• pepsin : ตัด hinge region ให้เป็น $2F(ab')_2$



• Fab fragment : ยึดจับกับ antigen

• Fc fragment : crystallizable



Antibody structure

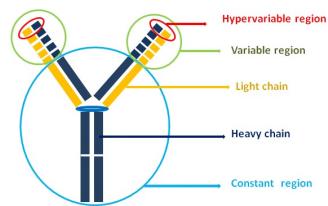


Image © medicalverge.in

CAR T cell

- chimeric antigen receptor T cell therapy
- ມີຄານສ່ວນດີໃນ tumor Ag recognition
- ໃນ single chain = ຍັງມີຕົວຕົວເຕີມ
- ພວກເຮົາ

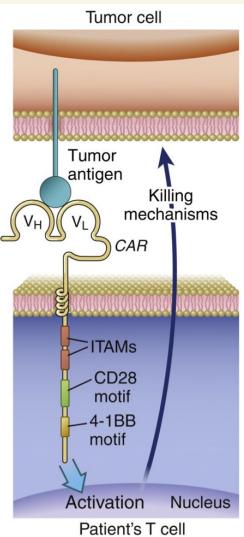
① ອອກແນບ CAR ກົບຕົວ tumor cell

② ອຳຕິດຕົວຕົວ T cell

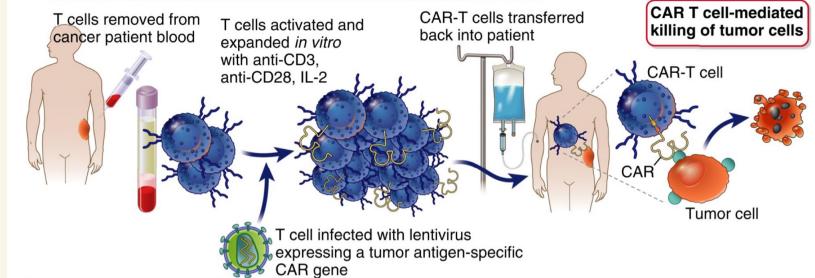
- transfection = ອຳຕິດຕົວ细胞
- transduction = ອຳຕິດຕົວ ດ້ວຍ virus

Tumor antigen recognition

Signaling for T cell activation



B Adoptive Transfer of Chimeric Antigen Receptor (CAR) T cells



Lymphocyte development

- germline organization of Ig

- heavy chain
 - variable (V)
 - diversity (D)
 - joining (J)
 - constant (C)
- light chain $\mu, \delta, \gamma, \alpha, \epsilon = \kappa \text{ & } \lambda$
 - variable (V)
 - joining (J)
 - constant (C)

- germline organization of TCR

- α chain
 - variable (V)
 - joining (J)
 - constant (C)
- β chain
 - variable (V)
 - diversity (D)
 - joining (J)
 - constant (C)

	Immunoglobulin			T cell receptor	
	Heavy chain	κ	λ	α	β
Number of variable (V) gene segments	~45	35	30	45	48
Number of diversity (D) gene segments	23	0	0	0	2
Number of joining (J) gene segments	6	5	4	50	12

Rearrangement

- V(D)J recombination

① តួ D-J ភាពកំណែ

② តួ V-(D)J ភាពកំណែ

③ transcription

④ splicing នៃ V(D)J-C ភាពកំណែ

⑤ translation

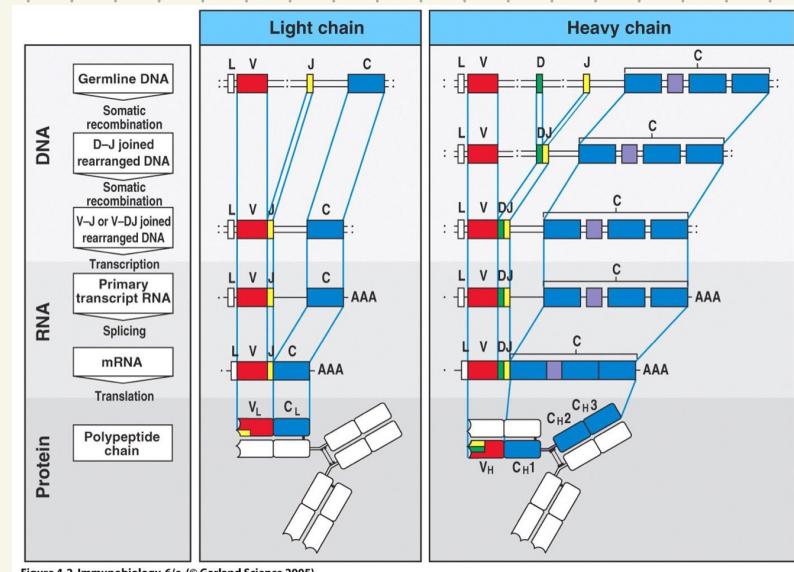
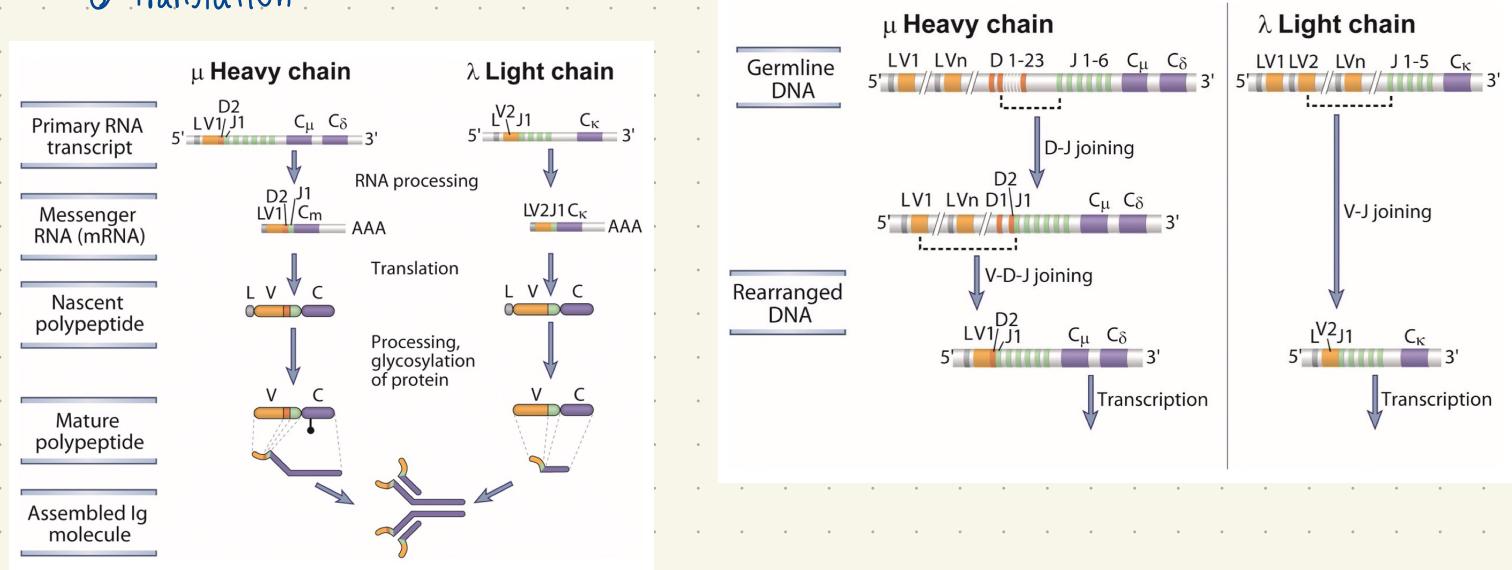


Figure 4-2 Immunobiology, 6/e. © Garland Science 2005



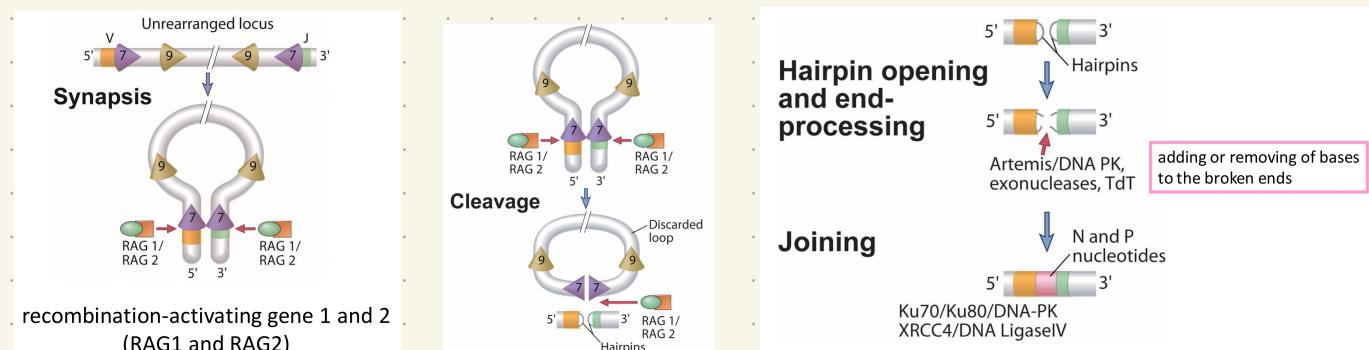
- V(D)J recombination mechanism

① តួ DNA ដែល RAG1 & RAG2 (recombination-activating gene)

↳ ខ្សោយ: developing T & B cell

② កំរាយទៅលើ modify ដំណឹង diversity

③ ផែិតកំណែ



• ពីនិងនិរន្តរ ទៅ antigen មួយ ឬទេ = immune repertoire

Selection

- เมื่อ幼稚淋白细胞 ที่มี functional receptor จะถูกกำกับ negative selection
- negative selection = ถ้าจับกับ self-antigen รึเปล่า

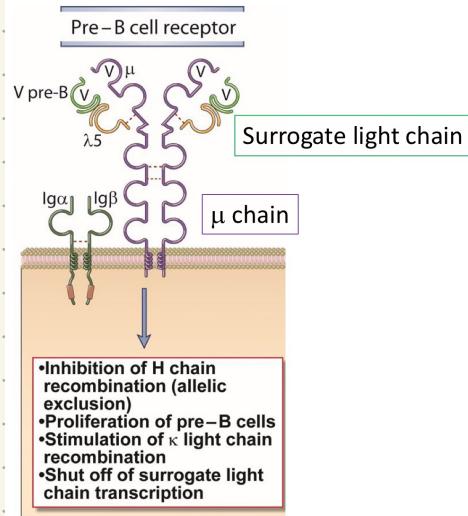
B cell dev.

① pro B cell

- $CD19^+$ (surface marker)
- เกต Ig μ (heavy) rearrangement = RAG

② pre B cell

- Ig μ chain จับกับ surrogate light chain
- ถ้า Ig μ functional = inhibit other rearrangement (allelic exclusion)
- ถ้า Ig μ non-functional = rearrange another chain สร้าง non-functional B cell จำนวนมาก
- หรือ kappa light chain rearrangement

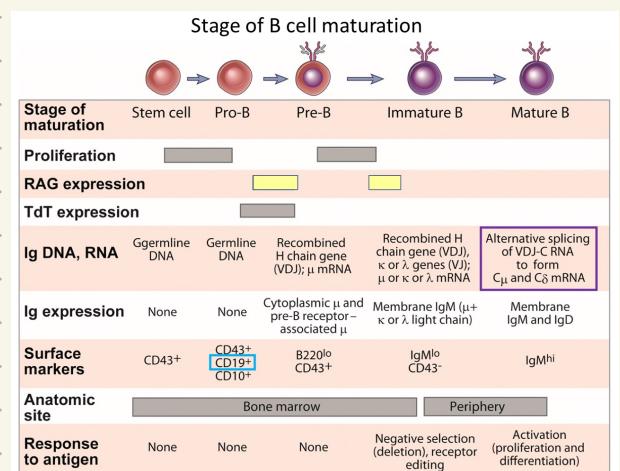


③ immature B cell

- kappa light chain จับกับ Ig μ = IgM
- IgM ทำ negative selection
- ถ้า kappa light chain functional = allelic exclusion
- ถ้า Kappa light chain non-functional = จะมี lambda chain สร้าง non-functional cell จำนวนมาก
- ไปพัฒนาต่อที่ spleen

④ mature B cell

- co-expression of IgM & IgD
↳ ห้อง剪接เลือก splicing constant region
- มี functional competency = ทำงานได้ดี



T cell dev.

① pre T cell

- TCR β chain rearrangement
- 若有功能的 TCR β functional \rightarrow β chain allelic exclusion

② double positive T cell

- 1 cell 表达 CD4 & CD8 = double positive
- 有 TCR α chain rearrangement
- TCR α 搭配 TCR β

③ single positive immature T cell

- CD3 = 表达 T cell 标记
- double positive cell 表达 CD4+ / CD8+ T cell
 ↳ 需要识别肽-MHC 复合物在 thymus = thymic education
- MHC 识别者 = self MHC = MHC restriction

positive selection

- 表达 T cell 表达 MHC 低亲和力 (low avidity)

• 表达 class I = CD8⁺

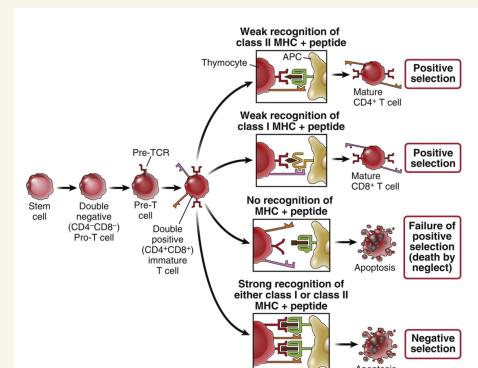
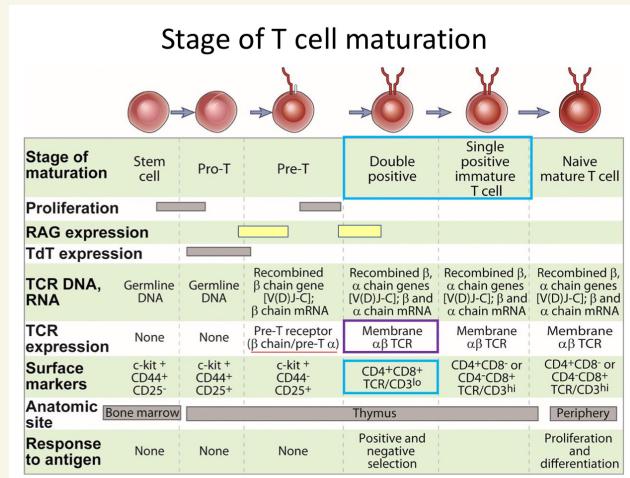
• 表达 class II = CD4⁺

negative selection

- 表达 T cell 表达 MHC 亲和力 = 调节/调节性 T cell

• 引起 autoimmunity

• 在 thymus 表达 MHC 的 T cell 增殖 = autoimmunity



Lymphocyte activation

T cell

- បង្កើតនៃការពិសោធន៍ជា activation

① T cell រីករាយ peptide-MHC complex

② T cell នីតិវិក cytokine

- IL-2 សម្រួលឱ្យ T cell កែតាខែតនៃការ autocrine & proliferation

③ ការពិសោធន៍ជាបន្ទាន់នៃ antigen

- signal នៃការពិសោធន៍ជា activation

① Ag

② costimulator

③ cytokine

- costimulator

• តុលាការ មិនមែន costimulator ត្រូវបាន MHC T cell នឹង activate

• CD28 & ICOS = សម្រួលឱ្យ រីករាយ B7-1 (CD80) & B7-2 (CD86)

• CTLA-4 & PD-1 = ចុងក្រោយ

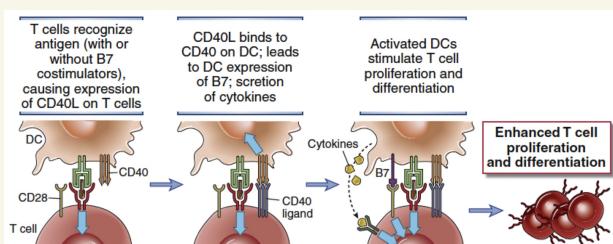
• ឯកសារ CD40 នៃ T cell activation

(នៃ APC)

(នៃ T cell)

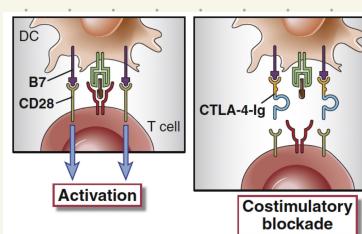
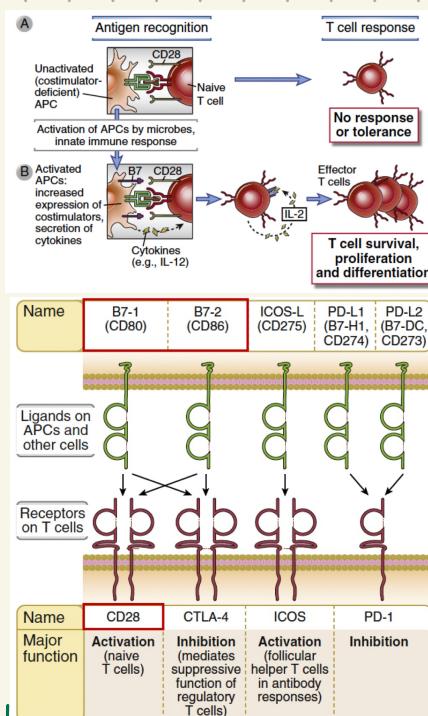
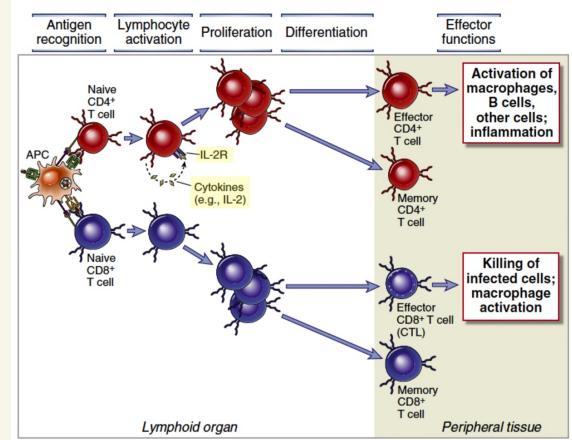
① តុលាការ មិនមែន B7 មានអាជីវកម្ម CD40 receptor ទៅចុងក្រោយ CD40 ligand

