

试题形式

- 一、选择题（每题1分，共50题）
- 二、名词解释（每个2分，共10题）
- 三、简答题（每题2分，共5题）
- 四、问答题（英文题，中文回答）
（共3题，20分）

卷面成绩占70%，作业占30%，共4次作业，补交无效

要求掌握内容

一、选择题（50个，50分）

（每次课2-6个题，专业名词为英文，基本概念需清楚，多为知识点引深内容）

二、名词解释（基本为课后习题内容，英文题目，翻译正确得1分，解释正确再得1分；每题2分，10个，20分）

三、简答题（5题，10分）

（专业名词为英文，课堂反复强调过的内容，只答标题，不细答）

四、问答题（3个英文问题，中文回答）（20分）

要求掌握内容

四、问答题（3个英文问题，中文回答）（其中一道为作业题）（20分）

1. 阻止微生物入侵的屏障
2. 天然免疫系统识别抗原的机制：模式识别，识别受体及其引发的下游效应
3. 吞噬细胞杀伤病原微生物的机制
4. 抗体的结构以及抗体识别的机制
5. TCR的结构以及TCR如何进行特异性识别
6. 抗原的处理及提呈：能够被 $\alpha\beta$ T细胞的受体（ $\alpha\beta$ TCR）识别的抗原是如何产生的？抗原提呈的不同途径：MHC-I 途径：提呈内源性抗原，MHC-II 途径：提呈外源性抗原
7. T细胞在胸腺发育中的阳性选择和阴性选择过程
8. B细胞对胸腺依赖抗原的应答过程，T细胞如何帮助B细胞进行应答
9. B细胞在生发中心进行抗体亲和力成熟的过程：体细胞高频突变，生发中心B细胞的阳性选择

recognition, effector, regulation, memory



The first lines of defense

Innate immunity
(immediate: 0-4h)

Innate immune cells

Innate Immune Response

**Early induced
Innate response**
(early: 4-96h)

inflammatory response

Adaptive Immune Response

**Adaptive
immune
response**
(late: > 96h)

Cell-mediated immune

Humoral immune

Immunodefense, Immunesurveillance, Homeostasis

Immunology

研究免疫系统结构与功能的学科

Immunobiology

研究免疫现象生物学基础的免疫学分支学科

Immune system

由免疫器官、免疫组织、免疫细胞、免疫分子和淋巴循环网络组成。

Immune System

Innate Immune System

- 1、模式识别
- 2、胚系编码
- 3、迅速应答
- 4、无记忆

物理、化学和微生物屏障、
免疫分子和固有免疫细胞

Adaptive Immune System

- 1、特异性识别
- 2、机体获得性
- 3、多样性
- 4、记忆性

T, B lymphocytes

Immune defense, Immune surveillance, Homeostasis

免疫系统具有区分“self”和“non-self”的能力

Immune response

凡是外来的就response

凡是宿主的就tolerance

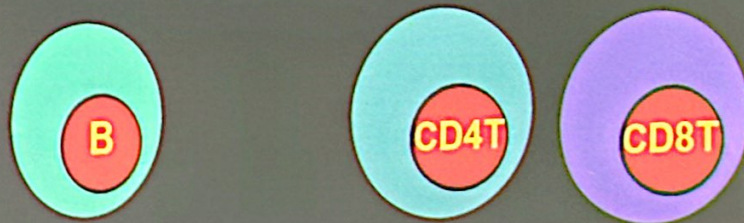
Immune response 程序

Immunological recognition, effector function,
regulation, memory

Innate Immune Cells

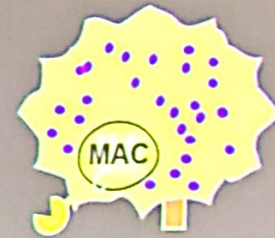
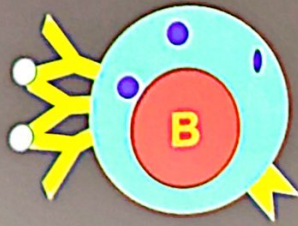


Adaptive Immune Cells



Immundefense, Immunesurveillance, Homeostasis

APC (Antigen Presenting Cells)



Central or primary lymphoid organs

BM

Thy

Peripheral or secondary lymphoid organs

Spleen

MIS

LN

Peripheral or secondary lymphoid organs

Spleen

MIS

LN

B

Activated
Effector

T

Blood and Lymph circulation

Inflammatory Site
(炎症部位)



Kenneth M. Murphy and Casey Weaver

Immunobiology (9ed)

**PART I An introduction to immunobiology
and innate immunity**

Chapter 2 Innate Immunity: The First Line of Defense

Section-1 Anatomic barriers and initial chemical defenses



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viruses,
bacteria
fungi,
protozoa,
worms.

Innate Immune System

Innate immunity

(immediate:0-4h)



The first lines of defense

Innate Immune Barrier

Mechanical, Chemical, Microbiological

Innate immune molecules

Lysozyme, Antimicrobial peptides: (Defensins, cathelicidins, RegIII, histatins)

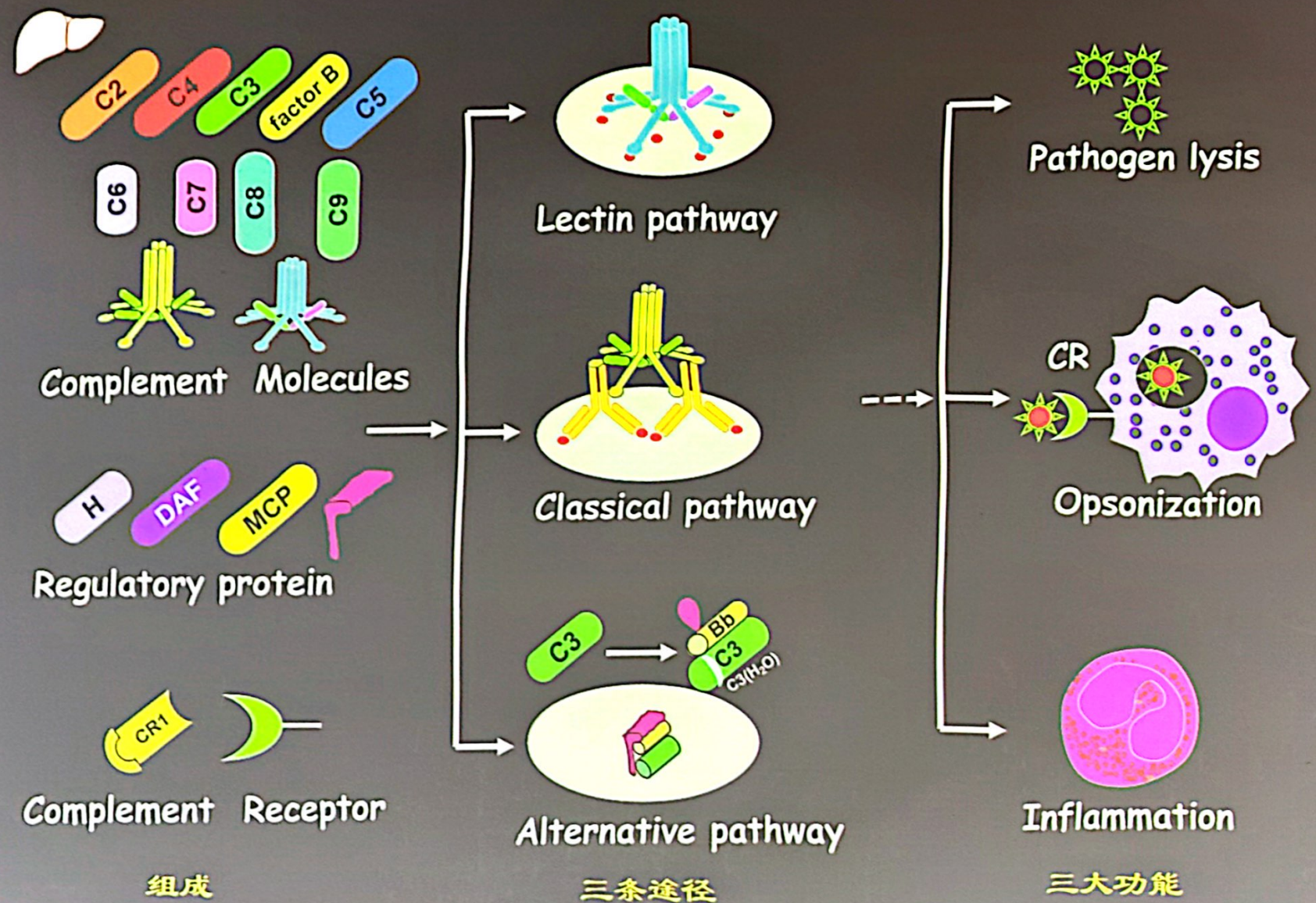
Complement system

viruses, bacteria fungi, protozoa, worms.

first barrier against infection

	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	Pulmonary surfactant	Enzymes in tears and saliva (lysozyme)
		Enzymes (pepsin)		
	β -defensins Lamellar bodies Cathelicidin	α -defensins (cryptdins) RegIII (lecticidins) Cathelicidin	α -defensins Cathelicidin	Histatins β -defensins
Microbiological	Normal microbiota			

The main component and effector actions of complement

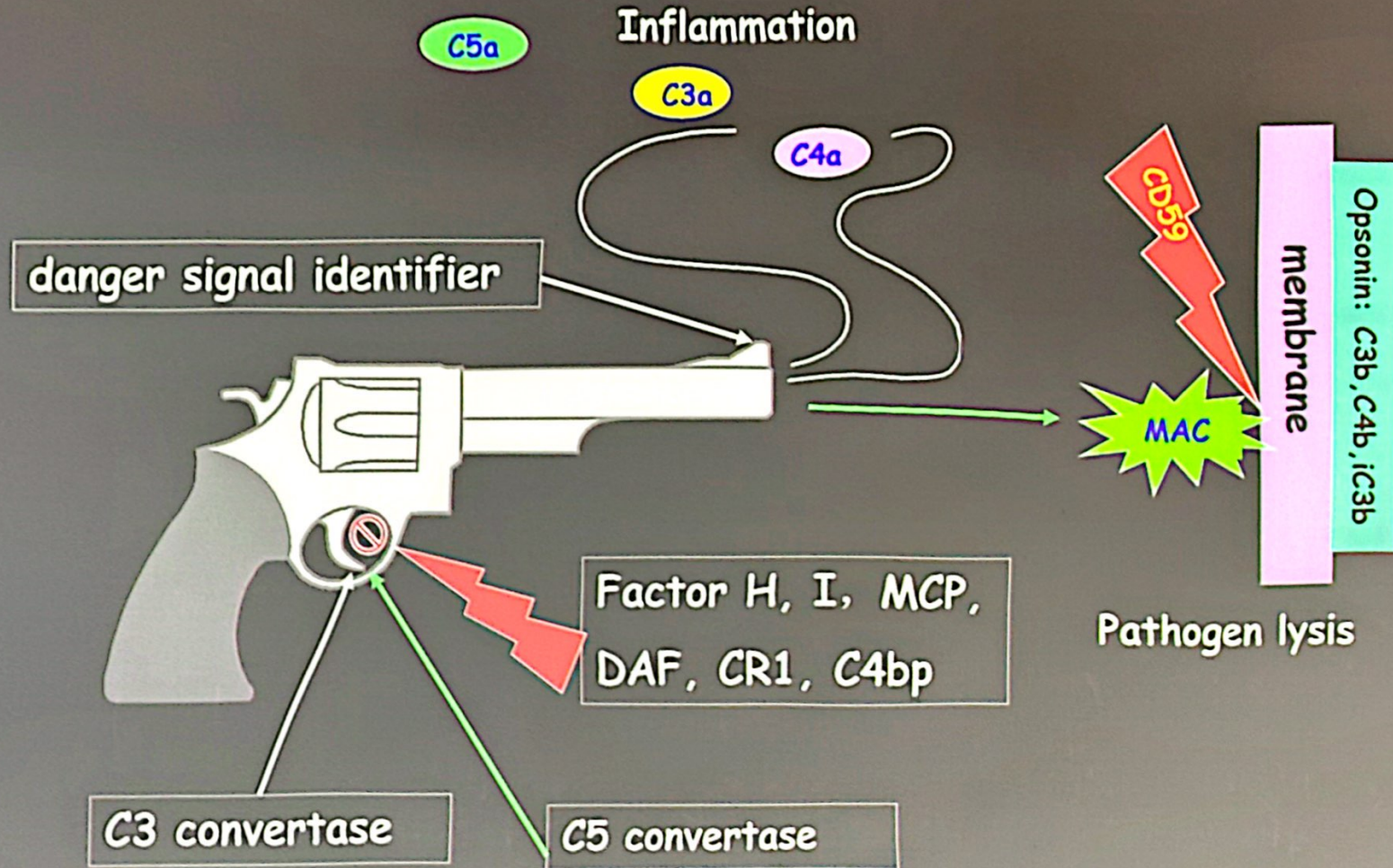


组成

三条途径

三大功能

The Complement System



viruses,
bacteria
fungi,
protozoa,
worms.

Innate Immune System

Innate immunity
(immediate:0-4h)



The first lines of defense

Innate Immune Barrier

Mechanical, Chemical, Microbiological

Innate immune molecules

Lysozyme, Antimicrobial peptides: (Defensins, cathelicidins, RegIII, histatins)