② សម្រួលឱ្យ APC ផ្តល់ B7 & cytokine



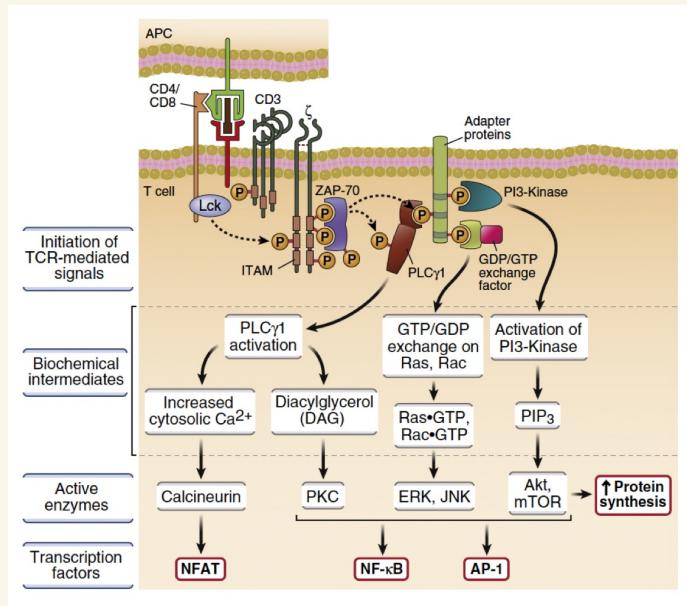
- clinical application

• សម្រួលឱ្យបង្កើត B7 នឹង T cell មុនពេលការ activate



• T cell signal transduction

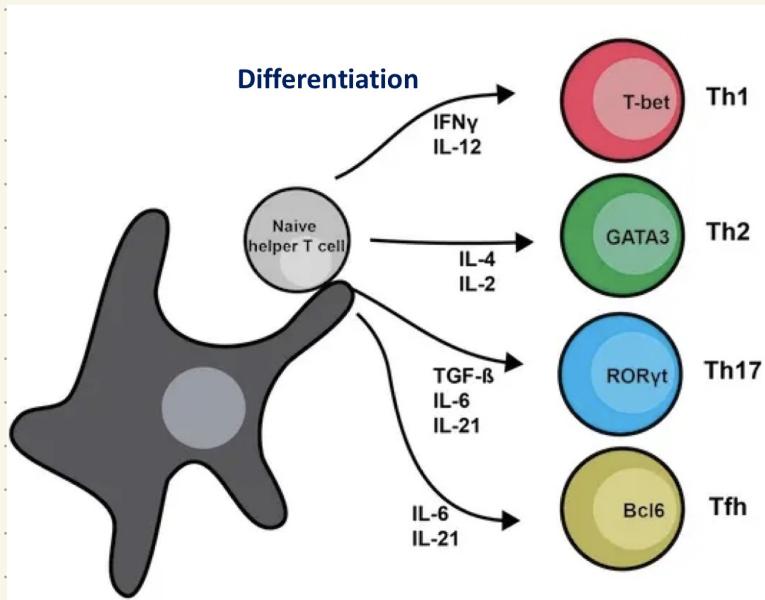
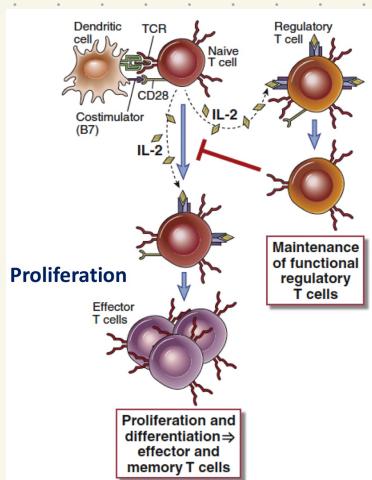
- เมื่อ TCR รับกับ Ag จะ CD4/8, CD3 & ζ (zeta) protein ก็จะส่งสัญญาณไป
ถึง transcription ของ T cell



- เมื่อที่น่อง cytokine ที่ T cell activation

• proliferation : IL-2

• differentiation



B cell

- B cell ແມ່ນອົງ 2 ກ່ຽວ

- T dependent B cell response

- B cell ຈະຕັບ Ag ຍູ້ກູ່ T cell

• ເຖິງ follicular B cell

- ສີ isotype switching & ↑ affinity ຫຼື memory B cell
(Ig ນາຍແນບ)

- T-independent B cell response

- B cell ອຸນ activate ຕ້ອງ Ag ຕອນວິທີນ spleen / lymph node / mucosal

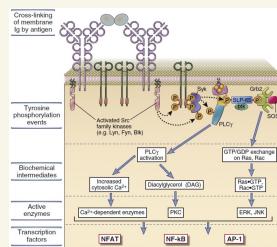
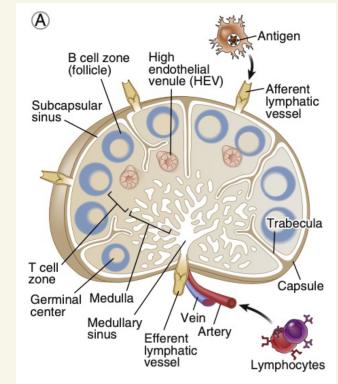
- ສີ IgM ທີ່ສ່ວນໃນນັ້ນ & ↓ affinity

- B cell activation

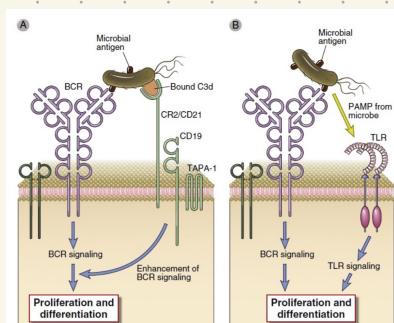
- ກຳດາ Ag ຈຶກກັນ BCR 2 ອົາ : cross-linking

- ກຳດາ Ag ຈຶປະໜາງ BCR & CR2/CD21 complement receptor

- ກຳດາ Ag ຈຶປະໜາງ BCR & Toll-like receptor



} innate receptor ມີກູ່ໃນ B cell



- ກຳໄກນວັດຫຼິດ B cell activation

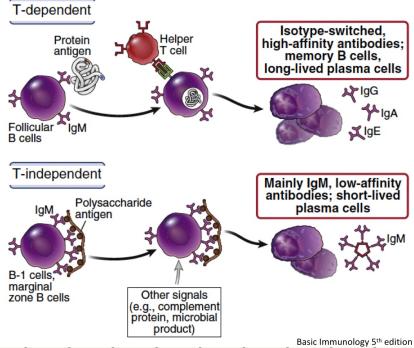
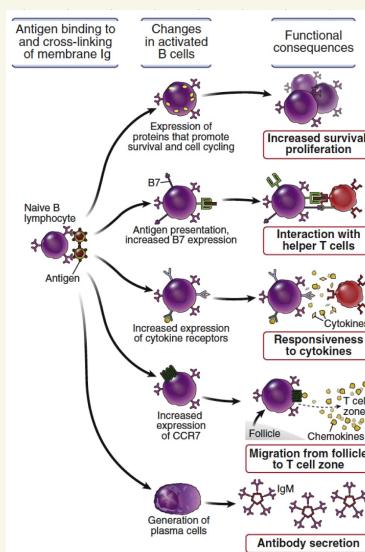
- B cell proliferation

- ໂອງ Ag ຍູ້ປິດ T cell

- ຕອນວິທີນຕ່າງ cytokine ດີບັນ

- ຍູ້ຕັ້ງ ສີ Ag ວິທີ = ຍູ້ຕັ້ງ chemokine

- ນົ່ວ່າ IgM



Basic Immunology 5th edition

• នរោងនៃ B & T cell

① T cell នឹង activate នៅ T zone ដែល APC

B cell នឹង activate នៅ B zone ដែល Ag
(primary follicle)

② B cell និង Ag ឆ្លើយ T cell នៅ T zone ដែល CD40 ឱ្យ B cell ឱ្យក្នុង CD40L ឱ្យ T cell

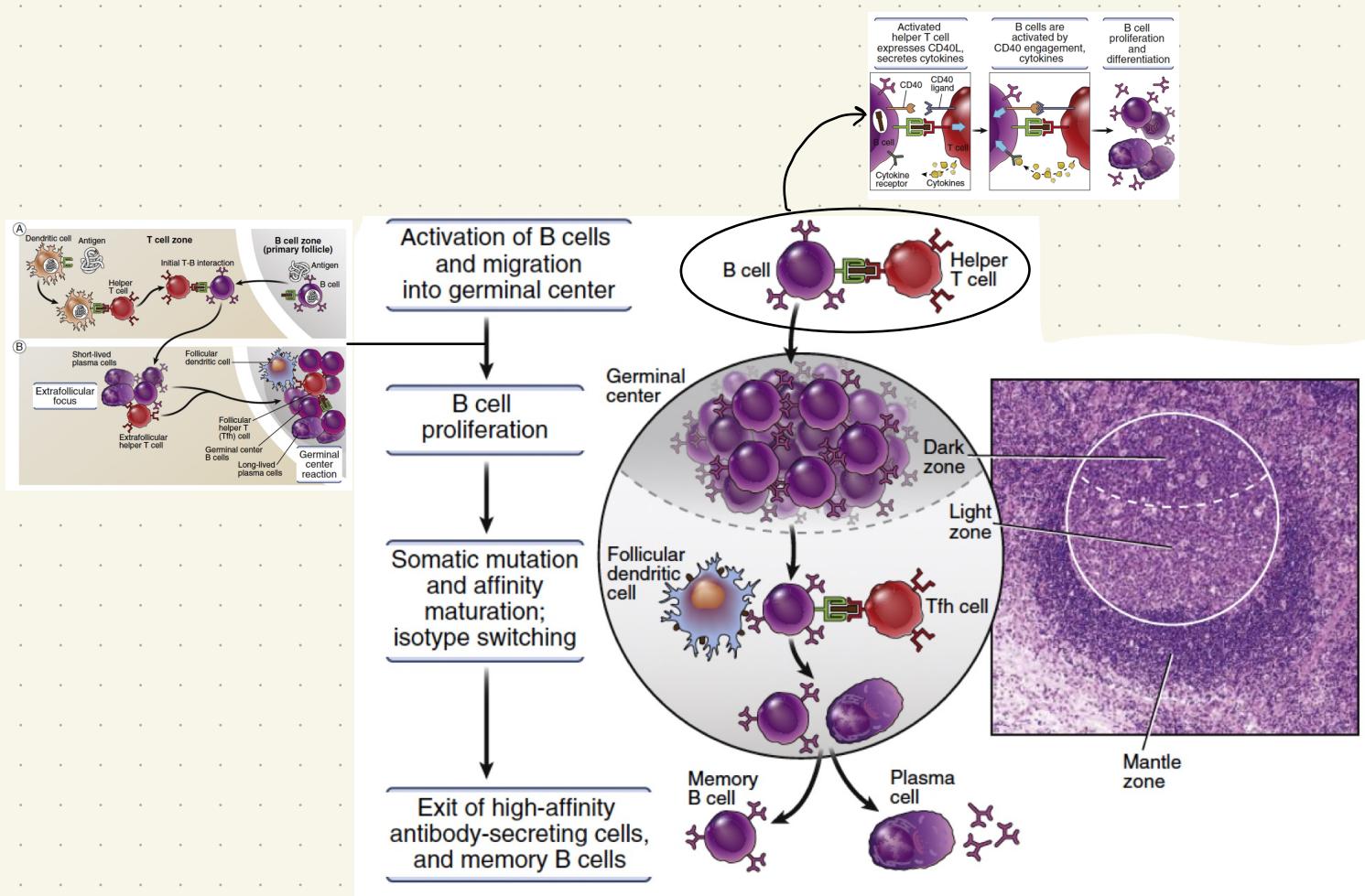
③ B cell នូវក្នុង follicle នៅដំឡើងនាម រាយក្រឹង dark zone of germinal center

follicular helper T (Tfh) cell & follicular dendritic cell នៅក្នុង follicle នូវក្រឹង light zone

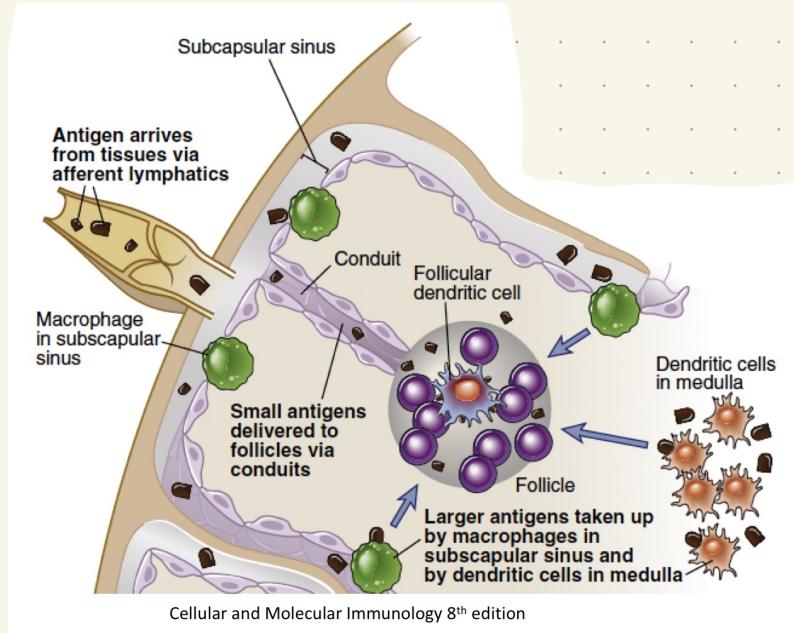
④ B cell នឹង isotype switching & somatic hypermutation (\uparrow affinity)

⑤ B cell នៅក្នុង light zone នៅក្នុង follicular dendritic cell នឹងក្រែងបរិសក្តី Ag
Tfh cell នឹងក្រែងបរិសក្តី Ag

⑥ B cell នឹង ៩ រាយក្រឹង memory B cell & plasma cell



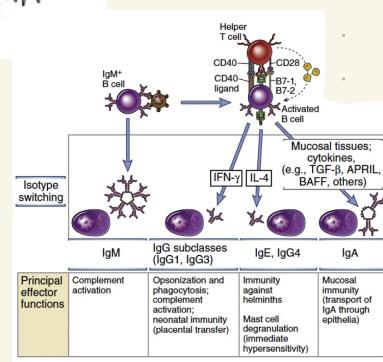
• នរោងក្នុង Ag & follicular B cell



Cellular and Molecular Immunology 8th edition

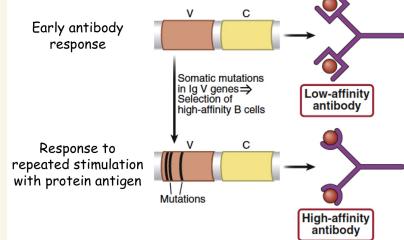
• ផលិត isotype switching

- សម្រេចតាម CD40L & cytokine នៃ T cell
- កំណត់ដោយ heavy chain



• នរោងក្នុង affinity

- កែតា somatic mutation of Ig V gene



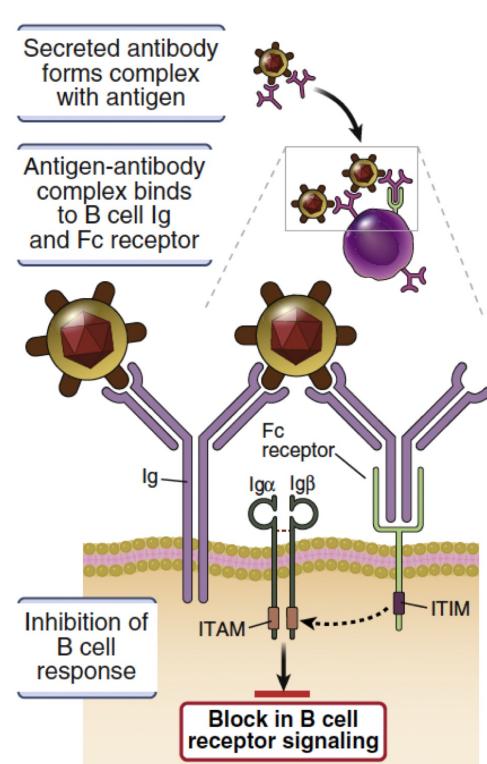
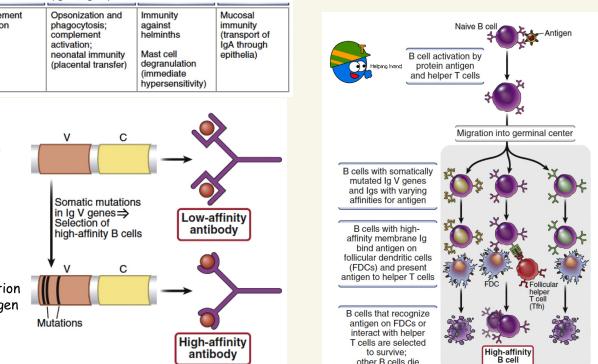
• antibody feedback

- កំណត់ដោយ terminate B cell activation

① Ab-Ag complex អាចបញ្ចប់ BCR & Fc receptor

↳ IgG ឱ្យបូន្ថែម Ag

② block activating signal on Ag receptor.



Adaptive effector responses

T helper cell

• T helper cell អំពីនេះ 4 ភ្លេង

- Th1
- Th17
- Th2
- Treg

• Th1 cell

• មិនតែខ្សោយការ intracellular microbe (phagocytosed) ទេស៊រត្រូវ macrophage

• transcription factor = T-bet

• សំគាល់ IL-12

• លំនា IFN γ

• Th1 dev.