Complement system

Innate immune cells

Innate Immune Response

Innate immunologic recognition



Effector function, Regulation

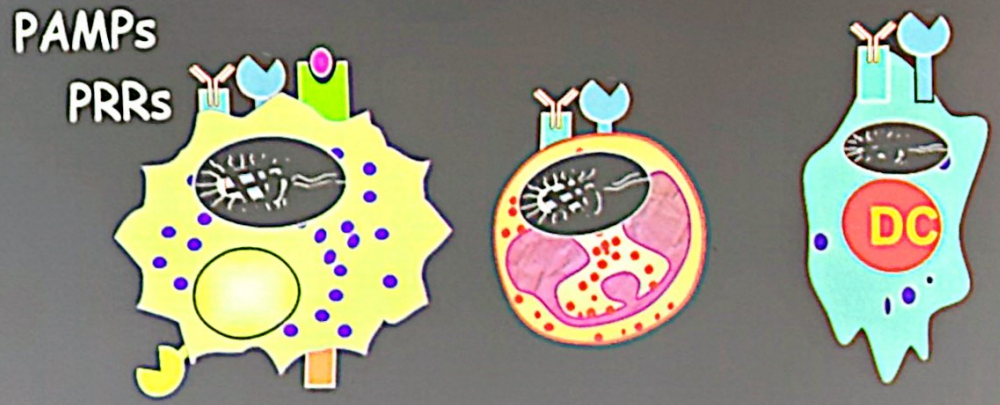
固有免疫系统是怎样识别和发挥效应的？

Process of phagocytosis

Phagocytes



Process of phagocytosis

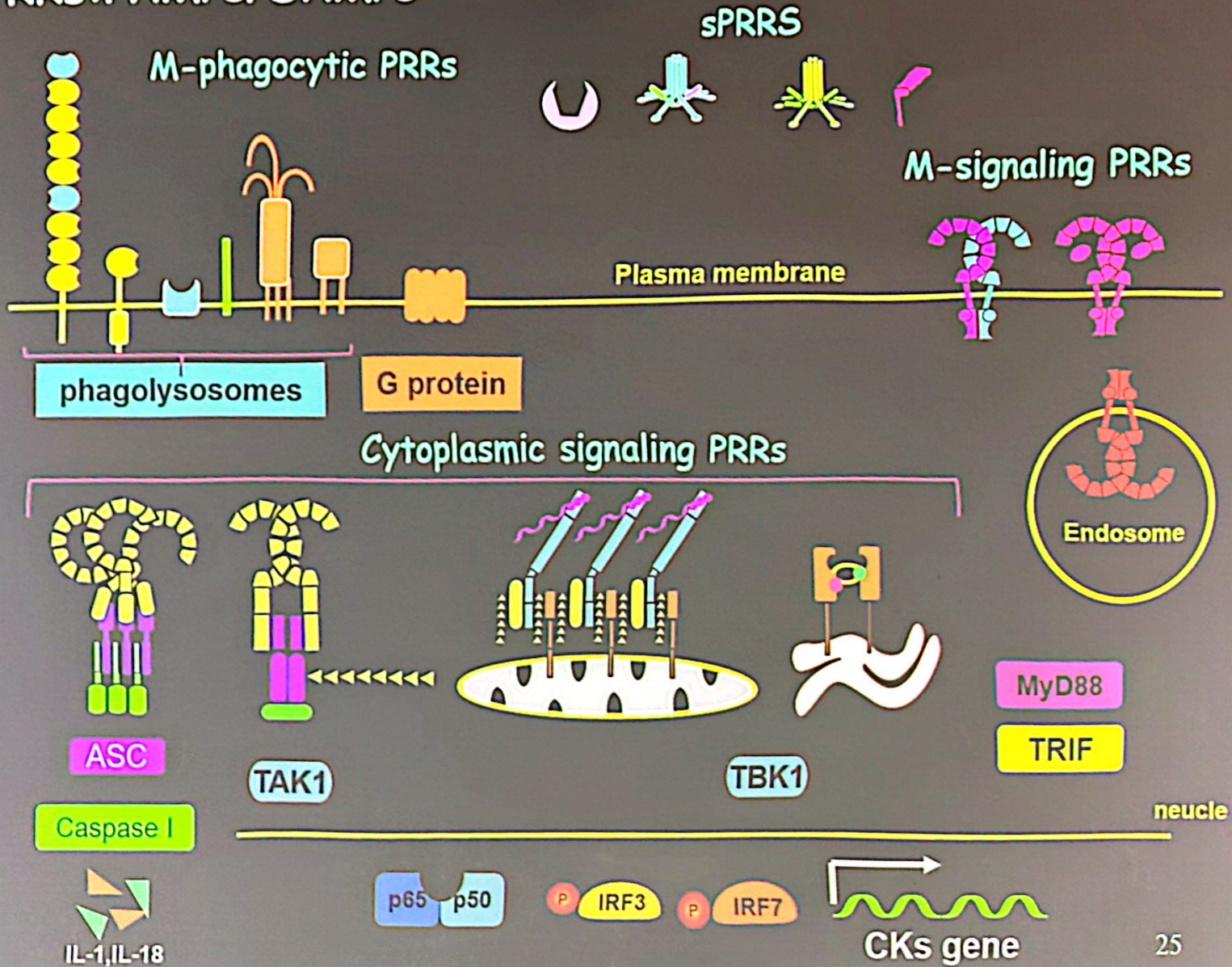


Recognition, ingestion, killed (digestion)

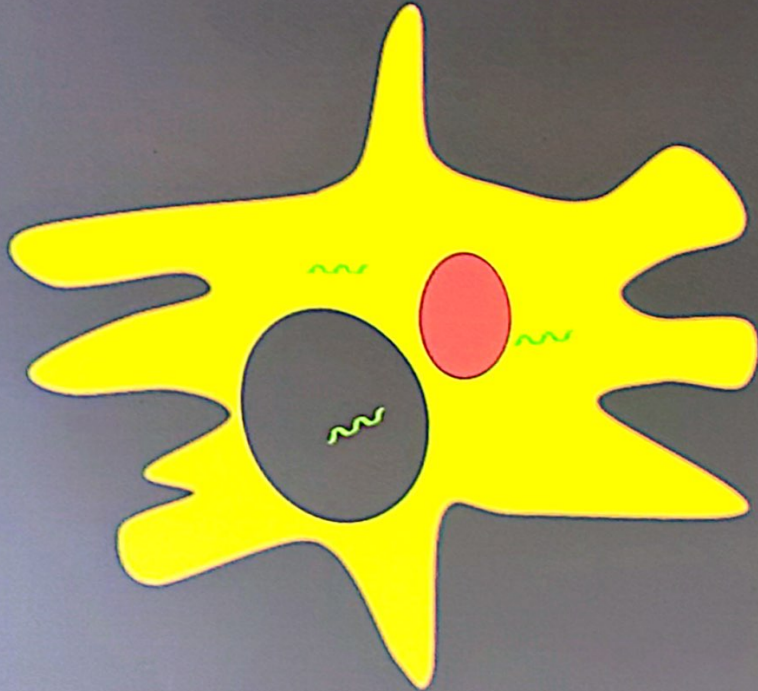
Mechanism

Respiratory burst, Acidification, NO

PRRs: PAMPs/DAMPs



Sensors of virus



TLR-3 (dsRNA),

TLR-7,8 (ssRNA),

TLR-9 (CpGDNA)

detect viral RNAs and
DNAs of extracellular
material entering the
endocytic pathway

cGAS (dsDNA)

RIG-I (ssRNA)

MDA-5 (dsRNA),

detect nucleic acids present
in the cytoplasm of a
virus-infected cell as a
result of viral replication

Immune system具有区分“self”和“non-self”的能力

Innate immunological
recognition

PAMPs

PRRs

Germline-encoded receptor
Pattern Recognition

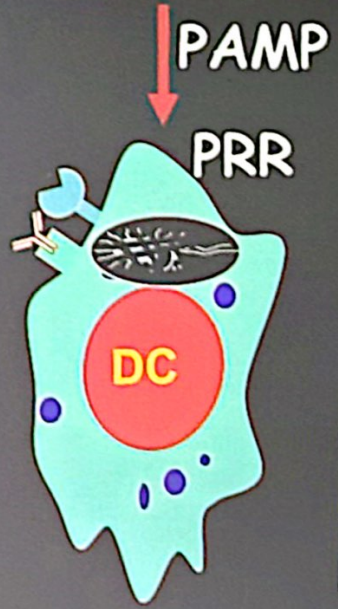
effector function, regulation

Innate immune response

viruses,
bacteria
fungi,
protozoa,
worms.

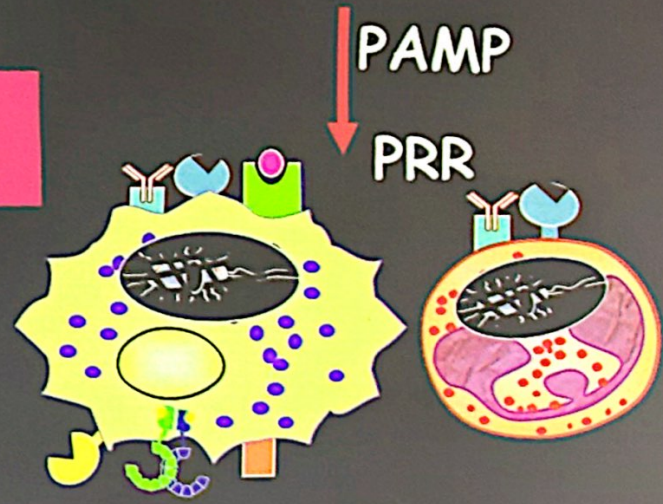
Barrier
Mechanical, Chemical, Microbiological
Innate immune molecules
Lysozyme, Antimicrobial peptides
Complement system

Innate immunity
(immediate:0-4h)



0-4h
inflammatory response

**Early induced
Innate response**
(early: 4-96h)



How to induce innate immune response?