① IL-12 (in dendritic cell & macrophage) & IFN γ (in NK cell)

② សំគាល់ transcription factor = T-bet, STAT1 & STAT4

③ ពីរុវ្ភារ់ naive CD4 \rightarrow Th1

④ Th1 ផ្តល់ IFN γ សំគាល់ Th1 ទៅ & សំគាល់ Th2 & Th17

• Th1 function (IFN γ)

• activate macrophage = កែតាត classical pathway of macrophage activation

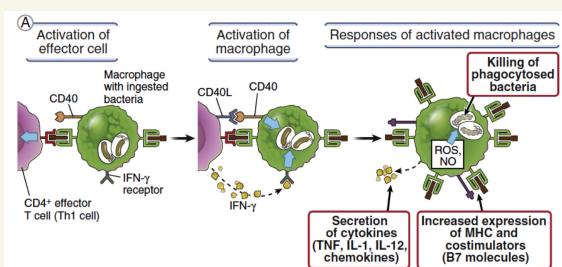
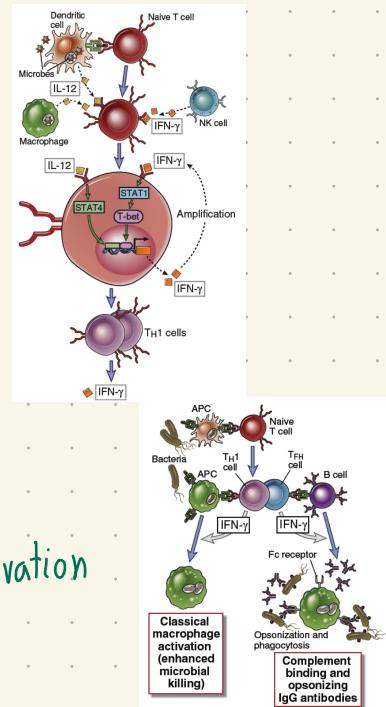
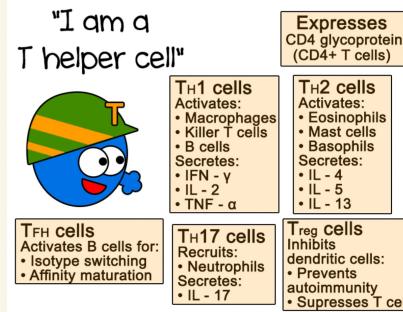
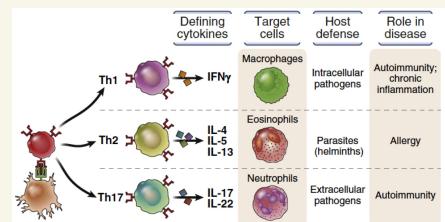
• នៅពី phagocytosed = លំនា ROS, NO & lysosomal enz.

• ផ្តល់ cytokine = TNF, IL-1, chemokine = leukocyte recruitment (inflammation)

IL-12 : Th1 differentiation & IFN γ production

• ពីរុវ្ភារ់ B7 & MHC : T cell activation

• នៅពី B cell = ពីរុវ្ភារ់ Ig \rightarrow IgG



• Th2 cell

- ชื่นตัวที่สำคัญ helminth จึงมีตัวนี้ mast cell & eosinophil
- ภัยเงียบ allergy
- transcription factor = GATA-3
- หลักตัวนำ = IL-4
- ผลิต = IL-4, IL-5 & IL-13

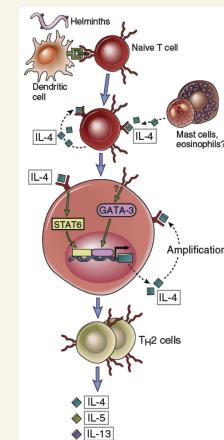
• Th2 dev

① IL-4 (T cell, mast cell & eosinophil)

② หลักตัวนำ transcription factor = GATA-3 & STAT6

③ ทำให้ naive CD4 → Th2

④ Th2 ผลิต IL-4 ยับยั้ง Th1 & Th17



• Th2 function

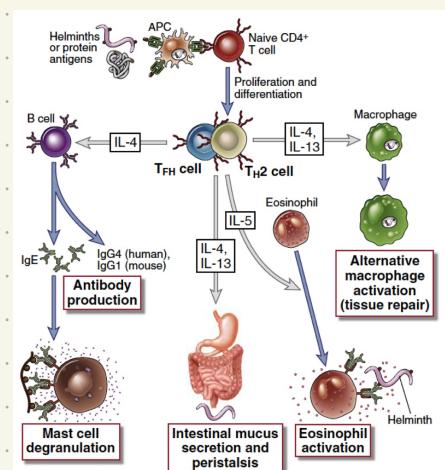
• IL-4 = เจรจา B cell ปล่อย Ig → IgE

• IL-5 = eosinophil

• IL-4 & IL-13

• mucosal barrier

• macrophage activation (alternative) + ยับยั้ง macrophage activation ให้ตาม Th1



classical & alternative macrophage activation

• classical (M1)

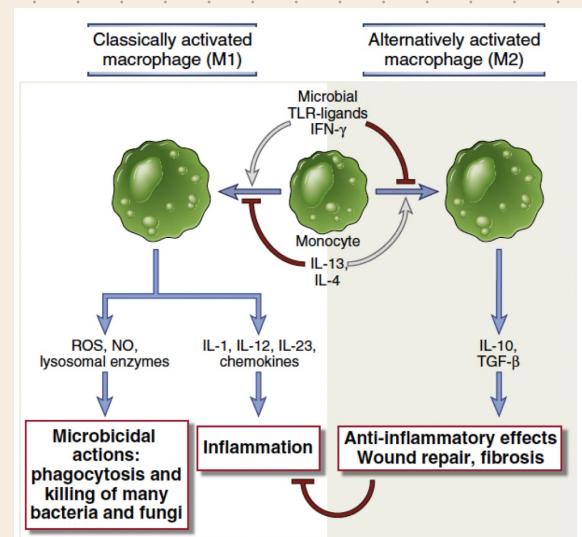
• IFN γ

• ภัยเงียบ inflammation

• alternative (M2)

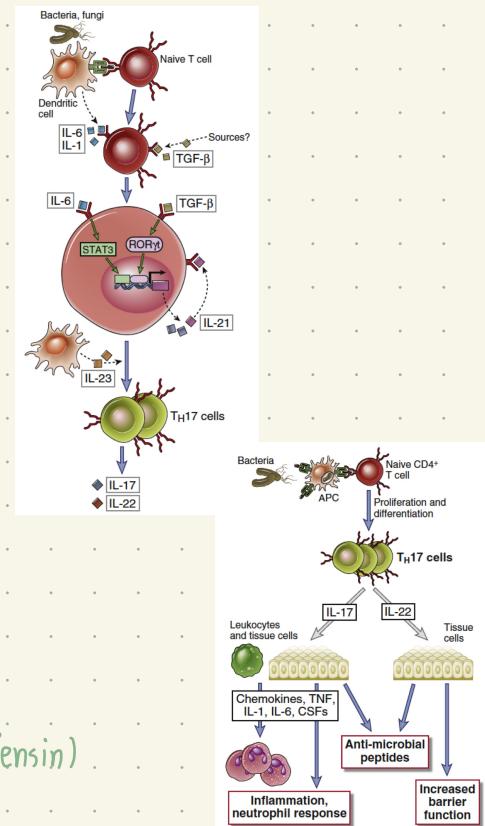
• IL-4 & IL-13 on Th2

• anti-inflammation → tissue repair & fibrosis



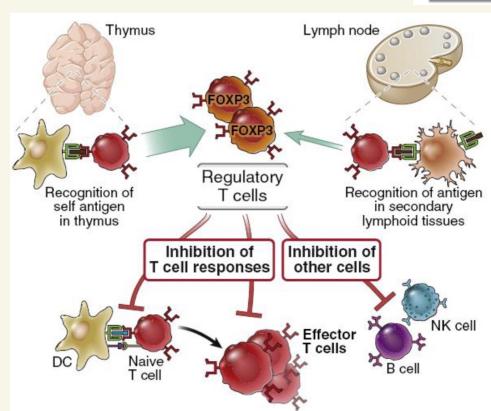
• Th17 cell

- ប៉ុន្មោះ extracellular pathogen
- កំណើនធ័រ autoimmune
- transcription factor : ROR γ t
- សេចក្តីផ្តើម : TGF- β , IL-6 & IL-1
- ផែនតារ : IL-17 & IL-22
- maintain តារ : IL-23
- Th17 dev.
 - IL-1 (APC), IL-6 (APC), TGF- β
 - សេចក្តីផ្តើម transcription factor : ROR γ t & STAT3
 - កំណើន naive CD4 \rightarrow Th17
 - APC ផែនតារ IL-23 យ៉ាងខ្លួន fungi & maintain Th17
- Th17 function
 - IL-17 : សេចក្តីផ្តើមនៃ chemokine
 - IL-17 & IL-22 : សេចក្តីផ្តើមសំគាល់ anti-microbial peptide (defensin)



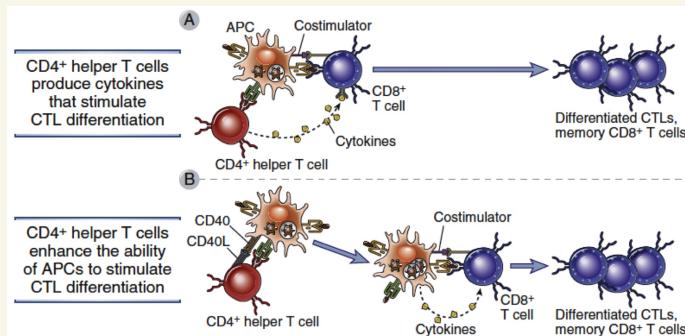
• Treg cell

- CD4 $^{+}$ CD25 $^{+}$ T cell
- អង្កេវ់ suppress immune response
- transcription factor : Foxp3
- អង្កេវ់ inhibitory cytokine : TGF β & IL-10



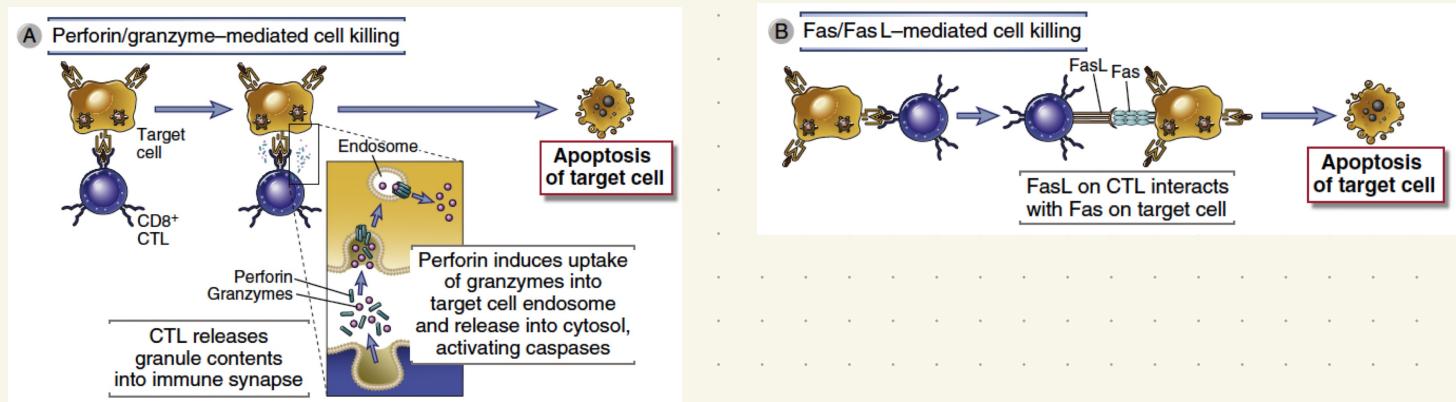
Cytotoxic T cell

- The following differentiation of CTL (cytotoxic T lymphocyte)



- mechanism of cytotoxicity នឹង 2 របៀប (the kiss of death)

- របៀប perforin & granzyme
 - perforin និង granzyme និត្តនកល់ cytosol នៃ target cell
- របៀប Fas/Fas L
 - FasL នូវ CTL ឲ្យឱ្យ Fas នូវ target cell



"I am a
killer T cell"



Expresses
CD8 glycoprotein
(CD8⁺ T cells)

- ① Recognize antigen combined with class I MHC (altered self cells)
- ② Receive signal for activation:
 - With CD4 T cell help: Cytokines (IL-2)
 - Without help: Activation by potent APCs
- ③ Releases cytotoxic proteins:
 - Perforin: Forms a pore for delivery of granzymes
 - Granzymes: Programmes cell to die (Induces apoptosis)
 - Granulysin: Stabs the cell (Creates holes in target membrane & destroys it)

Memory T cell

- Naive T cell ($CD45RA^+$) / memory T cell ($CD45RO^+$)

- memory T cell dev.

- ពេល T cell រាយការណ៍នាំការឃុំទៅ memory

- ចំណាំ naive T cell ក្នាយការណ៍ memory

- តម្លៃសមបំពេញ memory T cell

- មីនី anti-apoptotic protein = នាយកភាព

- slow proliferation & self-renew

- maintain តែង IL-7 & IL-15

- នៅក្នុង 3 រដ្ឋ

- central (TCM)

- នៅក្នុង lymphoid organ

- ដំឡើងនានាដឹកជឺ Ag \rightarrow ឈើ effector cell នៃ secondary response

- effector (TEM)

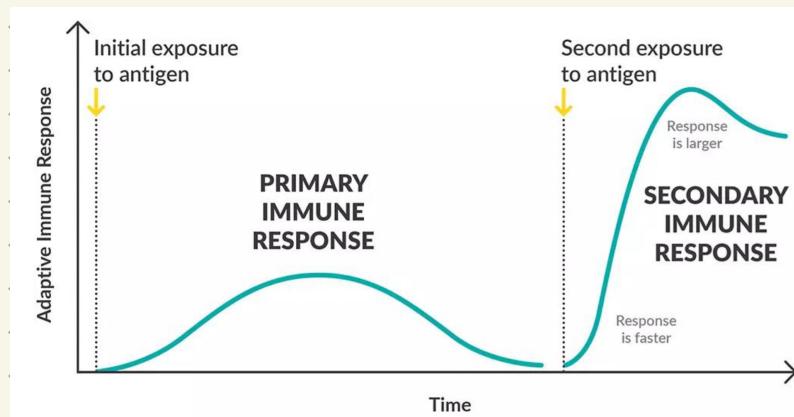
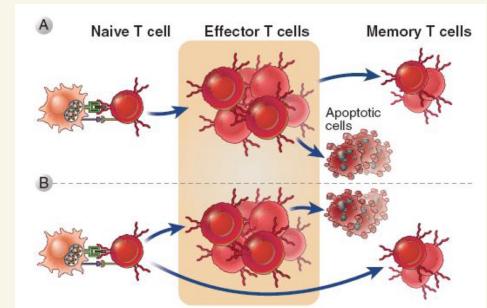
- នៅក្នុង circulation

- rapid effector response

- tissue-resident (TRM)

- នៅក្នុង tissue

- first line of defense





B cell

Ig 5 នៅ

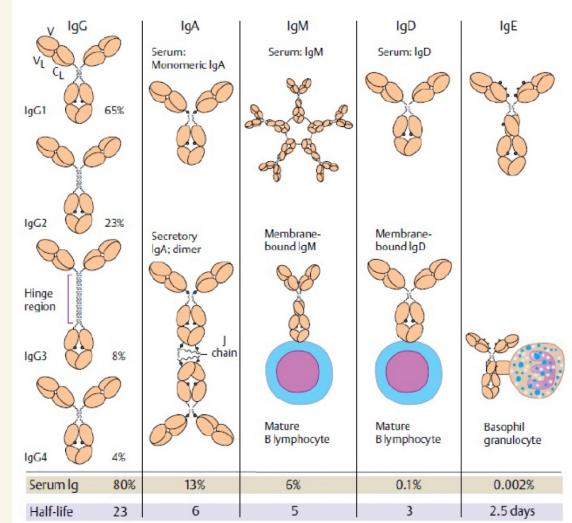
- IgG (common & $t_{1/2}$ ខ្ពស់)

- IgA

- IgM

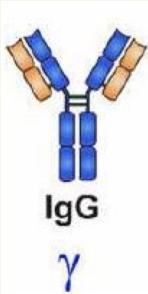
- IgD

- IgE



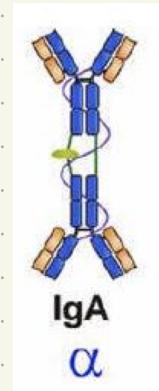
IgG

- main Ab in secondary response
- complement fixation & opsonization
- neutralize toxin & pathogen
- cross placenta = passive immunity



IgA

- secretion & milk
- monomer in circulation, dimer in secretion
- across epithelial cell = transcytosis
- in GI = gut infection

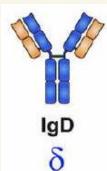


IgM

- immediate response
- monomer in B cell, pentamer in circulation (J chain)
- complement fixation
- BCR in B cell
- agglutination reaction



• IgD



• លោកស្រប B cell

• IgE

• លោកស្របស្អាត

• ចិត្តក្នុង mast cell & basophil សម្រាប់ពន្លាគំពង់ degranulation

• ធ្វើឱ្យ hypersensitivity (Type I) → histamine

• activate eosinophil

• ចិត្តក្នុង Fc receptor (FcεRI)



IgE

Fc Receptor	Affinity for Ig	Cell distribution	Function
FcγRI (CD64)	High ($K_d \sim 10^{-9}$ M); binds IgG1 and IgG3; can bind monomeric IgG	Macrophages; neutrophils; dendritic cells	Phagocytosis; activation of phagocytes
FcγRIIA (CD32)	Low ($K_d \sim 0.6-2.5 \times 10^{-8}$ M)	Macrophages; neutrophils; eosinophils; platelets	Phagocytosis; cell activation (inefficient)
FcγRIIB (CD32)	Low ($K_d \sim 0.6-2.5 \times 10^{-8}$ M)	Lymphocytes; DCs; mast cells; neutrophils; eosinophils; macrophages	Feedback inhibition of B cells; attenuation of inflammation
FcγRIIIA (CD16)	Low ($K_d \sim 0.6-2.5 \times 10^{-8}$ M)	NK cells	Antibody-dependent cellular cytotoxicity (ADCC)
FcεRI	High ($K_d \sim 10^{-10}$ M); binds monomeric IgE	Mast cells; basophils; eosinophils	Activation (degranulation) of mast cells and basophils

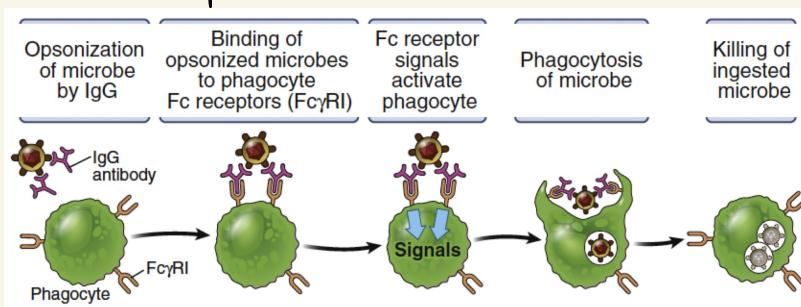
• mr neutralization toxin & microbe ឬ Ab

• block microbe entry

• block microbe binding

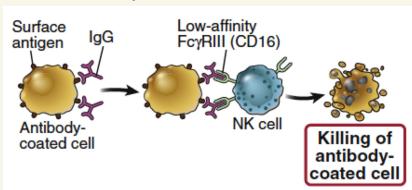
• block toxin binding

• Ab mediated opsonization



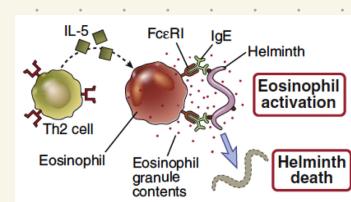
• antibody-dependent cellular cytotoxicity (ADCC)

• ទំនួន IgG ចិត្តក្នុង target cell ឬវិវីតុងក្នុង Fcγ receptor ឬ NK cell = NK cell ឬ NK cell ឬ neutrophil



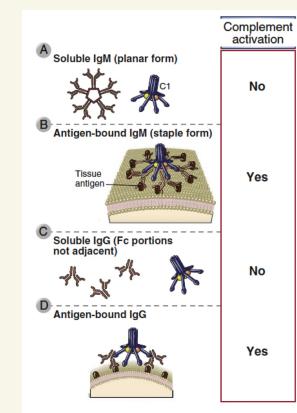
• IgE & eosinophil

• IgE ចិត្តក្នុង helminth ឬចិត្តក្នុង FcεRI ឬ eosinophil ក្នុង degranulation



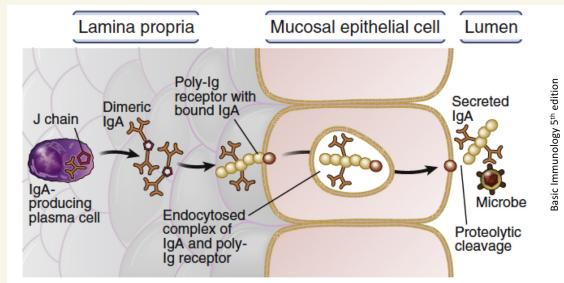
- Ag-Ab complex mediated complement activation

• ឧែត្តម្ភៃត្រូវ Ab ពេលចិញ្ចាប់ Ag.



- mucosal immunity

• poly-Ig receptor នៃ epithelial ទទួល J chain ដើរក្នុង IgA & IgM

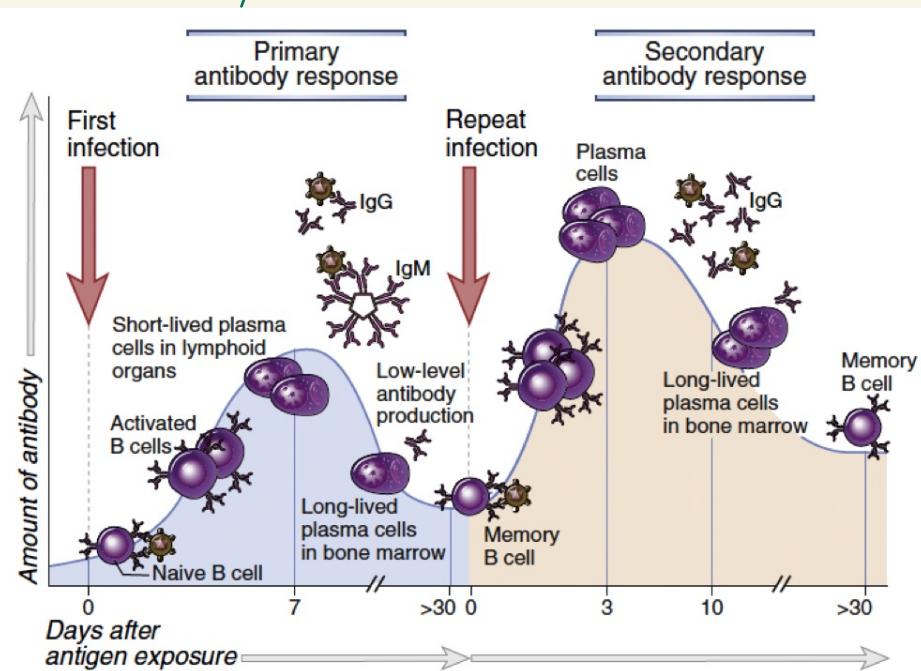


- neonatal immunity

• IgG ចិញ្ចាប់ neonatal Fc receptor (FcRn) នៃ placenta នៅក្នុងព័ព័ fetal circulation
 • គឺ FcRn អាចឈុំ IgG មិនឈុំឡាតាំង
 • FcRn-IgG complex នឹងចូល endosome និងចូល lysosome របស់
 • FcRn អាចរាយ IgG ក្នុងព័ព័ circulation = recycle

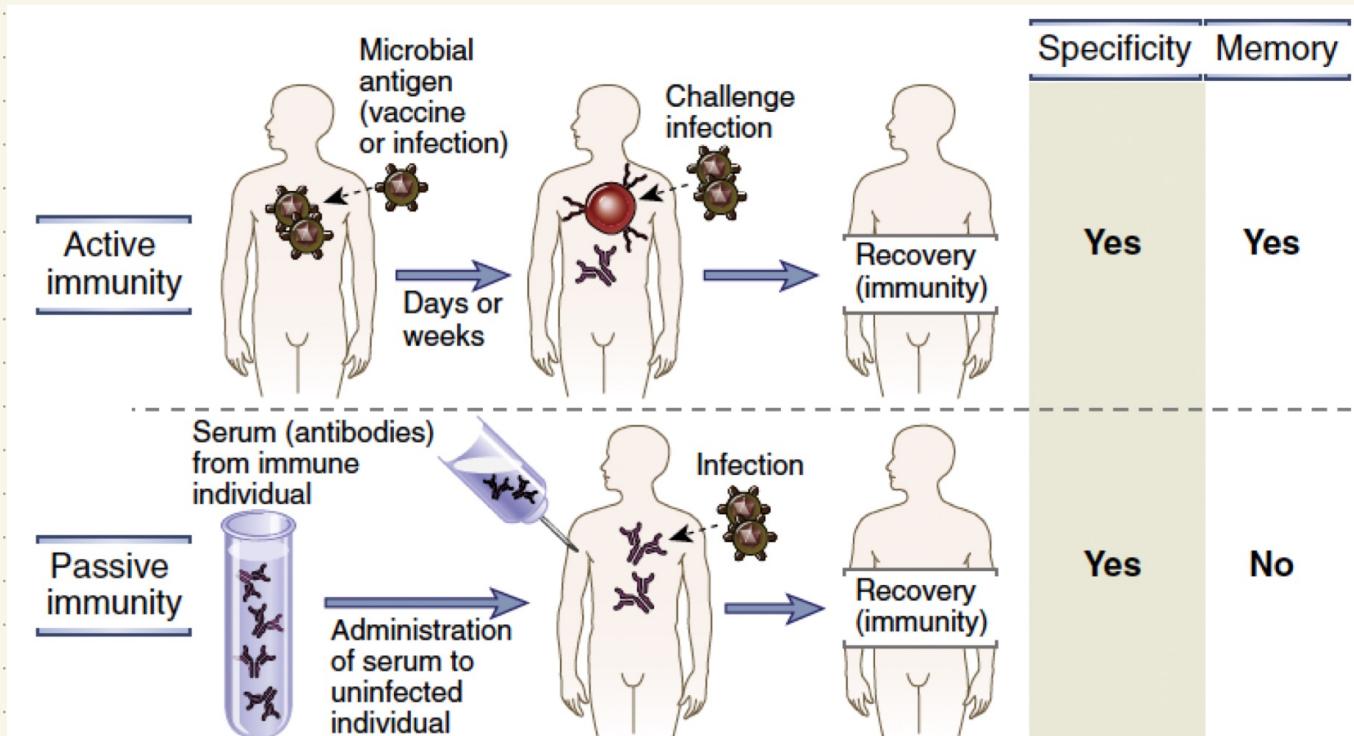
Memory B cell

- ឧែត្តម្ភៃត្រូវ Ab ក្នុងដំណឹងការព័ត៌មាន
- ចិញ្ចាប់ spleen > circulation & tissue
- មិន anti-apoptotic protein



Feature	Primary response	Secondary response
Peak response	Smaller	Larger
Antibody isotype	Usually IgM > IgG	Relative increase in IgG and, under certain situations, in IgA or IgE
Antibody affinity	Lower average affinity, more variable	Higher average affinity (affinity maturation)
Induced by	All immunogens	Mainly protein antigens

Application immunization

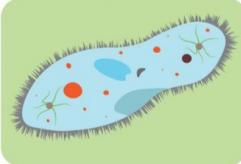


Acquired Immunity

Immunity that develops
during your lifetime

Active Immunity

Natural
Antibodies developed
in response to
an infection



Artificial
Antibodies developed
in response to
a vaccination

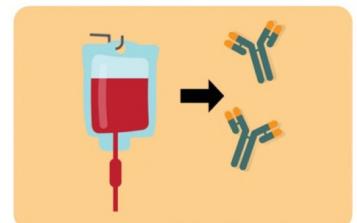


Passive Immunity

Natural
Antibodies received
from mother,
through breast milk



Artificial
Antibodies received
from a medicine,
from a gamma
globulin injection or infusion



Leukocyte migration

- กระบวนการ blood \Rightarrow tissue เพื่อ
 - effector of myeloid cell
 - effector of lymphoid cell

เข้าไปใน lymph node

- selectin : transmembrane glycoprotein
 - endothelial : P & E selectin
 - leukocyte : L selectin ที่ ligand คือ GlyCAM1 & MadCAM1

- integrin : surface protein
 - LFA-1

- $\alpha_4\beta_7$ ที่ ligand คือ MadCAM1

- chemokine : cytokine ที่เรียกว่า WBC chemoattractant
 - \uparrow ปริมาณ selectin & integrin
 - \uparrow affinity von integrin

neutrophil migration

① macrophage หลั่ง cytokine (TNF, IL-1) ทำให้ endothelia ที่ selectin & integrin \uparrow

(E > P)
② WBC จับกับ selectin ทำ rolling

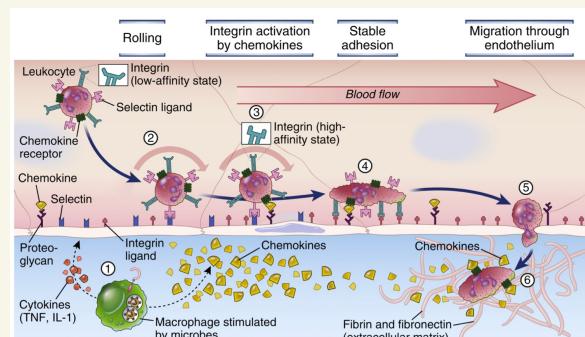
③ integrin เกิดการเปลี่ยนโครงสร้างทำ affinity \uparrow = high affinity binding

④ เกิด firm attachment

⑤ endothelia อาจ tight junction อาจ ทำให้ WBC ผ่านไป = transmigration

⑥ WBC นำ protein เช่น Ag

Family	Molecule	Distribution	Ligand (Molecule; Cell Type)
Selectin	P-selectin (CD62P)	Endothelium activated by histamine or thrombin	Sialyl Lewis X on PSGL-1 and other glycoproteins; neutrophils, monocytes, T cells (effector, memory)
	E-selectin (CD62E)	Endothelium activated by cytokines (TNF, IL-1)	Sialyl Lewis X (e.g., CLA-1) on glycoproteins; neutrophils, monocytes, T cells (effector, memory)
	L-selectin (CD62L)	Neutrophils, monocytes, T cells (naive and central memory), B cells (naive)	Sialyl Lewis X/PNA on GlyCAM-1, CD34, MadCAM-1, others; endothelium (HEV)
Integrin	LFA-1 (CD11aCD18)	Neutrophils, monocytes, T cells (naive, effector, memory), B cells (naive)	ICAM-1 (CD54), ICAM-2 (CD102); endothelium (upregulated when cytokine activated)
	Mac-1 (CD11bCD18)	Neutrophils, monocytes, dendritic cells	ICAM-1 (CD54), ICAM-2 (CD102); endothelium (upregulated when cytokine activated)
	VLA-4 (CD49aCD29)	Monocytes, T cells (naive, effector, memory)	VCAM-1 (CD106); endothelium (upregulated when cytokine activated)
	$\alpha_4\beta_7$ (CD49dCD29)	Monocytes, T cells (gut homing, naive, effector, memory), B cells (gut homing)	VCAM-1 (CD106), MadCAM-1; endothelium in gut and gut-associated lymphoid tissues



1. Cytokine release
2. Rolling
3. High affinity binding
4. Firm attachment
5. Transmigration
6. Moving to the site

- defect in neutrophil migration
- LAD1 (leukocyte adhesion deficiency)
 - defect in LFA1 (integrin) = CD18 gene

- LAD2
 - defect in E/P selectin ligand

- LAD3
 - defect in chemokine

• T cell migration

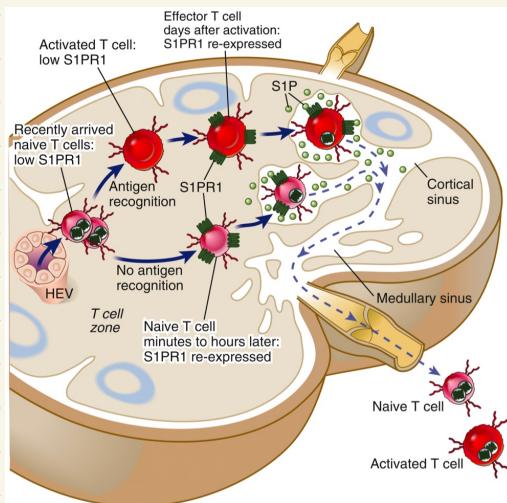
① naive T cell ออก thymus → blood

② เลี้ยง lymph node ผ่าน high endothelial venules

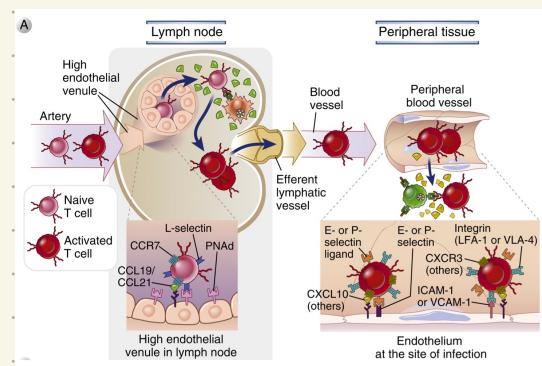
- รับ S1P (sphingosine 1-phosphate) มากใน blood & lymph น้อยใน tissue

- ผู้ที่รับ S1P ใน blood/lymph T cell จะมี S1PR มากขึ้น แต่จะมี integrin & selectin น้อยลง
 ↳ เนื่องจาก PNAd

- พอถูก S1P ใน lymph node T cell จะสัมผัติ S1PR กลับมา ทำให้ T cell กลับเข้าไปใน blood



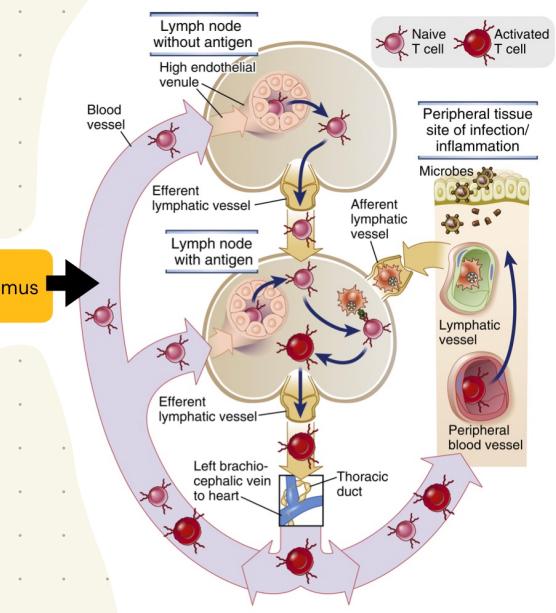
• เมื่อ S1PR inhibitor จะทำให้เป็น immunosuppressive



③ ตัว Ag = ต้อง activate แล้วไปที่ tissue

ตัว Ag = ออกที่อยู่ใน blood แล้วก็เข้าไปที่ lymph node

④ ที่ infection site จะมี defect ของ neutrophil migration



• B cell migration

① B cell in lymph node cross HEV

② within follicle

③ w^o antigen activate B cell → plasma cell & memory cell

④ o^ug^u germinal center = d^r Ab }

within bone marrow : d^r Ab } neogenesis S, PR & chemokine

within infection site

• memory cell

• central memory T cell : s^oo^gin lymphoid tissue

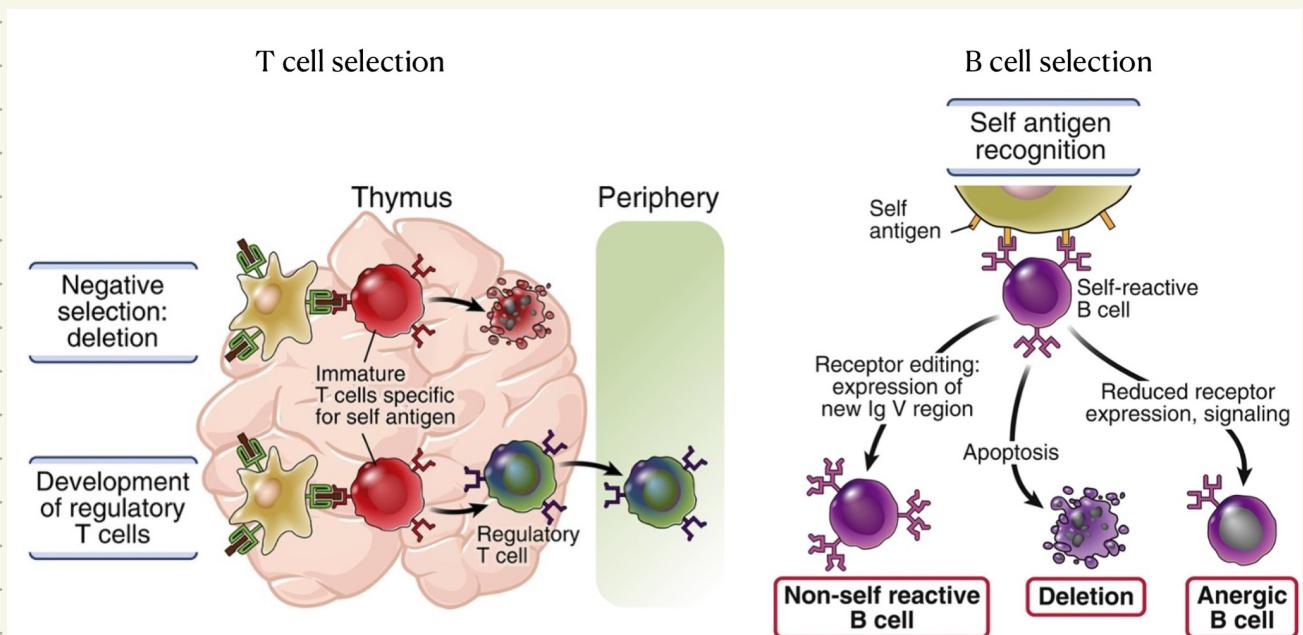
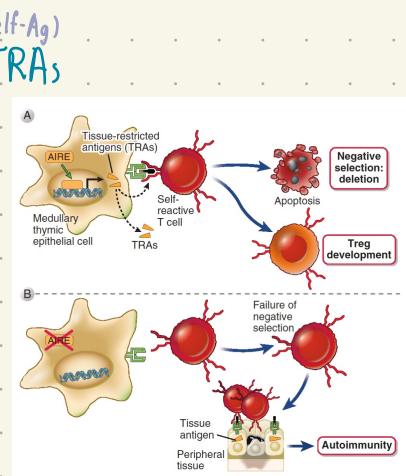
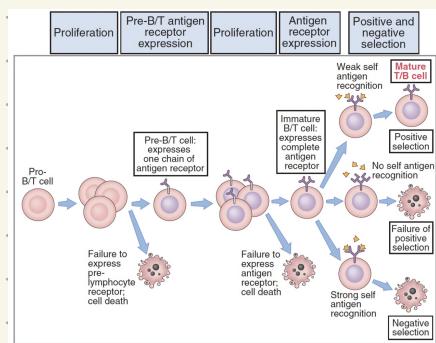
• effector memory T cell : s^oo^gin tissue