Lecture-05

Kenneth Murphy, Paul Travers, Mark Walport

Immunobiology (9ed)

**PART I An introduction to immunobiology
and innate immunity**

Chapter 3 Induced responses to Innate Immunity

Section-2 Induced innate responses to infection



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Immune Molecules

1. Cytokines (CKs):是由免疫细胞及组织细胞分泌的在细胞间发挥相互调控作用的一类小分子可溶性多肽蛋白。

a. 按结构分类: ① IL-1 family; ② Hematopoietin superfamily (IFN family); ③ TNF family; ④ Chemokine family。

b. 作用方式: ① 自分泌 (autocrine); ② 旁分泌 (paracrine); ③ 内分泌 (endocrine)

c. 作用特点: ① 多效性 (pleiotropy); ② 重叠性 (redundancy); ③ 协同性 (synergy); ④ 拮抗性 (antagonism); ⑤ 网络性 (Network)。

2. Chemokines: 能使细胞发生趋化运动的小分子细胞因子。

a. 结构: 均含有4个半胱氨酸 (cysteine, C) 并形成2个内部的二硫键。

b. 受体结构: 均为与G蛋白相结合的穿膜7次的跨膜蛋白。

3. Cell-Adhesion molecules (CAM): 是介导细胞与细胞之间、细胞与基质之间相互附着的分子的总称。

招募 immune cells 最重要的3个CAM家族为 ① selectin family; ② integrin family; ③ Ig superfamily (IgSF)。

Innate immune cells

1. Neutrophils: are first wave to enter an inflamed site
2. ILCs: produced CKs to provide protection in early infection.
ILCs: NK, ILC1, ILC2, ILC3, TLI
ILC1: IFN γ
ILC2: IL-5, IL-13
ILC3: IL-22, IL-17
3. NK cells: receptors: recognition of altered/missing self
Activating receptors : ITAM: NCRs and NKG2D
NCRs: NKp30, NKp44, NKp46 } (altered self)
NKG2D: ligand: MICA/B }
Fc receptors (CD16) : ADCC.
Inhibitory receptors : ITIM ; MHC class I molecules;
prevent NK cells from killing normal host cells. (missing self)
Killing mechanisms: 1. NCR/NKG2D-cytotoxic granules;
2. TRAIL/Fas; 3. ADCC.

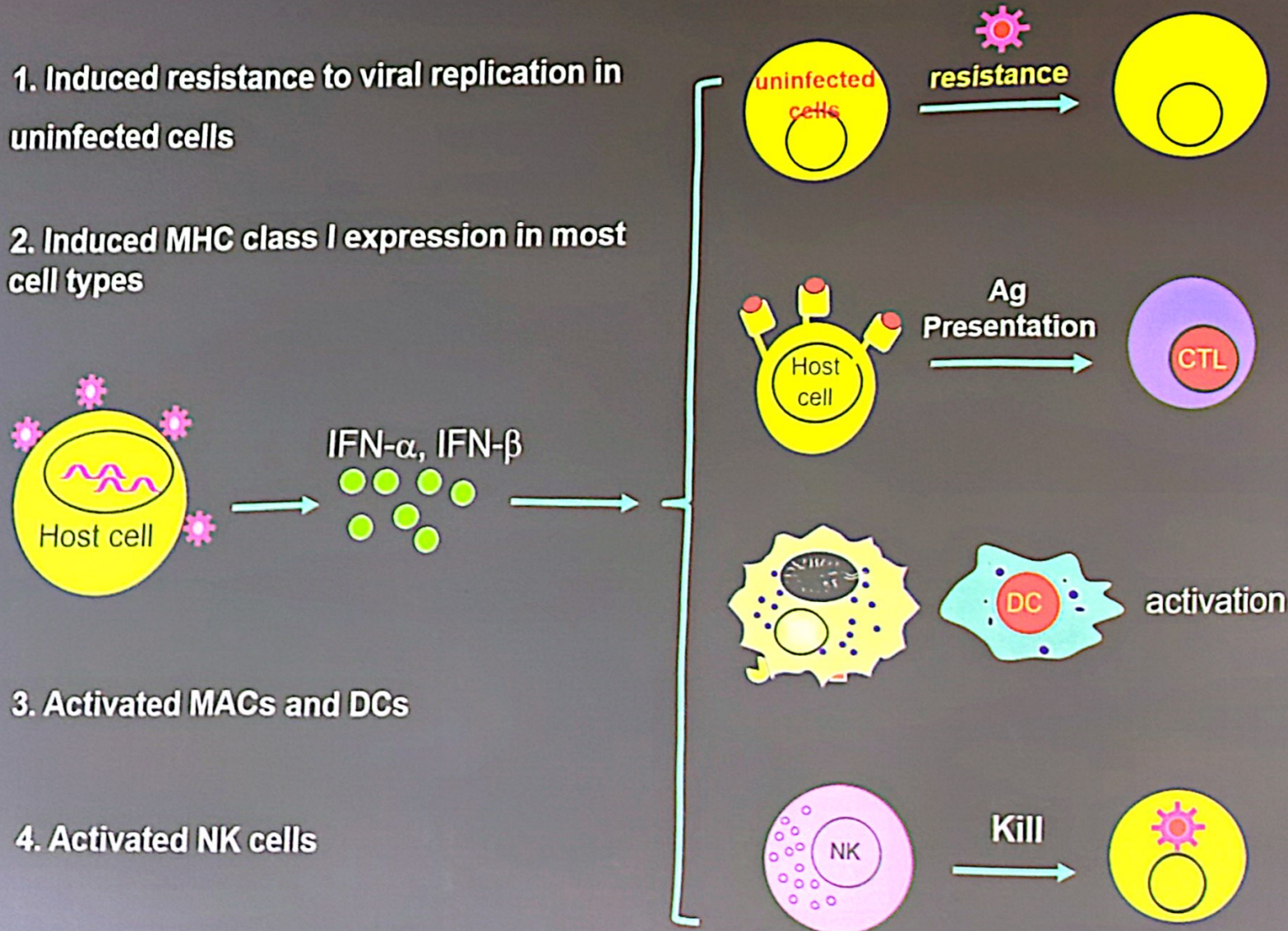
major functions of IFN α/β

1. Induced resistance to viral replication in uninfected cells

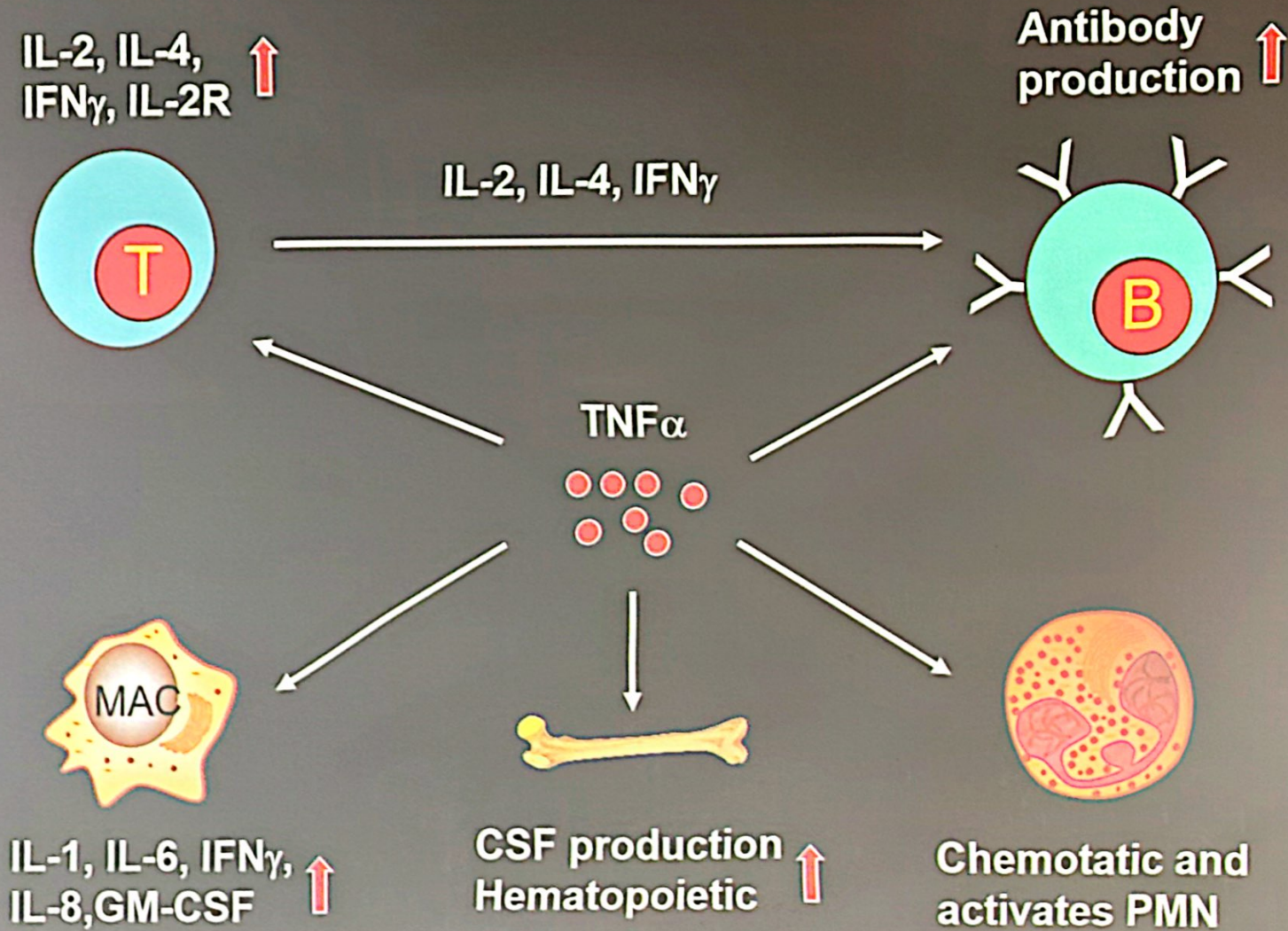
2. Induced MHC class I expression in most cell types

3. Activated MACs and DCs

4. Activated NK cells



major functions of $TNF\alpha$



Innate Immune System

viruses,
bacteria
fungi,
protozoa,
worms.



Epithelial Barrier
Mechanical, chemical, microbiological

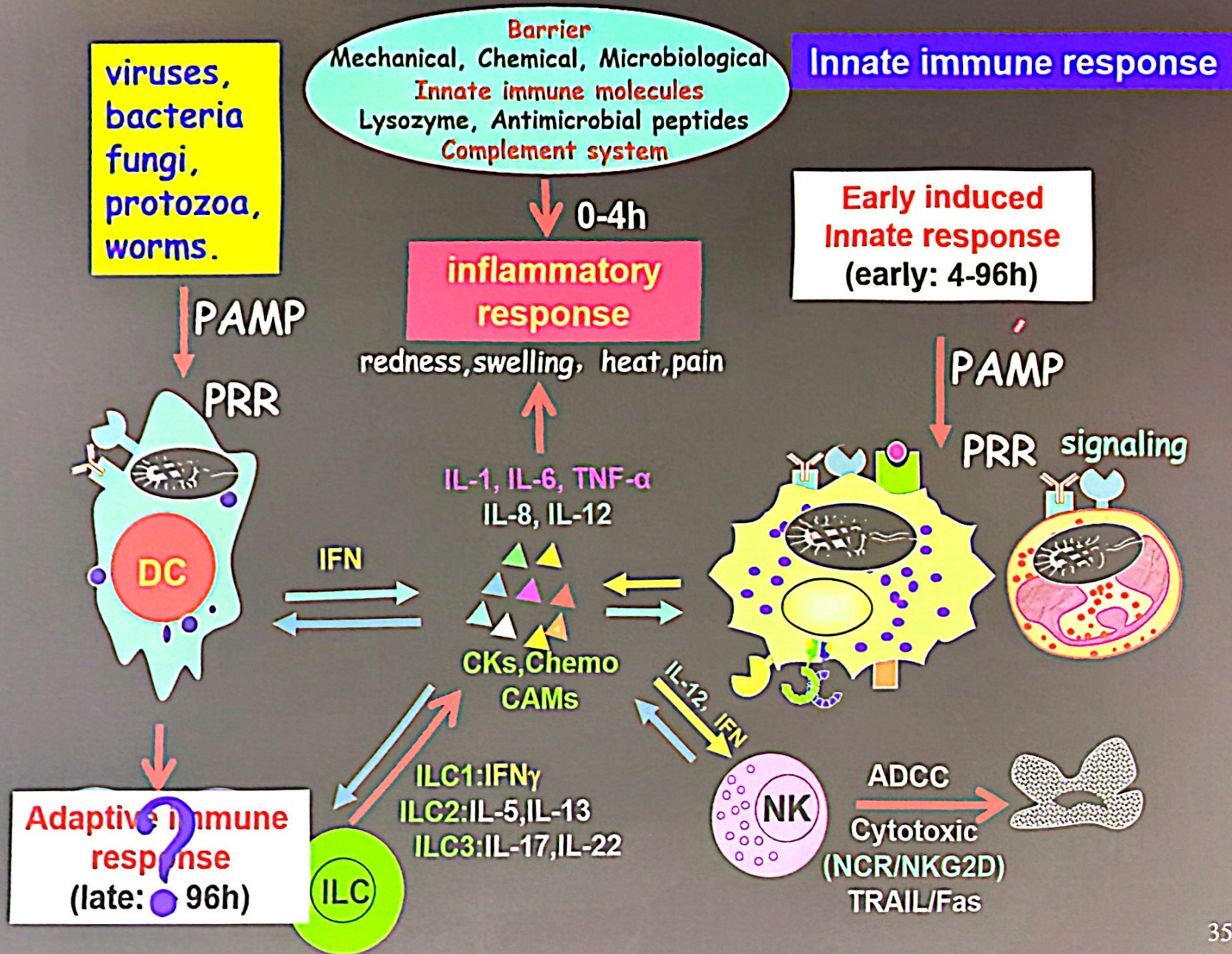
Innate immunity
(immediate:0-4h)

Innate Immune molecules
Lysozyme, Antimicrobial peptides
Complement, **CKs, Chemo, CAMs**