• memory B cell : o^ug^u bone marrow : Ig-producing plasma cell



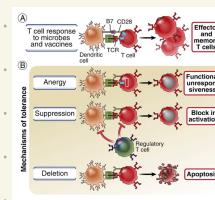
Immunoregulation

- tolerance : non-self reactive cell
 - tolerogen = Ag កែងចាំនូវការ tolerance
 - autoimmunity = មិនមែន self-tolerance
 - central tolerance
 - primary lymphoid organ
 - T cell cell នៃ thymic medulla ទៅក្នុង MTEC នៃ TRAs
 - positive : ចុះក្នុង self-Ag តុលធម៌
 - negative : ចុះក្នុង self-Ag តុលធម៌
 - cell ផ្សាយ 2 នៅក្នុង apoptosis ដែលរាយការណ៍ Treg
 - AIRE gene ដំឡើ self-peptide នៃបោរិយាល័យ APC
- ↳ ក្នុងនេះមិនមែនសេចក្តីរៀង = មិនមែន selection = autoimmunity



• peripheral tolerance

- ເກົ່າໄດ້ 3 ກຳສັ່ນຕື່ມ anergy , Treg & apoptosis

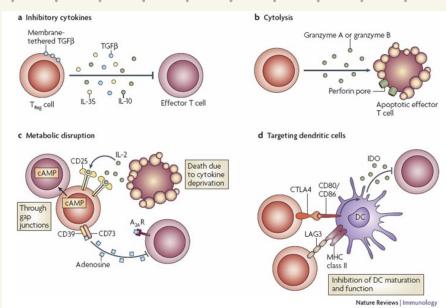
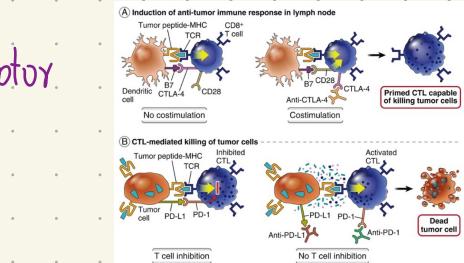
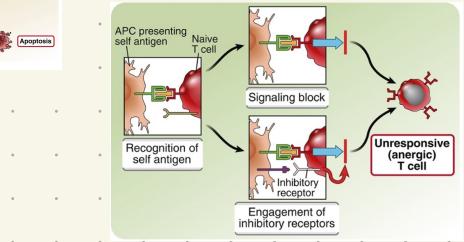


• anergy

- APC ກຳສັ່ນ self-Ag ຫຼືມໄລຍະ co-stimulatory signal
- APC ກຳສັ່ນ self-Ag ອັບນຸ່ງ T cell ດັບ inhibitory receptor
 - CTLA4 (ct cell) → B7 (APC)
 - PD1 (ct cell) → PD-L1 (APC)

• Treg cell

- ນັ້ນ inhibitory cytokine : IL-10 & TGF- β
- granzyme & perforin
- IL-2R (CD25) ແມ່ນ IL-2 ມີ T cell ດິຈິນໄວ່ວິນ
- CTLA-4 ອັບກັນ DC ດິຈິນນັ້ນ IDO ໄປຂັ້ນພໍ T cell & presenting Ag ປູມໄວ້



- ໂດຍ Treg ເຄີມມາ CD4 T cell ທີ່ມີ self-reactive transcription factor = FoxP3 $^{+}$

• ເລກທອງນຸ່ມ: 100 CD4, CD25 & FoxP3

• apoptosis

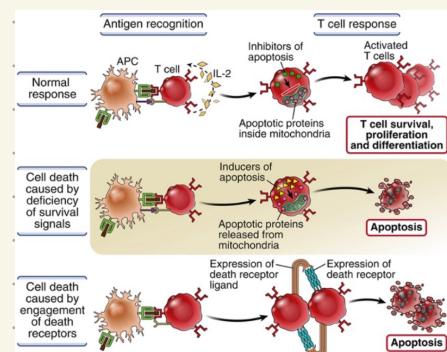
- ເຊີ່ມ anti-apoptotic protein ປູມໄວ້

• Fas / FasL

• ບົບ B cell

- anergy

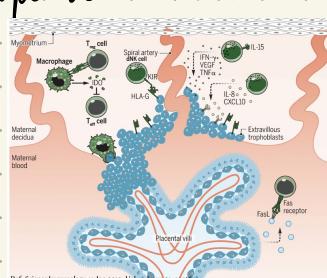
• ເຖິງ lymph node ປູມໄວ້ : apoptosis



- ບົບ pregnancy ລະທີ maternal immune response = ຕົວຈິງຂັບປັງ = immunologically privileged site

• FasL ລັດຕາກໍໄປບັນກັນ Fas receptor

• Treg ພອມໄວ



privileged site

• immunologically privileged site = ប្រទេសដែលមិនមែនទំនាក់ទំនង immune មែនទំនាក់ទំនង

• មែនមែន lymphatic access

• មែន inhibitory mediator = TGF- β

• មែន FasL

• eye, testicle, CNS = ក្នុងអ្នកទំនាក់ទំនង autoimmune / រវាង immune MHC II Ag នៃ

• sympathetic ophthalmia = ពាណិជ្ជកម្មនៃព័ត៌មាន immune មែនទំនាក់ទំនង

• multiple sclerosis = CNS ដែលបានចាប់ផ្តើមនៅ Ag MHC II Ag នៃimmune រវាងព័ត៌មាន CNS

Sympathetic ophthalmia

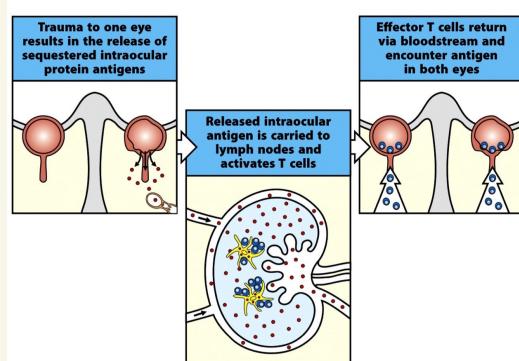
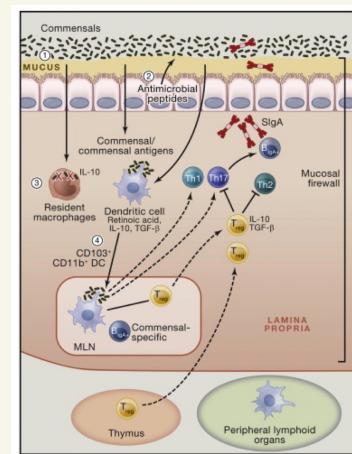
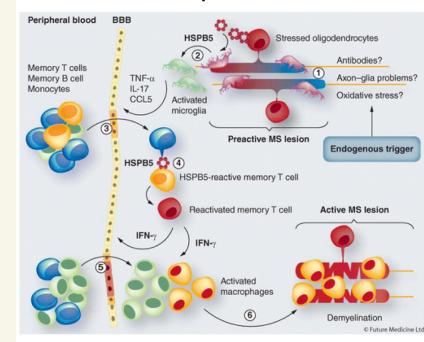


Figure 14-8 Immunobiology 7ed. © Garland Science 2008

Multiple sclerosis



• mucosal immunity

• mucus ក្នុងប៊ូតីនីប៉ាតីរី នៃកំណែ enterocyte

• enterocyte នៃកំណែ anti-microbial peptide

• DC & macrophage នៃកំណែ IL-10 (inhibitory cytokine)

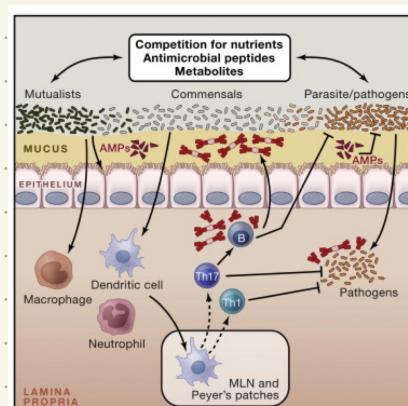
• DC នៃកំណែ Treg \rightarrow នៃកំណែ IgA

• gut microbiome នឹងរក្សាយ immune

• នឹងរក្សាយ pathogen

• នៃកំណែ antimicrobial peptide

• នៃកំណែ host cell នឹងកំណែ pathogen



Immune response to infection

Extracellular bacteria

- innate responses

 - neutrophil & macrophage = inflammation

 - complement system

 - NET = neutrophil

- adaptive response

 - B cell

 - neutralization

 - opsonization

 - activate complement system

 - Th17

 - inflammation = IL-17 & TNF

 - macrophage = IFN- γ

- immune evasion

 - 偽抗原 Ag

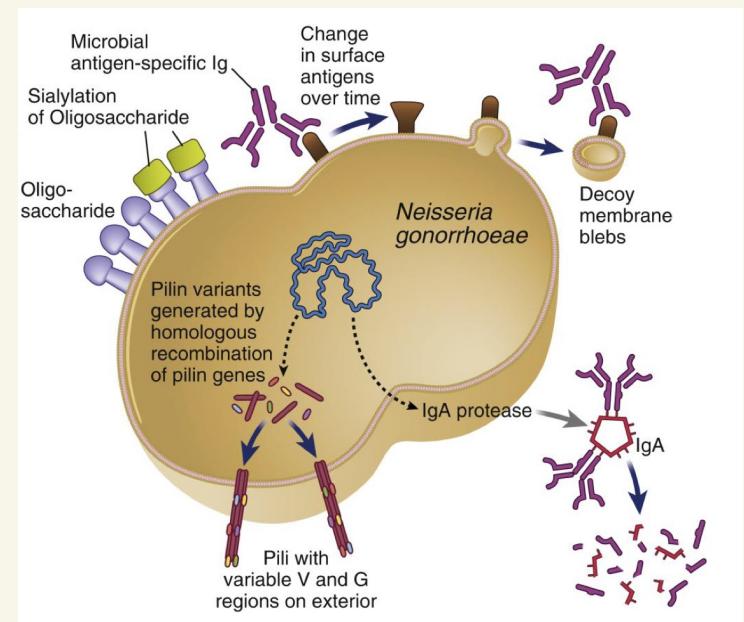
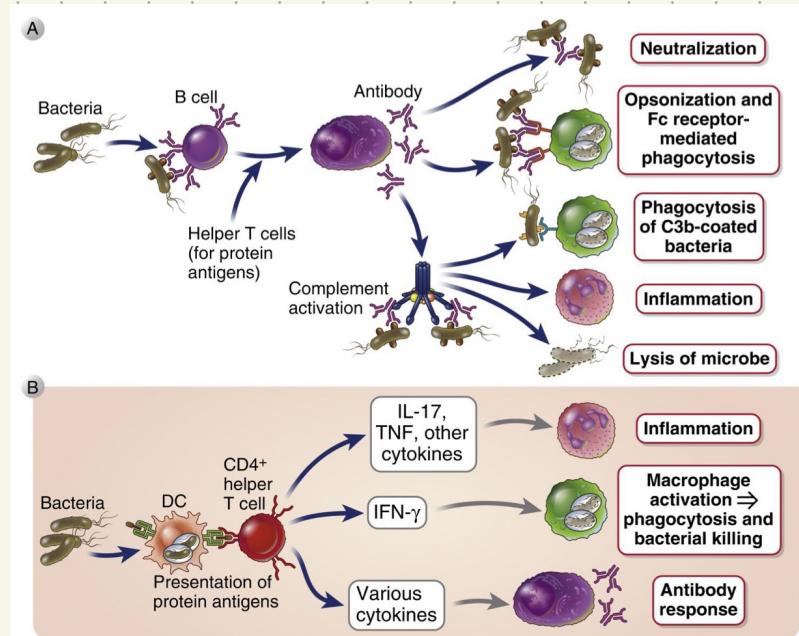
 - gonococci หรือ pili protein หลอกหลอน

 - capsule

 - polysaccharide-rich = หลอก phagocytosis

 - sialic acid capsule = หลอก complement

 - decoy = หลอก Ag หลอกไปล่อ

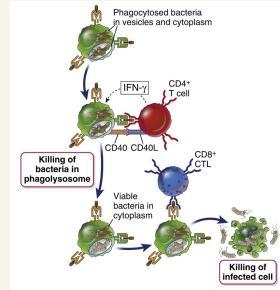


Mechanism of Immune Evasion Extracellular Bacteria	Examples
Antigenic variation	<i>Neisseria gonorrhoeae</i> , <i>Escherichia coli</i> , <i>Salmonella typhimurium</i>
Inhibition of complement activation	Many bacteria
Resistance to phagocytosis	<i>Pneumococcus</i> , <i>Neisseria meningitidis</i>
Scavenging of reactive oxygen species	Catalase-positive bacteria (including staphylococci and many others)

Intracellular bacteria

- innate response

- NK cell & type 1 ILC : ផែន IFN- γ នៃពុក neutrophil & macrophage
- PRRs (TLR & NLR) : ទរវាជុប Ag នៃលក្ខណៈ & នៃពុក type 1 IFN



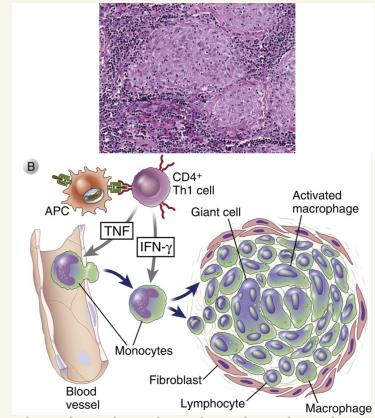
- adaptive response

- Th1 : នៃពុក phagocyte
- CD8 : សាក់តាក់នុគត់ phagolysosome (infected cell)
- granulomatous inflammation (TB)
- delayed type hypersensitivity (DTH) reaction

- macrophage & Th1 ធ្វើនូវ TB ត្រួមទៅការធម្មជាតិ
- ឈឺហំតាន់ fibrosis (connective tissue) នូវបាន

- ពាណិជ្ជកម្មនៃ leprosy = ឯក immunopathology

- tuberculoid
 - ធ្វើឡាងនៃ strong cell-mediated response
 - Th1 ↑
 - ↓ bac នៃ lesion



- lepromatous
 - កំណើនលេខវិធី defective cell-mediated response
 - ↓ Th1
 - ↑ bac នៃ lesion



Mechanism of Immune Evasion	Examples
Intracellular Bacteria	
Inhibition of phagolysosome formation	<i>Mycobacterium tuberculosis</i> , <i>Legionella pneumophila</i>
Inactivation of reactive oxygen and nitrogen species	<i>Mycobacterium leprae</i> (phenolic glycolipid)
Disruption of phagosome membrane, escape into cytoplasm	<i>Listeria monocytogenes</i> (hemolysin protein)

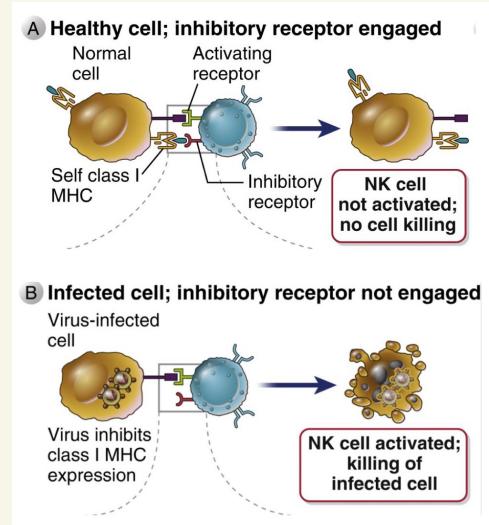
Fungi

- innate immunity
 - phagocyte
 - neutrophil & macrophage
 - TLR, lectin (dectin) & mannose receptor : ตรวจ fungi PAMPs
 - ROS & lysosome
 - complement system
 - candida
 - ein alternative & lectin pathway : ทำ opsonization
- adaptive immunity
 - Th17 : extracellular fungi
 - candida
 - ต้อง PAMPs & dectin ภูมิ fungi
 - Th1 : intracellular fungi
 - *Histoplasma capsulatum* & *Cryptococcus neoformans*
 - ต้อง macrophage
- immune evasion
 - stealth : หลีก PAMPs บน PRR
 - capsule
 - melanin
 - biofilm
 - decoy
 - dimorphism

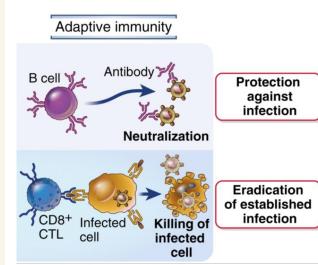
- control
- complement inhibition
- ฉบับ phagocytic process - titan cell (*C. neutromans*)
- ฉบับ phagosome maturation - รวมกับ lysosome ให้ถูกต้อง
- apoptosis induction
- attack
 - น้ำสีฟ้าทึบๆ ROS/RNS
 - น้ำสีฟ้า เป็นผล oxidative stress
 - enzyme = superoxide dismutases - SODs & catalases - CATs
 - non-enzyme = melanin, mannitol & trehalose
 - พิษต่อร่องรอยของเชื้อไวรัสในเซลล์