**Early induced
Innate
response**
(early: 4-96h)

Immunedefense, Immunesurveillance, Homeostasis



Adaptive Immune Response

BCR/TCR
Immune Recognition

Immune system具有区分“self”和“non-self”的能力

Adaptive Immune Response

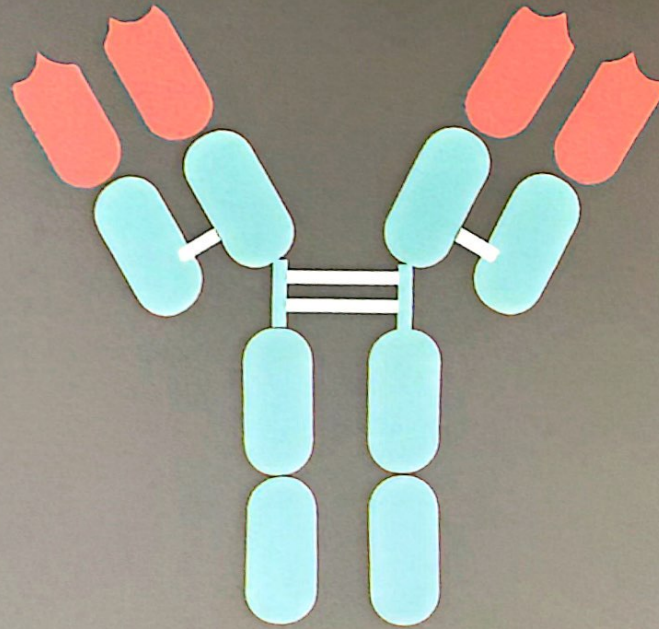
Adaptive immunologic recognition

Specificity

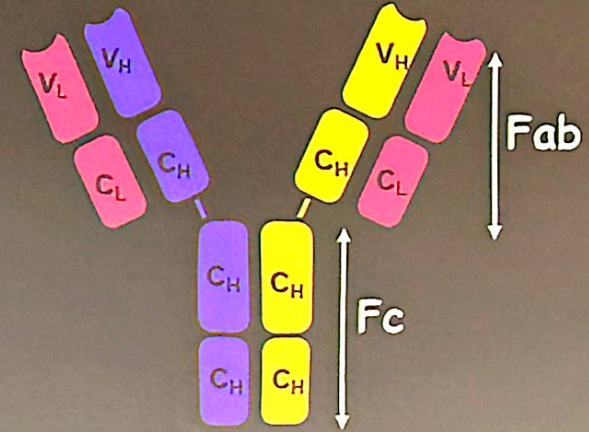
effector function, regulation, memory

A structure of a typical antibody molecule

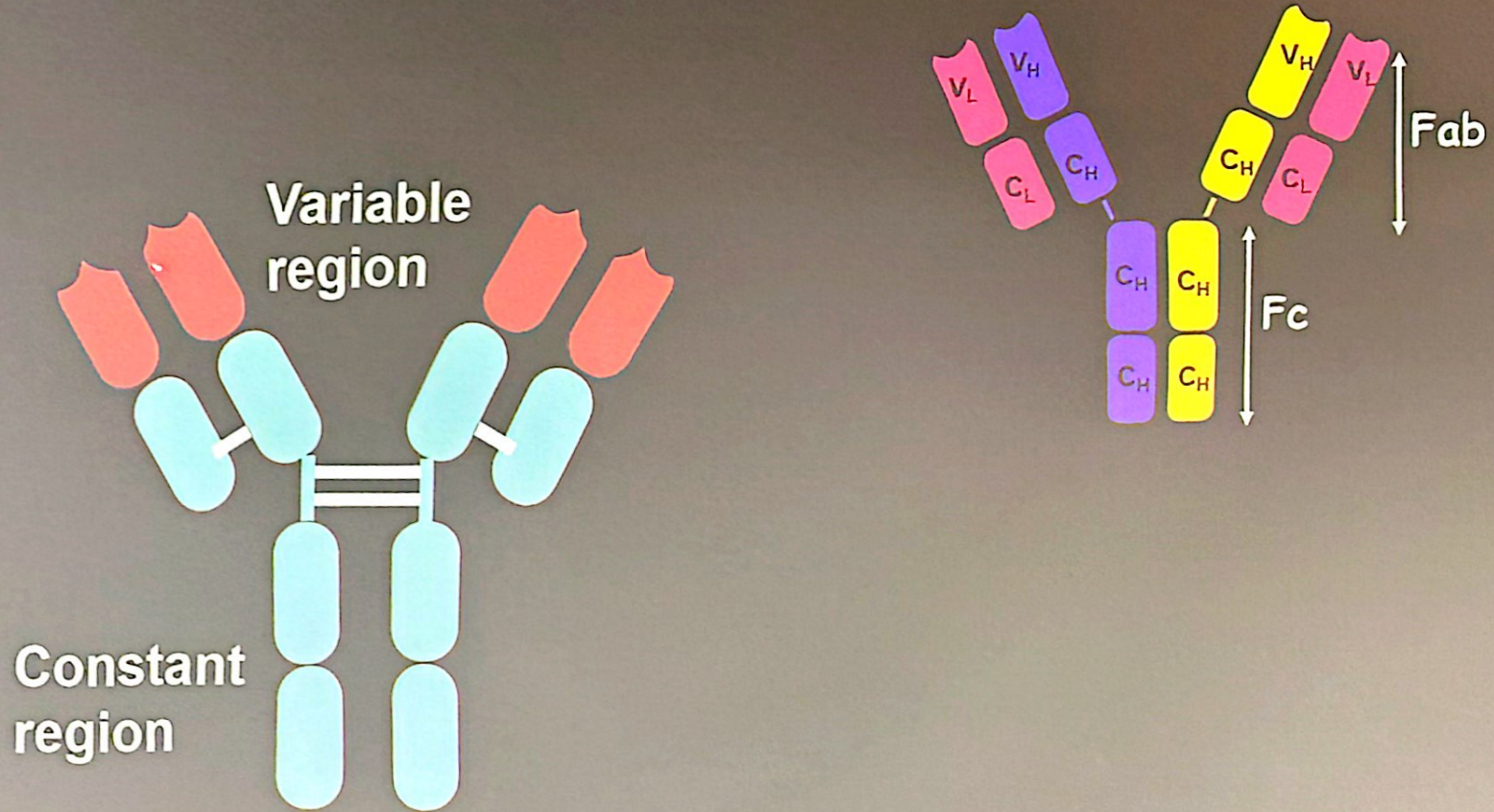
N terminus



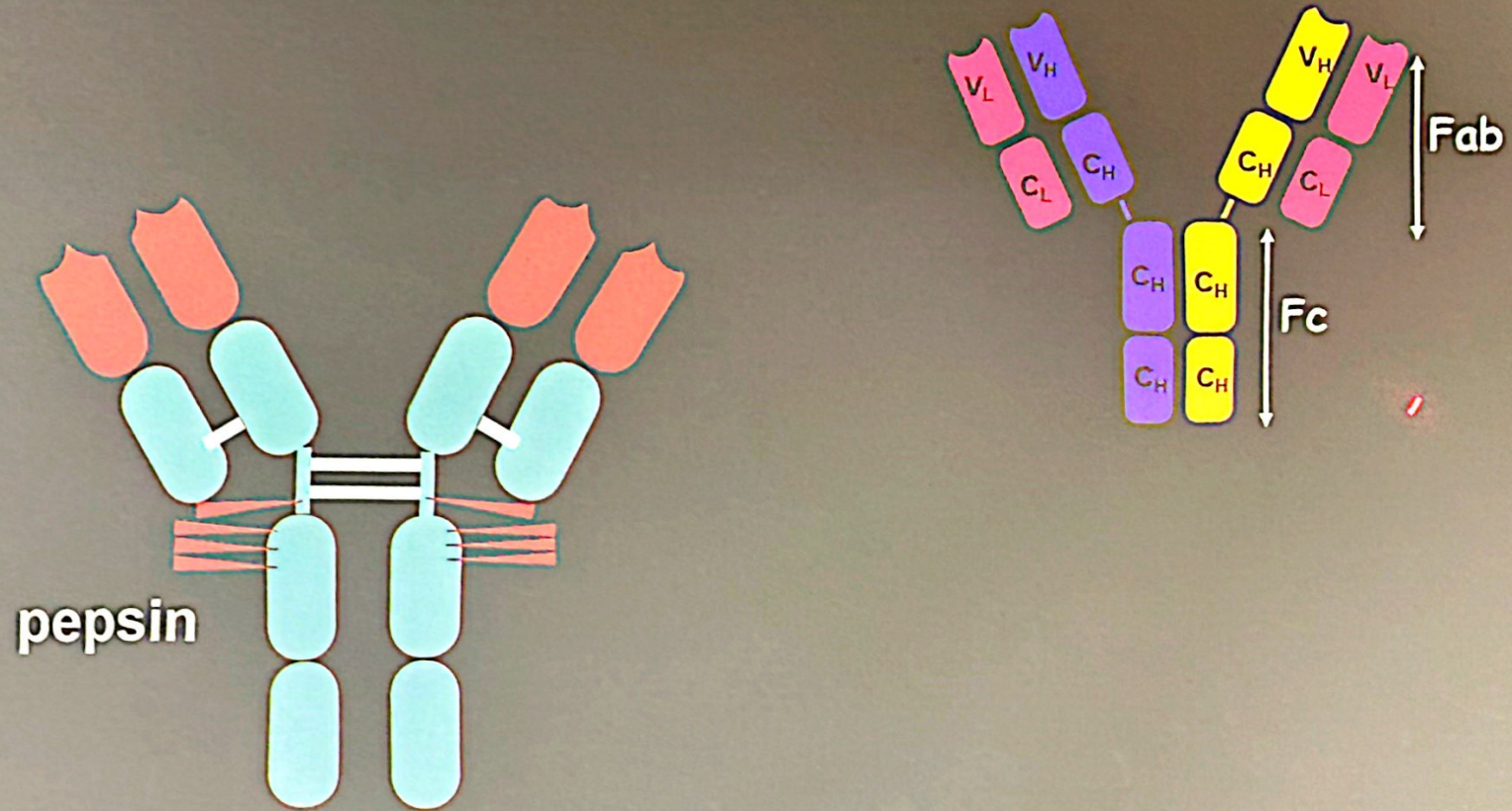
C terminus



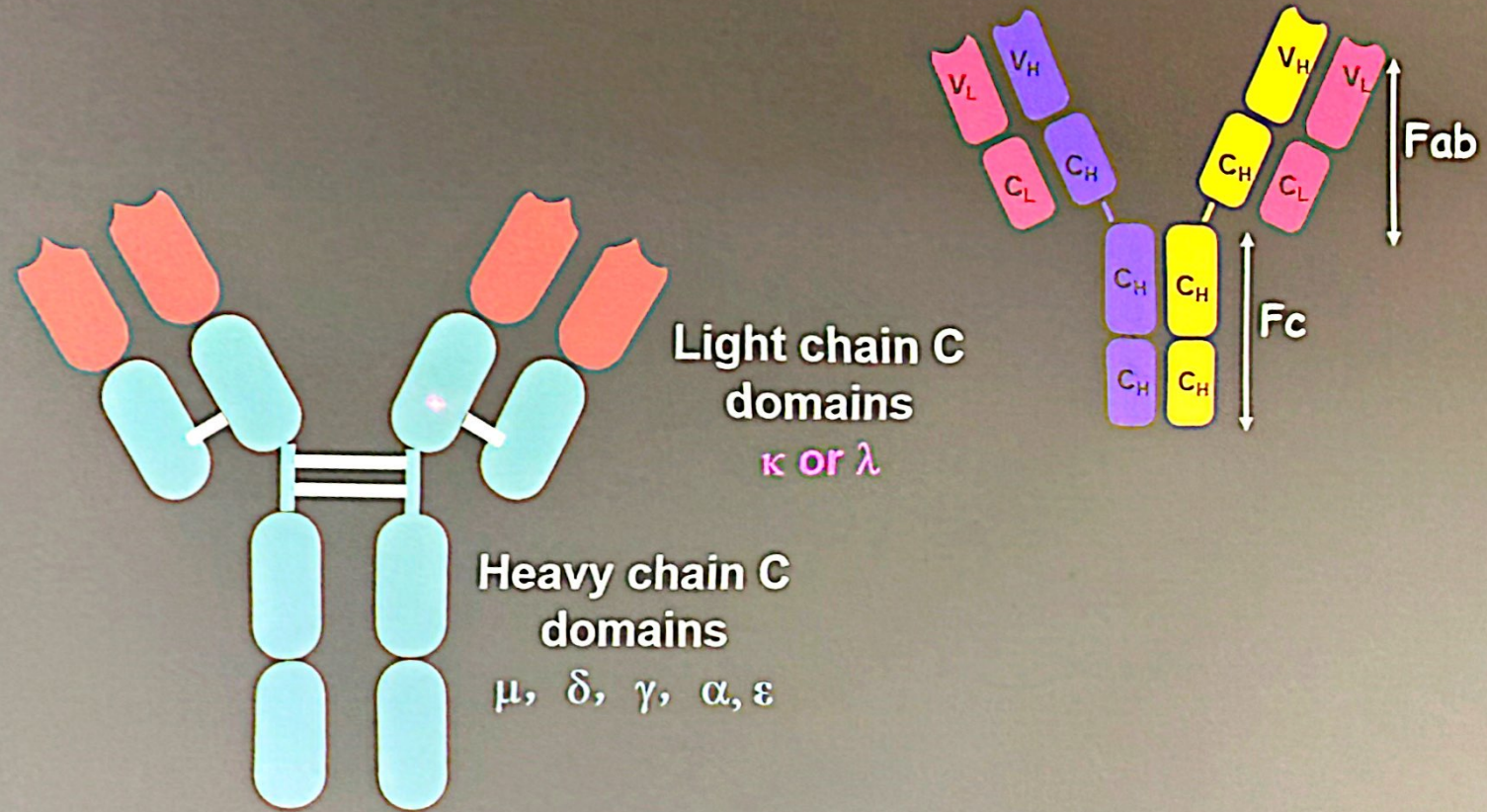
A structure of a typical antibody molecule



A structure of a typical antibody molecule



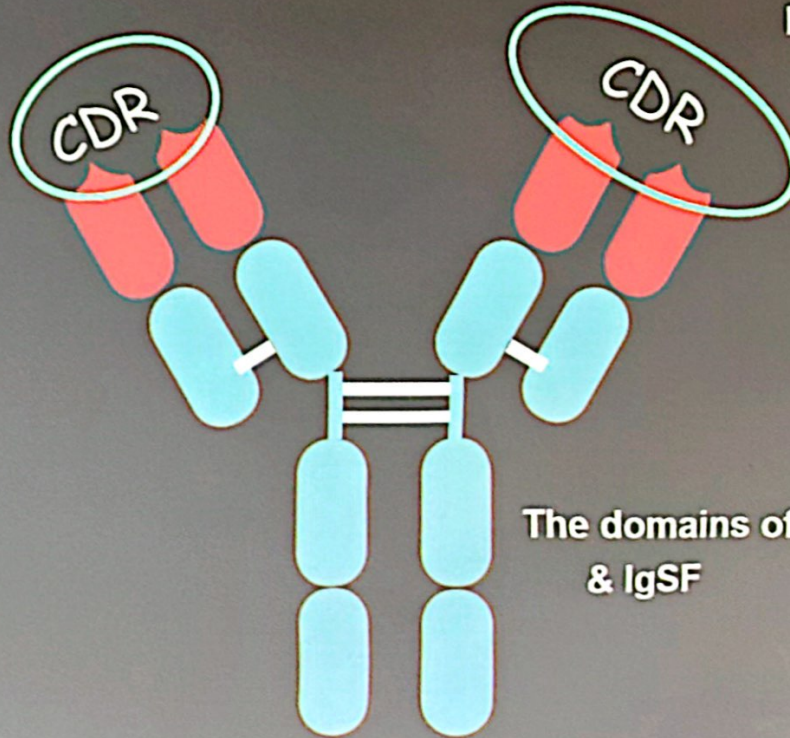
A structure of a typical antibody molecule