Virus

- innate immunity
 - type I IFN (IFN α / β)
 - ผ่านติดอยู่ infected cell & plasmacytoid DC
 - ทำให้เกิด IFN & antiviral
 - ยับยั้งการทึบ virus replication
 - NK cell
 - DNA virus = herpesvirus & human papilloma virus
 - virus ทำให้ cell ไม่มี MHC 1 - NK cell ทึบไม่ได้



- adaptive immunity
 - Ab ต้านไวรัส เอ็มบี
 - IgA = mucosal infection
 - การต่อต้าน opsonization & complement



- CD8+ in infected cell

- latent infection

- \downarrow herpesvirus & HIV

\hookrightarrow chickenpox, HSV1 & EBV

- viral DNA \downarrow cell \downarrow immune evasion

- influenza reactivation

- immunopathology

- infection \downarrow immune evasion

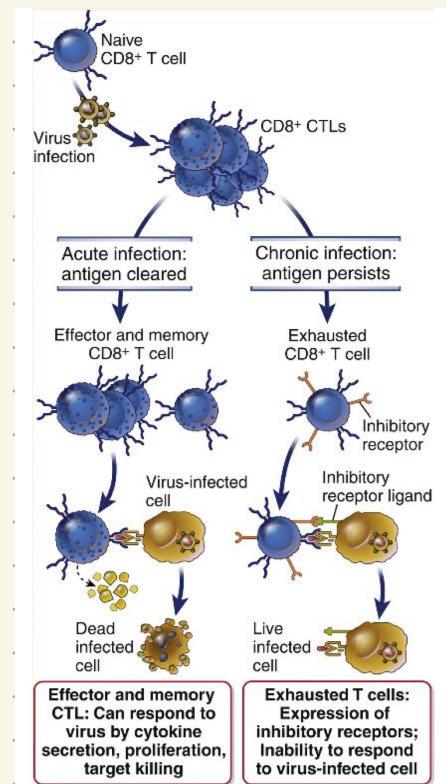
- hepatitis B virus = CD8+ \uparrow apoptosis

- SARS-CoV2 = systemic inflammatory & cytokine storm

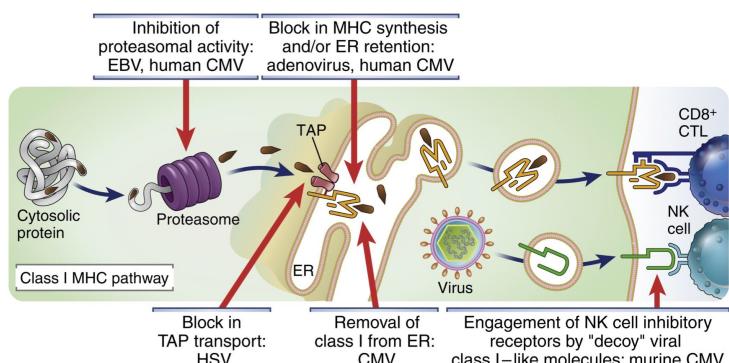
- dengue virus = Ab-dependent enhancement \downarrow cytokine storm

\hookrightarrow Ab \downarrow \downarrow cytokine storm

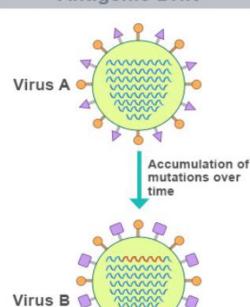
Mechanism	Example
Interference with viral antigen processing and presentation	HSV (ICP47), EBV (EBNA-1), HIV (Nef, Tat), HPV (E5), CMV (UL6)
Evasion of NK cell function	HIV (Nef), EBV (EBNA-1), CMV (UL40, UL18)
Inhibition of cell apoptosis	Adenovirus (RID complex and E1B), HIV (Nef), EBV (BHRF-1)
Destruction of T cells	HIV
Interference with antiviral cytokines and chemokines	EBV (IL-10 homologue), CMV (US28 chemokine receptor homologue), vaccinia virus (IL-18-binding protein), HIV (Tat chemokine activity)
Inhibition of complement action	HSV, pox viruses
Inhibition of DC maturation	HSV, vaccinia virus
Frequent antigenic variation	Influenza virus, HIV
Infection of immune privileged site	Measles virus, VZV and HSV (neurons)
Immune exhaustion	HIV, HCV, HBV



Interfering with antigen presenting processing and presentation

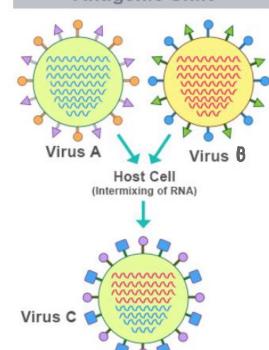


Antigenic Drift



Influenza

Antigenic Shift



Parasite

- innate immunity

- protozoa

- កំណត់ឱយ phagocytosis

- ទរស់នុប៉ាយ TLR2 (plasmodium) & TLR4 (toxoplasma gondii)

- helminth

- កំណត់ឱយ eosinophil នូវ phagocyte និង microbicidal

- នរោង alternative pathway of complement

- adaptive immunity

- protozoa

- Th1 និង macrophage

- CD8 និងការការពារ plasmodium នាមឃើញឱ្យការពារ

- helminth

- Th2

- IL4 : IgE

- IL5 : eosinophil

- នរោង macrophage = ហេដែល delayed-type hypersensitivity ហេដែល granuloma របស់ខ្លួន

- immune evasion

- ផ្សេងៗ surface Ag

- plasmodium : ផ្សេងៗ Ag នៃ stage of life cycle

- trypanosoma brucei : ផ្សេងៗ Ag

- ភ័ត៌មាន៖ ផ្សេងៗ

- ឯកសារ cell / cyst

- ឯកសារ intestinal lumen

- អង្គភាព immune effector : CD8 & complement

- ယုပ္ပါယ် immune response
- leishmania အေးကြား Treg
- plasmodium & Trypanosoma မန် inhibitory cytokine

Pathogens ☆ !!	Innate	Adaptive
Extracellular bacteria	Phagocytosis Complement	Antibody
Intracellular bacteria	Macrophage (usually resist phagolysosome)	CD8 T cell-> CTL CD4 T cell -> Th1
Fungi	Similar to bacteria	
Virus	Type I IFN NK cell	Antibody CTL
Parasites	Various depending on their characteristic	

Hypersensitivity

• immun tolerance ไม่

• self tolerance = autoimmunity ไม่ immun typ 1 > 4.

• tolerance to innocuous Ag = allergy ไม่ immun type 2,3,4

• tolerance to fetus = abortion

• tolerance to allograft = graft rejection

• autoimmune disease

• อุบัติเหตุ type 2-4

• ไม่เฉพาะเจาะจง 2 ชั้น

• organ specific

• type 1 diabetes = typ 4

• good pasture's = typ 2

• multiple sclerosis = typ 4

• graves' disease = type 2

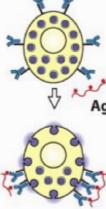
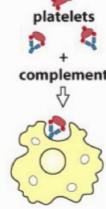
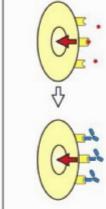
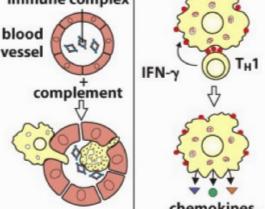
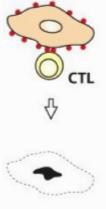
• myasthenia gravis = type 2

• systemic

• rheumatoid arthritis = type 4

• SLE = typ 3

Autoimmune diseases involve all aspects of the immune response			
Disease	T cells	B cells	Antibody
Systemic lupus erythematosus	Pathogenic Help for antibody	Present antigen to T cells	Pathogenic
Type 1 diabetes	Pathogenic	Present antigen to T cells	Present, but role unclear
Myasthenia gravis	Help for antibody	Antibody secretion	Pathogenic
Multiple sclerosis	Pathogenic	Present antigen to T cells	Present, but role unclear

Immune reactant	Type I	Type II		Type III	Type IV		
	IgE	IgG		IgG	T _H 1 cells	T _H 2 cells	CTL
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Cell-surface receptor	Soluble antigen	Soluble antigen	Soluble antigen	Cell-associated antigen
Effector mechanism	Mast-cell activation	Complement, Fc ^{RI} cells (phagocytes, NK cells)	Antibody alters signaling	Complement, phagocytes	Macrophage activation	IgE production, eosinophil activation, mastocytosis	Cytotoxicity
							
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies	Some drug allergies (e.g. penicillin)	Chronic urticaria (antibody against Fc ^{RI} alpha chain)	Serum sickness, Arthus reaction	Allergic contact dermatitis, tuberculin reaction	Chronic asthma, chronic allergic rhinitis	Graft rejection, allergic contact dermatitis to poison ivy

Type I immediate hypersensitivity

- Ab : IgE
- Ag : soluble Ag
- cell : Th2, mast cell/basophil, eosinophil
- example : allergy, anaphylaxis, drug allergy (some)
- allergic disease
 - airway : asthma, rhinosinusitis, conjunctivitis
(过敏性)
 - skin : urticaria, angioedema, atopic dermatitis, contact dermatitis
 - systemic : food, drug, insect, anaphylaxis
- mechanism

- ① Th2 ရှုက္ခားတို့မှ အကျဉ်းသတ် B cell မျှော်လျော် အကျဉ်းသတ် \rightarrow IgM \rightarrow IgE : sensitization
- ② IgE ပြုထွက်၍ mast cell / basophil အား FcεR1
- ③ ပြန်လည် Ag ခြေဆံ : re-exposure
- ④ mast cell ထဲမှာ histamine

- allergen
 - Ag အမြန် immediate hypersensitivity (type I)
 - ယူရော် Th2

- protein = မျှော်ဆန်း၊ ဂိုဏ်၊ ဓရမ်၊ ဓမ္မဆု
- haptene = ဦး
- Th2 = များ IL4-5-13 & ပြုလုပ် အကျဉ်းသတ် \rightarrow IgM \rightarrow IgE
- mast cell/basophil
 - histamine : vascular permeability, bronchoconstriction, intestinal hypermotility
 - TNF : inflammation
 - enz. (tryptase) : tissue damage

Diseases	Clinical presentation
Anaphylaxis (systemic immediate hypersensitivity)	Hypotension, edema in several tissues, vascular leakage, urticaria-angioedema, N/V/D, LOC
Food allergy	Itchy skin-mucosa, urticaria-angioedema, anaphylaxis
Allergic rhinoconjunctivitis	Itchy watery eyes & nose, sneezing esp. upon allergen exposure/early morning
Allergic asthma	SOB, wheezing, cough

Type 2

- Ab : IgG
- Ag : ព័ត៌ម្យបន្ទូល cell membrane
- mechanism
 - Ab និង complement → opsonization (C3b, C5b) = phagocytosis
= AIHA, thrombocytopenia, pernicious anemia (intrinsic factor)
 - Ab និង complement → inflammation (C3a, C5a)
= Ab-mediated glomerulonephritis, goodpasture's, pemphigus vulgaris, rheumatic
 - Ab ឱ្យចុះក្នុង normal receptor ទូទៅ ឬមានអារីឌីជាប់ពាក្យសាងទៅខាងក្រោម
 - TSH receptor = graves' disease
 - ACh receptor = myasthenia gravis
 - insulin receptor = insulin resistant diabetes

Type 3 immune complex hypersensitivity

- Ab : IgG
- Ag : soluble Ag
- mechanism
 - ① រំលែកយក Ag ឱ្យចុះក្នុង
 - ② កំណែ Ag-Ab complex
 - ③ និង phagocyte & complement គួរព FcR
 - DNA & nucleoprotein = SLE (systemic lupus erythematosus)
 - HBV Ag = polyarteritis nodosa
 - Strep Ag = poststreptococcal glomerulonephritis.
 - various protein = serum sickness

• សំណើឱ្យពារកំណត់ដែល systemic នៅក្នុងសំណើឱ្យនេះមានរាយការណ៍

• serum sickness

• cause : គីត foreign Ag (serum)

• សិទ្ធិ : arthritis, rash, fever

• arthus reaction

• គីត Ag ឲ្យដើរ subcu សែន host ក្នុង Ab

• សិទ្ធិ : local cutaneous vasculitis + tissue necrosis

Type 4

• WBC : Th1, Th2 & CTL

• Ag : soluble Ag & cell-associated Ag

• mechanism

• delayed type (DTH)

• ឥឡូវ Ag ក្នុងភាគខ្សោយ → Th1 & CD8 ឬ IFN γ : inflammation

• Type I diabetes, multiple sclerosis, contact dermatitis, inflammatory bowel disease
(islet cell) (myelin-CNS) (skin) (GI cell)

rheumatoid arthritis (joint synovium), peripheral neuritis (myelin-peripheral nerve)

nickle allergic dermatitis, tuberculin test \hookrightarrow guillain-barre syndrome.

• ឥឡូវក្នុង granulomatous inflammation ឧប. TB

• direct killing

• ឥឡូវ Ag ក្នុងភាគខ្សោយ → CD8 នៃ cell តិចខ្លះ ឬ virus កំឡុងការឱ្យបានកិច្ច

• post-viral autoimmune myocarditis (coxsackie virus)

• viral hepatitis ងាយបាន

Cancer immunology

- tertiary lymphoid structure (TLS) - ក្នុងខែង WBC នៃសំលាក់តាម lymph node នៅទីតាំង
- ទូទៅ immune cell កំពើរប៉ុងក្រោម tumor គុណភាព inflammation/tumor

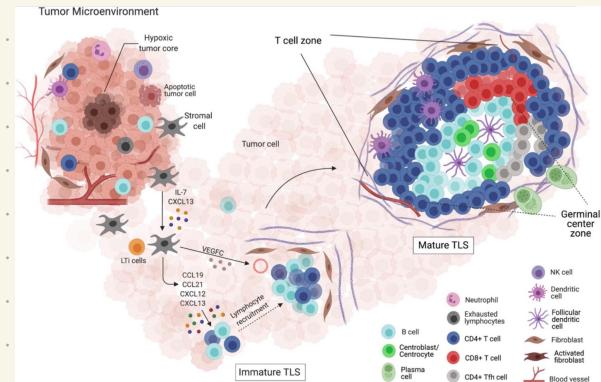
- follicular DC
- follicular Th
- CD8 (MHC I)

immune surveillance

- កំណត់ការ cell ដែលបាត់ នៃការកំណត់ការ
- តែងតាំងការកំណត់ការ cancer = immunodeficiency → transplantation, AIDS
- តំបន់ tumor cell ដែលអាចចូលចាយនូវនឹងការ immune ការកំណត់ការ cancer

tumor Ag

- mutated self gene product
 - proto-oncogene : Ras
 - tumor suppressor gene : p53
 - random gene : p91
- normal cell protein
 - overexpression : Her2, tyrosinase, MART, gp100
→ ក្រោមពាណិជ្ជកម្ម differentiation
 - dedifferentiated : CEA, AFP
↳ carcinoembryonic Ag = colon cancer
- glycolipid/protein
 - mucin : Muc1, CA19-9, CA125
 - ganglioside : GM₂, GD₂
- oncogenic virus product : virus កំរែក្នុងក្រោម tumor
 - cervical cancer : HPV : E6, E7 protein } DNA virus
 - B lymphoma : EBV : EBNA1 protein }
 - T cell leukemia : HTLV-1 (human T-cell lymphotropic virus) → RNA virus



• innate immune response

• NK cell

- ตัวที่ไม่มี MHC 1

- ตัวที่มี viral Ag

• macrophage

- มี tumoricidal & IFN γ

- lysosomal enz.

- ROS

- NO

- tumor necrosis factor

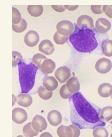
• cytokine

- TNF = ร่องรอย coagulation \rightarrow tumor necrosis & apoptosis

- IL12, IL15 & type 1 interferon = กระตุ้น NK cell

• adaptive immune response

- CD8 คือ primary mechanism = downy cell



- tumor infiltrating lymphocyte (TIL) = tumor cell + CD8

- CD4 คือผู้ให้ทึบสี cytokine กระตุ้น CD8

- IFN γ กระตุ้น macrophage

- B cell ผู้ให้ Ab & APC ให้ T cell

- Ab รับกัน Ag นำต้นทางประจักษ์ ให้ T cell รับไวต่อ protein

- antibody-dependent cell-mediated cytotoxicity = IgG

- complement-mediated cytotoxicity

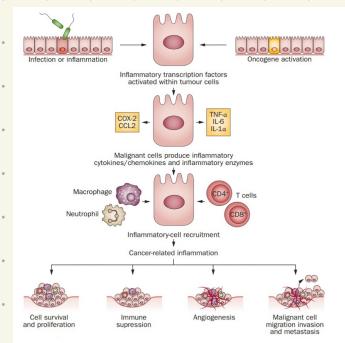
cancer-immune cycle

- ① DC សំនួល neoantigen ដែលវាយការងារ cancer cell
 - ② DC យកទៅ draining lymph node (DLN)
 - ③ present Ag ទៅ T cell ជាមួយ MHC I > MHC II = cross presenting
 - ④ antigen-recognizing cancer-specific T cell មែនក្នុង tumor នៃ blood
 - ⑤ CD8 នៃ cancer cell
 - perforin & granzyme
 - FasL - Fas
 - ⑥ ឯកសារ cancer cell សម្រាប់ផ្តល់ neoantigen មែនត្រូវ ① នូវ
-
- The diagram illustrates the 7 steps of the cancer-immune cycle:
- ① Release of tumor antigen
 - ② Tumor antigen presentation by APCs
 - ③ T cell priming and activation
 - ④ T cell trafficking to tumors
 - ⑤ T cell infiltration into tumors
 - ⑥ Recognition of tumor cells by T cells
 - ⑦ Killing of tumor cells
- Each step includes associated therapies:
- Step 1: NP-boosted phototherapy, NP-boosted chemo/radiotherapy, NP-boosted oncolytic viral therapy
 - Step 2: DC-targeted vaccine and immuno-adjvant delivery with NPs, NP-enhanced antigen presentation
 - Step 3: LN-targeted vaccine and immuno-adjvant delivery with NPs
 - Step 4: Overcome stromal barrier with NPs, Reprogram TME with NPs
 - Step 5: T cell-targeted CAR and TCR expression with NPs
 - Step 6: T cell-targeted CAR and TCR expression with NPs
 - Step 7: NP-boosted immune checkpoint blockade, Delivery of T and NK cell activators with NPs, Reprogram TME with NPs

Treg របស់ក្រុង cancer

- transcription factor = Foxp3 (forkhead box protein P3)
- និងក្រុង anticancer immunity
- cancer-related inflammation

- ① inflammation / oncogene នឹង proinflammatory transcription factor
- ② និងចំណេះចំណេះ cytokine, chemokine & inflammatory enzyme
- ③ នៃ tumorigenesis



circulating tumor cell (CTC)

- CTC នៃទូទៅ tumor-specific immune cell នៅក្នុង cell ដែលការពារ
 - និង CTC នៃទូទៅ immune
 - (classic) (tumor-associated Ag)
 - និង MHC I នៃទូទៅ TAA : នៅ MHC I នូវ នូវ NK cell នៃ
 - និង HLA-G (nonclassic MHC I gene) : និង immune evasion
 - Fas/FasL : apoptosis T cell ក្នុង
 - Chaperone of Fas receptor
 - Delivery of FasL to target cells leading to apoptosis of effector cells
 - Delivery of FasL by target cells which blocks downstream signaling
 - CD47-mediated signaling (don't eat me) : បង្កើ SIRPa នៃ macrophage និងការការពារ
 - និងទូទៅ hypoxia : និង bone marrow ដែលត្រូវការការពារ និង immune កែលការ
 - programmed cell death protein 1
 - immune checkpoint : PD1/PDL1 & CTLA4 (T cell) ឬ cytotoxic T lymphocyte-associated Ag 4 (T cell)
-
- The diagrams illustrate:
- Evasion mechanisms:**
 - CD47 - SIRPa interaction: "Don't eat me" signal
 - Anti-CD47 mAb: Prevents "Don't eat me" signal
 - Immune checkpoints:**
 - PD1 - B7-1/B7-2 interaction
 - CTLA4 - B7-1/B7-2 interaction
 - Anti-PD1 mAb: Prevents PD1-B7 interaction
 - Anti-CTLA4 mAb: Prevents CTLA4-B7 interaction

- cancer therapy
 - PD1 / PDL1 inhibitor
 - targeting cytokine
 - targeting TNF α (inflammation)
 - Anti-TNF α ပုံစံ၏ rheumatoid arthritis & chrohn's disease : infliximab & etanercept
 - or inhibit TNF α အကြောင်းကancer
 - targeting inflammatory cell
 - မျှော်လွှာ T cell မြတ်ဆောင်ရေး အကြောင်းကancer cell ဓမ္မအနေဖြင့်
 - CAR T cell

Immunosuppressant

ໄຟລິນັກສົມ ADR ອອກແດ່ນາງຕົວ

- immunological drug
 - immunosuppressant : organ transplantation, autoimmune & cytokine storm.
 - immunostimulant - immuno deficiency, antitumor & viral infection
- immunosuppressant ແນວໃນ 2 ພະຍານ
 - non-specific
 - specific
 - ສືບ ADR ເຊື້ອ:
 - corticosteroid
 - antimetabolite
 - alkylating agent

▪ ນັກທະກຳອານຸອົງ immunosuppressant

① inhibition of gene expression of inflammatory

② ລດ ຕຽບຮັງ lymphocyte

③ ຍັນຍັງ activation ວວລາ lymphocyte

④ ອີບ Ab ລວມກະເວນ lymphocyte

⑤ neutralize cytokine / cytokine receptor

⑥ ຍັນຍັງ APC

⑦ ຍັນຍັງ leukocyte adhesion

⑧ ຍັນຍັງ complement

} lymphocyte

① inhibition of gene expression of inflammatory = glucocorticoid (corticosteroid)

- target : T cell > humoral immunity

- indication

- transplantation : prednisone & methylprednisolone

- autoimmune : prednisone, prednisolone & dexamethasone

- cytokine storm (covid) : dexamethasone

- mechanism : ချက်ချွမ်း glucocorticoid receptor ကြော်ပြန် gene transcription သူ့ inflammatory mediator

- ADR : less bone marrow suppression

② ဆုတေသန lymphocyte = cytotoxic agent

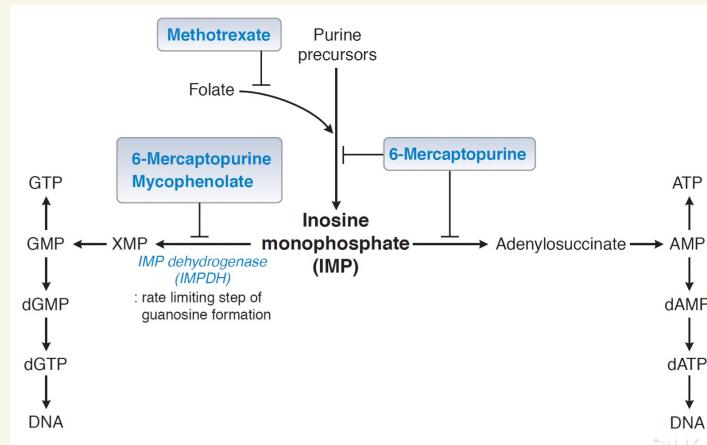
- antimetabolites

- target

- cell ဖိုးဆုတေသန bone marrow & GI : azathioprine & methotrexate

- lymphocyte B & T cell : mycophenolate

- mechanism



- azathioprine

- mechanism : ဦး prodrug ပို့ပြိုကြရန် glutathione အားဖြင့် 6-mercaptopurine (6-MP)

- indication : transplantation & autoimmune

- ADR : bone marrow suppression

	Azathioprine Methotrexate	Mycophenolate
	Older antimetabolites	Newer antimetabolites
Cytotoxicity	Rapid dividing cells in bone marrow & GI	lymphocyte B & T cell
Indication	Cancers Transplantation Autoimmune diseases	Transplantation Autoimmune diseases
Side effects	Bone marrow suppression GI toxicity (nausea, diarrhea) Alopecia	Leukopenia GI toxicity

• methotrexate

- mechanism = folate analog
- indication = autoimmune
- ADR
 - bone marrow suppression
 - 抑制 folic acid = 抑制 BM suppression

• mycophenolate mofetil toxic than azathioprine / methotrexate

- mechanism
 - MMF = inhibitor of inosine monophosphate dehydrogenase (IMPDH) type II
 - 阻止 lymphocyte 合成 purine on de novo synthesis = 阻止 IMPDH
- indication = transplantation
- ADR : GI discomfort
- alkylating agent
- target = 毒害 DNA replication 通过 conjugate alkyl group 到 DNA
- indication

- cancer

- autoimmune

- transplantation

• cyclophosphamide

- target = B cell

- ADR

- leukopenia, cardio toxicity & alopecia

- bladder cancer on acrolein

③ រួចការណ៍ activation នៃ lymphocyte

- mechanism

① TCR activation នឹងការ Ca^{2+} ↑

② calcineurin activation ← cyclosporin, tacrolimus

③ calcineurin និង activate NFATc T cell specific transcription factor

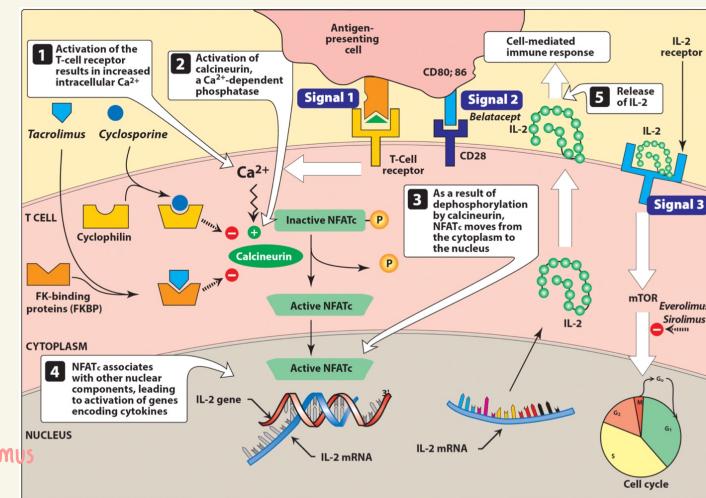
④ NFATc ឱ្យខ្សោ និង ឱ្យ cytokine gene activate

⑤ T cell នៃ IL-2

⑥ IL2 receptor នឹង IL2

⑦ mTOR សម្រួលិត់ cell cycle ← sirolimus

↳ mammalian target of rapamycin, everolimus, zotarolimus



- promote transition from G1 → S phase

	Cyclosporine	Tacrolimus	Sirolimus
Binding protein	Cyclophilin	FKBD	FKBD
Target protein	Calcineurin	Calcineurin	mTOR
IL-2 production	↓	↓	○
Cellular response to IL-2	○	○	↓

Synergistic effects

- calcineurin inhibitor = minimal BM suppression

- cyclosporine

- នៅក្នុង fungus

- bind to cyclophilin

- indication = transplantation, autoimmune disease & ophthalmic solution

- ADR

- metabolize ដោយ CYP3A4

- minimal BM suppression

→ severe dry eye syndrome

• tacrolimus

- **bäion bacteria**
- bind to = **Fk-binding protein (FKBP)**
- indication = transplantation, မြန်မာပို့ဆေးမှု
- အောက် လောက် မြန်မာပို့ဆေးမှု cyclosporine
- ADR
- metabolize ပါ။ **CYP3A4**
- minimal BM suppression
- mTOR inhibitor = sirolimus (rapamycin), everolimus, zotarolimus
- **sirolimus (rapamycin)**
 - **bäion bacteria**
 - bind to = **Fk-binding protein (FKBP)**
 - indication = transplantation (kidney), drug-eluting stent
↳ reduce proliferation of endothelial cell
 - ADR = metabolize ပါ။ **CYP3A4**

Drug interaction

- CYP3A4 inducer = rifampin
- CYP3A4 inhibitor
 - erythromycin
 - ketoconazole, itraconazole
 - ritonavir
 - grapefruit juice

Side effects	Cyclosporine	Tacrolimus	Sirolimus
Nephrotoxicity	Most common	Most common	-
Neurotoxicity	Tremor	Tremor, headache, seizure, hallucination	-
Hypertension	50%	35%	40-50%
Hyperlipidemia	↑ LDL	-	↑ LDL & TG
Hyperglycemia & diabetes	✓	✓	-
Hepatotoxicity	✓	-	-
Potassium level	Hyperkalemia	Hyperkalemia	Hypokalemia
Unique side effect	Gingival hyperplasia Hirsutism	Alopecia	Leukopenia Thrombocytopenia Delayed wound healing

More severe than cyclosporine

④ វិធី Ab សំខាន់ lymphocyte.

- mab = monoclonal Ab

- monab = mouse

- ximab = human/mouse

- zumab = humanized

- mumab = human

- cept = fusion protein

- Fc human + receptor

- neutralizing Ab : នឹង Ab បង្កើត effect

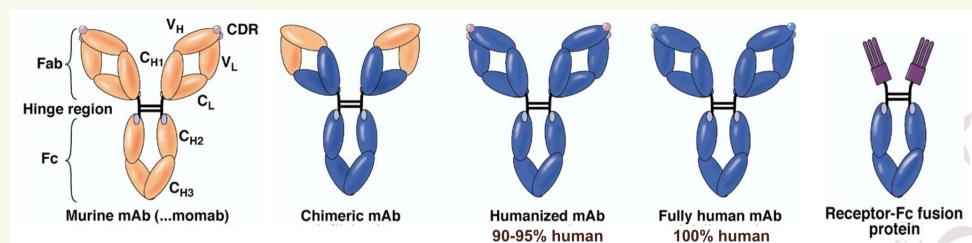
- HAMA : human anti-mouse Ab

- HACA : human anti-chimeric Ab

- HAHA : human anti-human Ab

មានក្នុងទំនាក់ទំនង

មេចក្នុងការ



• antithymocyte globulin

- ឬ polyclonal Ab

- target : សំណើ T cell ក្នុង

- indication : transplantation

- ADR

- សំរាប់ infection

- កំតែ T cell activation : នៅក្នុង cytokine កំពុង fever : cytokine-release syndrome

• OKT3 / muromonab - CD3 ເກີຍ

- murine monoclonal antibody targeting CD3
- target : CD3 T cell
- mechanism = CD3 ທຳນາເກົ່າກົນ Ag recognition ວອງ T cell (CD4 & CD8)
- indication : transplantation
- ADR
 - T cell activation : fever
 - MAHA : anaphylaxis

• basiliximab

- target : CD25 (IL2 receptor) activated T cell
- mechanism = IL2 ໄປ້ງນາມໄດ້ມີນາມຂອງ T cell ໂດຍ CD25 ມີລະບົບໃນ activated T cell
- indication : transplantation
- ADR
 - GI discomfort
 - ໜ້າຕິດ cytokine release syndrome
 - anaphylaxis

• rituximab

- target : CD20 mature B cell
- indication
 - CD20 non-hodgkin's syndrome
 - autoimmune

• ADR

- neutropenia : ຮົກສະດັກ G-CSF
- anemia

⑤ neutralize cytokine / cytokine receptor

• infliximab, adalimumab

- target : TNF α

- indication : autoimmune

- ADR

- \uparrow $\text{m}\ddot{\text{o}}\text{r}\text{g}$ infection

- \uparrow $\text{m}\ddot{\text{o}}\text{r}\text{g}$ lymphoma

• certolizumab pegol

- mechanism

- Fab + PEG (polyethylene glycol)

- $\text{y}\ddot{\text{a}}\text{j}\ddot{\text{a}}$ Fc $\text{m}\ddot{\text{l}}\text{v}$

- $\text{y}\ddot{\text{a}}\text{j}\ddot{\text{a}}$ antibody-dependent cell mediated cytotoxicity $\text{m}\ddot{\text{l}}\text{v}$ effect $\text{m}\ddot{\text{o}}\text{r}\text{g}$

- $\text{i}\ddot{\text{m}}\text{o}$ neutralizing Ab $\text{m}\ddot{\text{o}}\text{r}\text{g}$

- $t_{1/2}$ $\text{m}\ddot{\text{o}}\text{r}\text{g}$

- indication : autoimmune

- ADR

- \uparrow $\text{m}\ddot{\text{o}}\text{r}\text{g}$ infection

- \uparrow $\text{m}\ddot{\text{o}}\text{r}\text{g}$ lymphoma

• etanercept

- target : TNF α

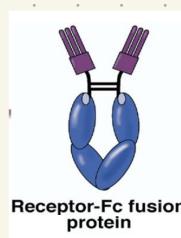
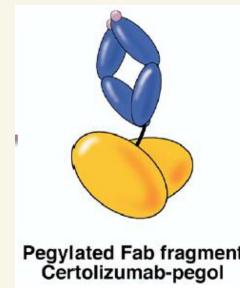
- mechanism : Fc + receptor

- indication : autoimmune

- ADR

- \uparrow $\text{m}\ddot{\text{o}}\text{r}\text{g}$ infection : latent TB & HBV

- \uparrow $\text{m}\ddot{\text{o}}\text{r}\text{g}$ lymphoma



- anakinra

- target = IL1

- indication

- autoimmune

- cryopyrin-associated periodic fever syndrome (CAPS) = IL1 高

- ADR = neutropenia

- tocilizumab

- target = IL6

- indication

- autoimmune

- cytokine storm (covid)

⑥ ຢັບຢັງ APC

- chloroquine & hydroxychloroquine

- mechanism = ຢັບຢັງຕາຫີ່ Ag presenting process ໂດຍມໍາເນີນ pH 9 ສະລຸງໄຟລູ
protein ປົມຄູກຂອງນິນ peptide

- target = Ag presenting process

- indication

- antimalarial

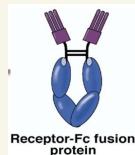
- autoimmune

- ADR ← ອອກສວນ

- retinopathy - chloroquine > hydroxychloroquine

- QT prolongation

- belatacept



- Fc + CTLA-4

- target = $\beta 7$ (co-stimulation) សំគាល់ abatacept

- indication = transplantation

- ADR

- post-transplant lymphoproliferative disorder (CNS)

- anemia, diarrhea, UTI, edema

⑦ ផ្សេងៗ leukocyte adhesion

- natalizumab

- target = $\alpha 4$ integrin

- mechanism

- ការបង្កើត integrin និងការចុះចុង leukocyte trafficking

- $\alpha 4\beta 1 + VCAM1 = CNS$

- $\alpha 4\beta 7 + MAdCAM1 = gut$

- indication = autoimmune

- ADR : ↑ នរោង progressive multifocal leukoencephalopathy (PML)

⑧ ផ្សេងៗ complement

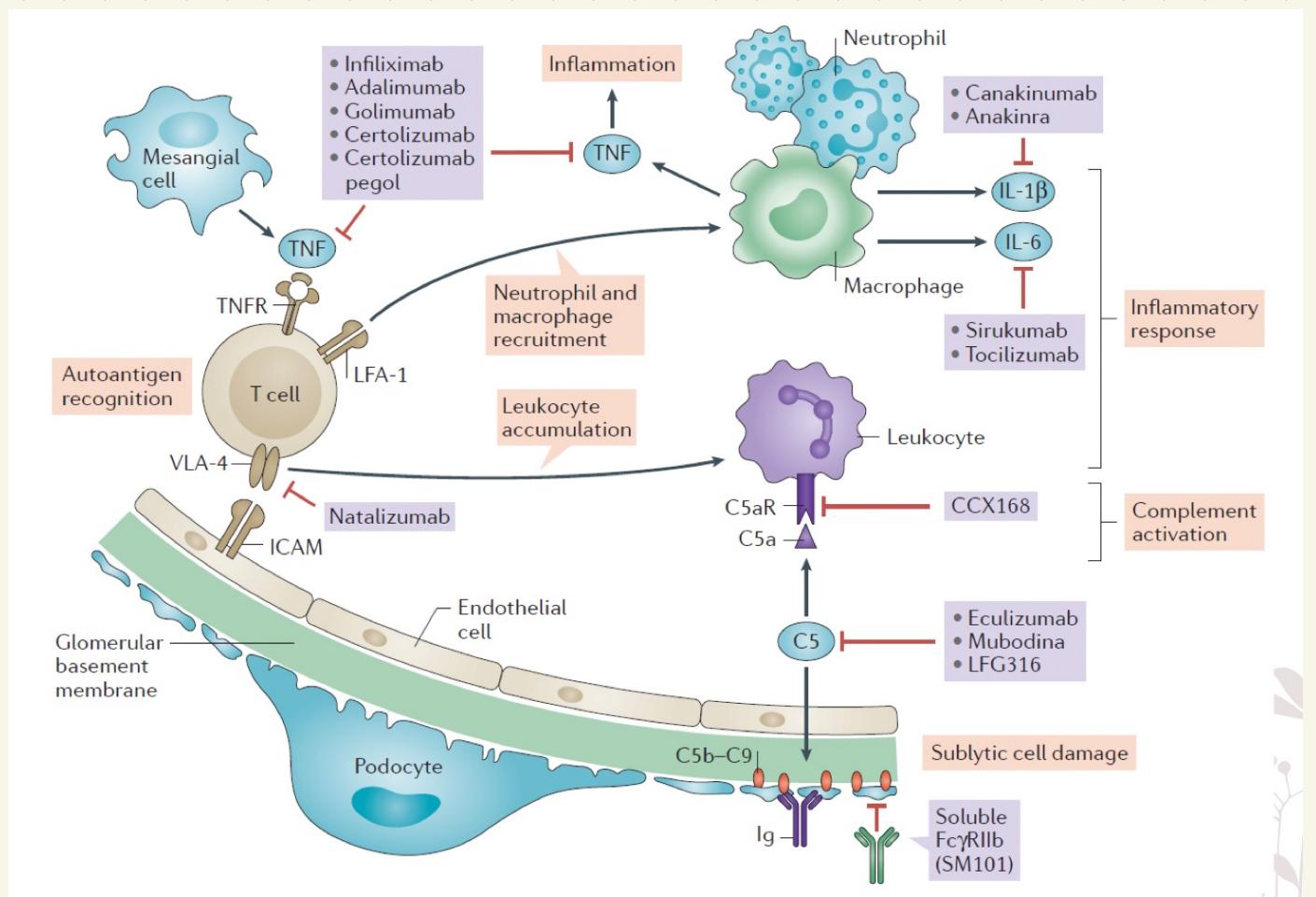
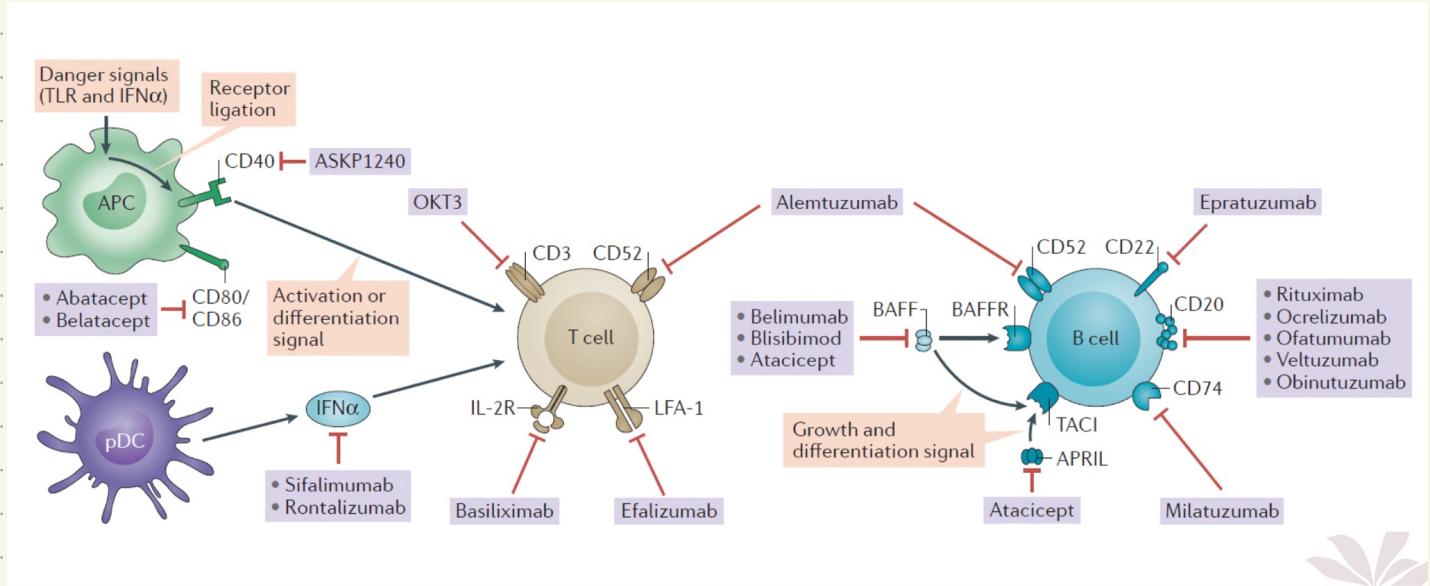
- eculizumab

- target = C5 trigger MAC

- indication = paroxysmal nocturnal hemoglobinuria (PNH)

- ↳ complement activate នូវក្រុង RBC

- ADR : ↑ នរោង infection → meningococcal

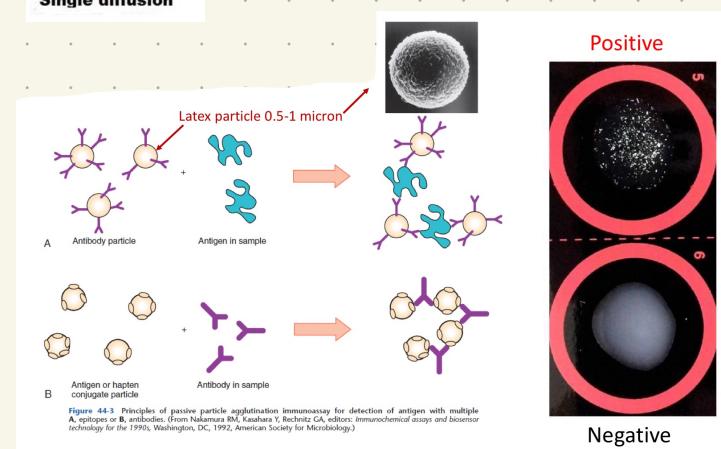
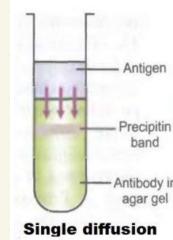
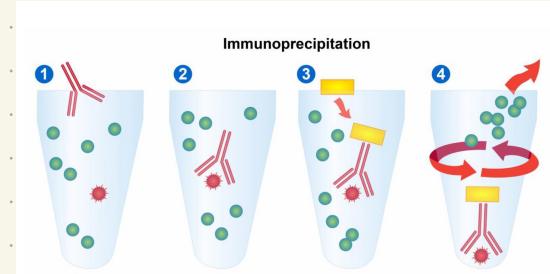


Immunodiagnosis

- immunoassay = test ຫົວໜ້າຂອງ Ag ດ້ວຍໃຊ້ Ab & Ag
- analyte = molecule ຫຼື ອາວເຄວົດໃນ immunoassay
- ປະເກດຂອງ immunoassay
 - precipitation
 - agglutination
 - solid phase - signal
 - lateral flow
 - flow cytometry

Precipitation

- immunoprecipitation = liquid phase
 - ① ໂຕ Ab ໄປຈັບກັນ Ag = Ag/Ab complex
 - ② ຈິ້ນໝູ Ag/Ab complex ດາວໂຫລດ



Agglutination

- particle agglutination
 - ① ໂຕ Ab ທາງອັນນາ particle ແລ້ວໃຈຮັກກັນ Ag
 - ② Ab ຈັບກັນ Ag ທີ່ໃນຕາຕະກວານ
- clinical application

- anti-HIV Ab
- treponema pallidum Ab (syphilis)

• hemagglutination

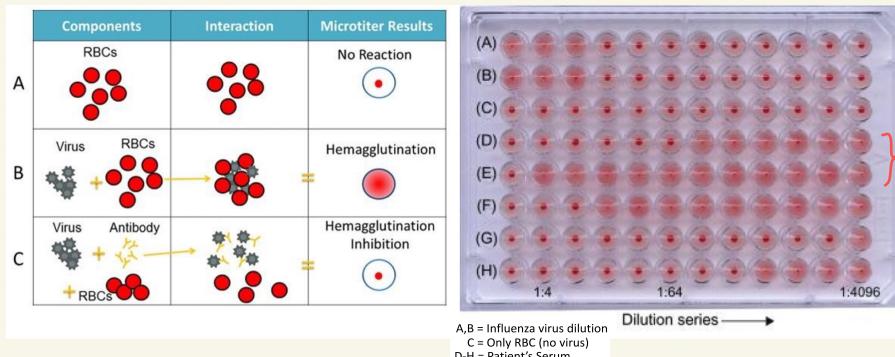
- detect Ag នូវ RBC = ឱ្យលោ ABO Ag
- detect abnormal auto-Ab ក្នុងការឱ្យសម្រាប់ infection : cold agglutinin នៃ mycoplasma
- clinical application

• ABO blood

- mycoplasma infection (cold coagglutinin)

• hemagglutination inhibition *

- virus + RBC = hemagglutination
- virus + RBC + Ab (serum) = រួចតាម hemagglutination
- convalescent serum = រួចតាម Ab នៅថ្ងៃទី 2W ពេលការ 4 ឬជាការពិនិត្យ



• clinical application

- human influenza virus Ab

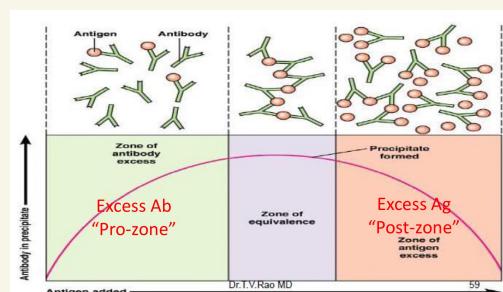
• ផែនដី

- low sensitivity

- វិធានធម្មគំនែ qualitative

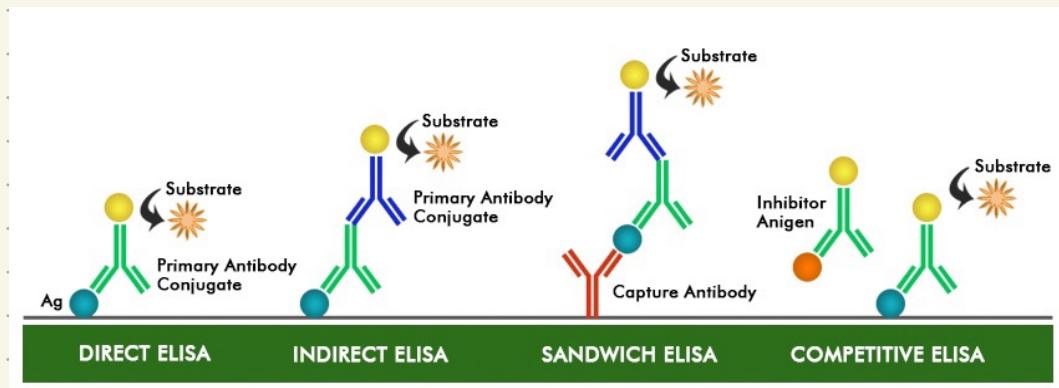
• កំណែ pro-zone / post-zone phenomenon *

- prozone = Ab មេះ: } false negative
- postzone = Ag មេះ:



Solid phase-signal

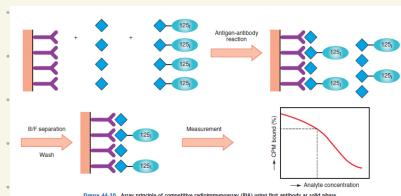
- enzyme immunoassay (common)



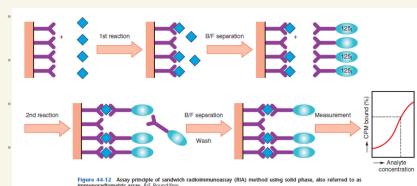
- direct ELISA = օղ Աբ կիսնել Ag
- competitive ELISA = օղ Ագ և Ագ համար էնզ. կատալիզ Աբ
- մաժայթավոր : Ag դժվար էլո:
- լածոցը լավագույն :

- radioimmunoassay

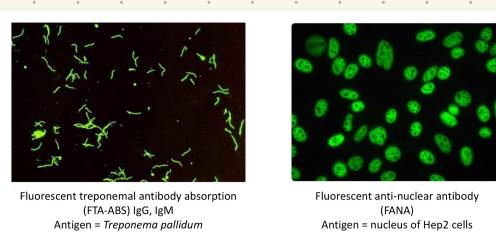
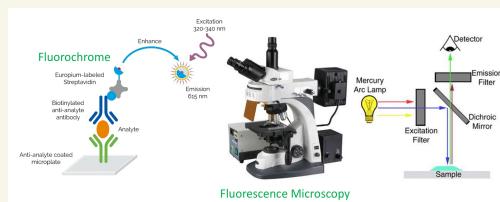
- competitive



- sandwich

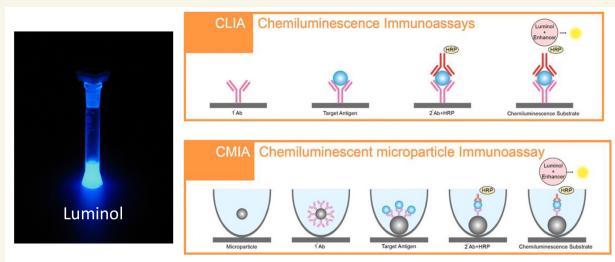


- fluorescence immunoassay



- application = autoimmune & congenital syphilis

- chemiluminescence immunoassay (էլեկտրո ջայլումինիսենս)

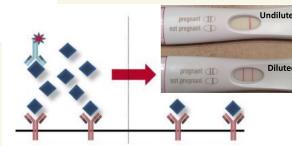
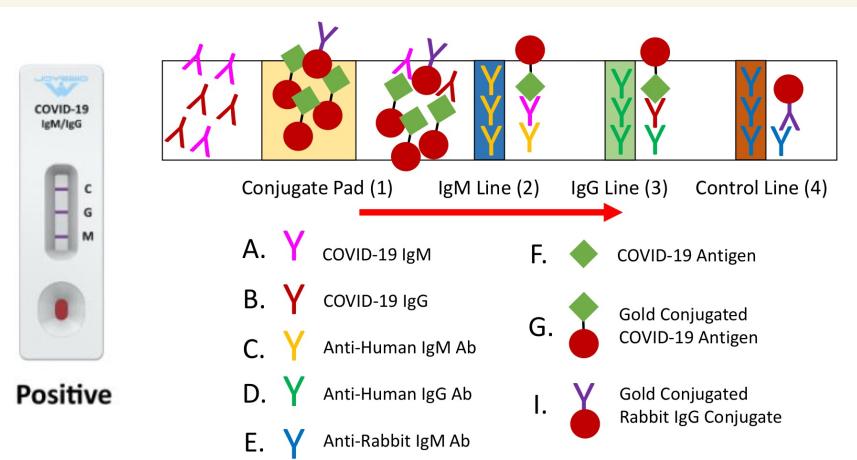


Lateral flow

ផែតានកម្រិត

- ① ឯក Ab_1 , នឹងចុចរវាង Ag នូវ conjugate pad ត្រូវ $\text{rabbit Ab} \& \text{Ag}_1$
- ② ទូរសព្ទ conjugate pad ឲ្យបាន test line ត្រូវ Ab_2 ដីចុចក្នុង $\text{Ab}_1 = [\text{Ag}_1] - \text{Ab}_1 - \text{Ab}_2$
- ③ ទូរសព្ទ test line ត្រូវ Ab_3 ដីចុចក្នុង rabbit Ab : $\text{rabbit Ab}] - \text{Ab}_3$

និង gold conjugated



- ពី Ag មិនអាចចិត្តរាយបាន false negative = hook effect
- clinical application

- pregnancy test = urine β -hCG (Ag)
- HIV
- SAR-CoV-2 = nucleocapsid protein
- food contaminant detection kit
- influenza A/B
- *S. pyogenes*
- amphetamine, morphine
- bacteria-fungus identification

Flow cytometry

- បានពិនិត្យទំនួល

① យកសែរ cell ដោយលើ laser ត្រូវ cell

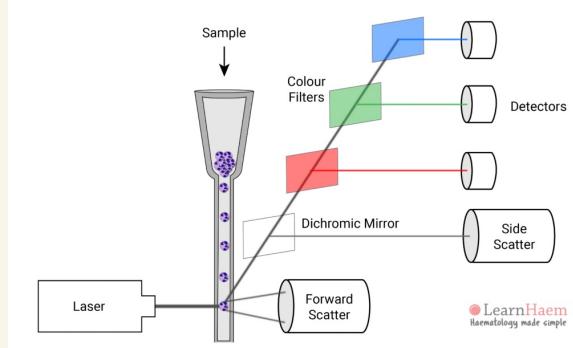
② detector ចុចចារម្មាយបង្ហាញ នៃលេខណីទំនួល cell

• ភាពិស់នឹង fluorescence ចុចក្នុង protein នៃលេខណី detector រួច

clinical application

• CD4 count in AIDS

• ង្ហោះ leukaemia : immunophenotyping



LearnHaem
Haematology made simple

Assay validation parameter

		True Diagnosis 'Gold Standard'		Prevalence = Disease Pos/All Samples = $(a+c) / (a+b+c+d)$
		Disease Positive $a+c$	Disease Negative $b+d$	
Test Results	Test Positive $a+b$	True Positive (a)	False Positive (b)	"Positive Predictive Value" (PPV) = True Pos/Test Positive = $a / (a+b)$
	Test Negative $c+d$	False Negative (c)	True Negative (d)	"Negative Predictive Value" (PPV) = True Neg/Test Neg = $d / (c+d)$
		"Sensitivity" = True positive rate = True Pos/Disease Pos = $a / (a+c)$	"Specificity" = True negative rate = True Neg/Disease Neg = $d / (b+d)$	

Scenario 1	
Test A	
in asymptomatic people	
Prevalence 10%	
SAR-CoV-2 +	SAR-CoV-2 -
10	90
ATK +	
ATK -	

Sensitivity = 70%
Specificity = 95%

PPV =
NPV =

Scenario 2	
Test A	
in suspected symptomatic patients	
Prevalence 50%	
SAR-CoV-2 +	SAR-CoV-2 -
50	50
ATK +	
ATK -	

Sensitivity = 70%
Specificity = 95%

PPV =
NPV =

Scenario 1	
Test A	
in asymptomatic people	
Prevalence 10%	
SAR-CoV-2 +	SAR-CoV-2 -
10	90
ATK +	
ATK -	

Sensitivity = 70%
Specificity = 95%

PPV = $7/11 = 64\%$
NPV = $86/89 = 97\%$

Scenario 2	
Test A	
in suspected symptomatic patients	
Prevalence 50%	
SAR-CoV-2 +	SAR-CoV-2 -
50	50
ATK +	
ATK -	

Sensitivity = 70%
Specificity = 95%

PPV = $35/37 = 95\%$
NPV = $48/63 = 76\%$