The interaction of the antibody molecule with specific antigen

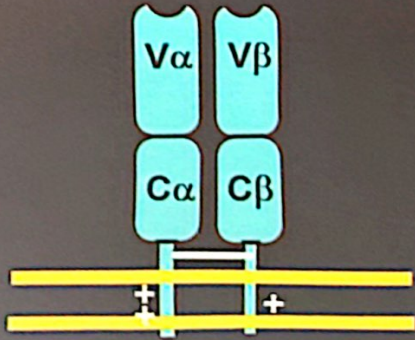
Antigen and haptan

AD (epitope),
linear epitope
conformational epitope

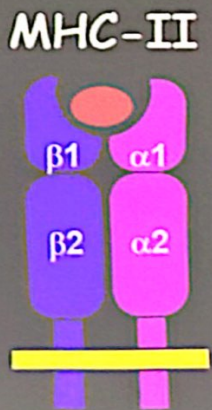
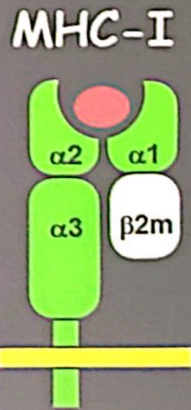


Forces of Ag-Ab interactions

The domains of an Ig
& IgSF

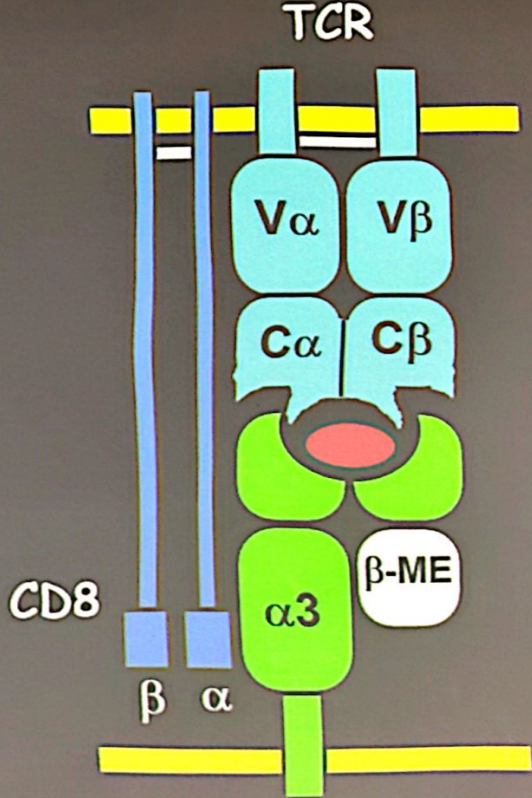


The structure of TCR



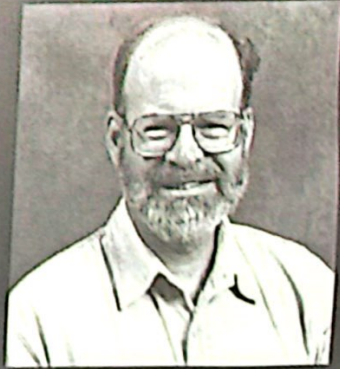
The structure of MHC

TCR recognition
双识别限制性



Specific recognition





Lecture-07

Kenneth Murphy, Paul Travers, Mark Walport

Immunobiology (8ed)

PART II The recognition of antigen

Chapter 5 The Generation of Lymphocyte Antigen Receptors

Section-1 Primary immunoglobulin gene rearrangement



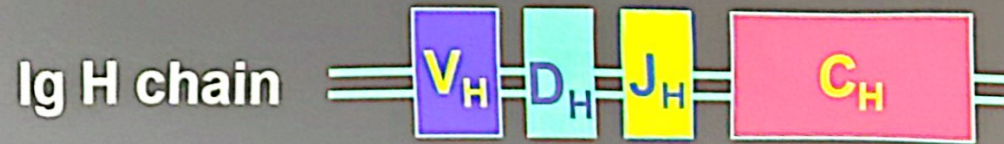
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How does generate complete genes that encode Ig?



Development

Lymphocyte-specific: RAG1/2: RSS

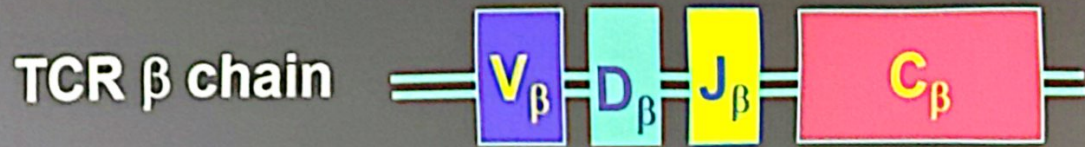


How does generate complete genes that encode TCR?



Development

Lymphocyte-specific: RAG1/2: RSS



D_β to J_β , $D_\beta J_\beta$ to V_β and $V_\beta D_\beta J_\beta$ to C_β



V_α to J_α and $V_\alpha J_\alpha$ to C_α

How does generate the diversity of the immunoglobulin/TCR repertoire?

1. Combinatorial diversity
2. Junctional diversity
3. Source of diversity
4. Somatic hypermutation

How does generate the diversity of the immunoglobulin/TCR repertoire?

1. Combinatorial diversity



2. Junctional diversity



3. Source of diversity



4. Somatic hypermutation



How many immunoglobulin classes in human?

5 domain IgM: pentamers and hexamers

4 domain IgD

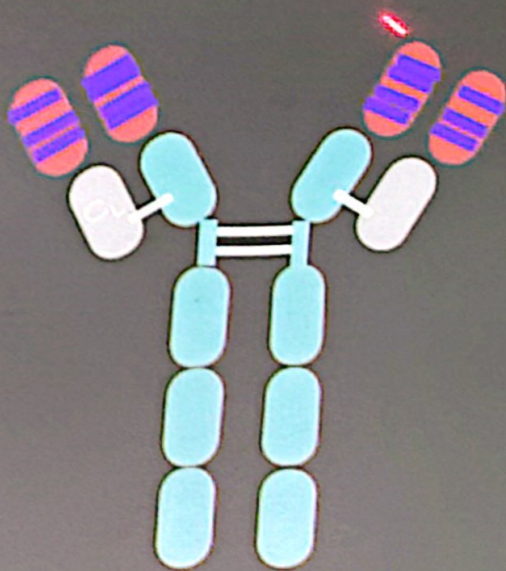
4 domain IgG: IgG1, IgG2, IgG3, IgG4

4 domain IgA: IgA1, IgA2, dimerisation

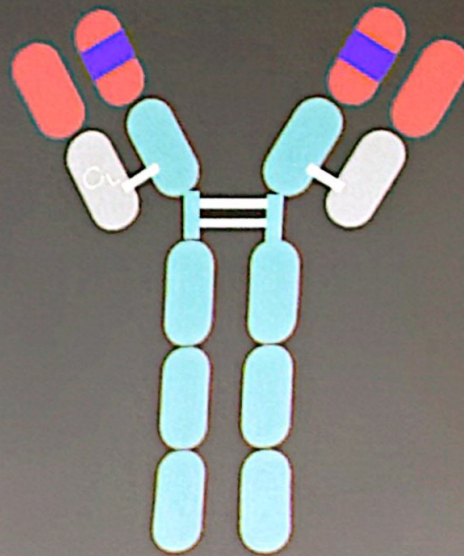
5 domain IgE

How does generate the secondary diversification of the antibody repertoire?

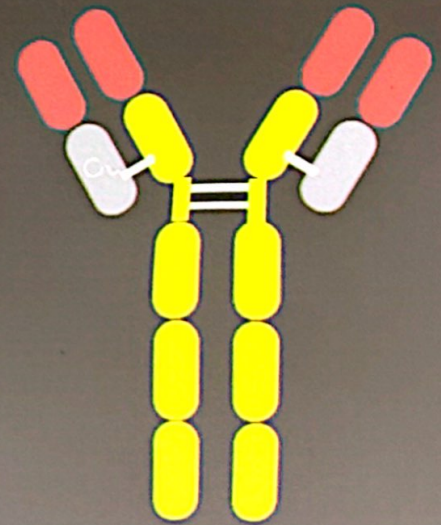
Somatic hypermutation



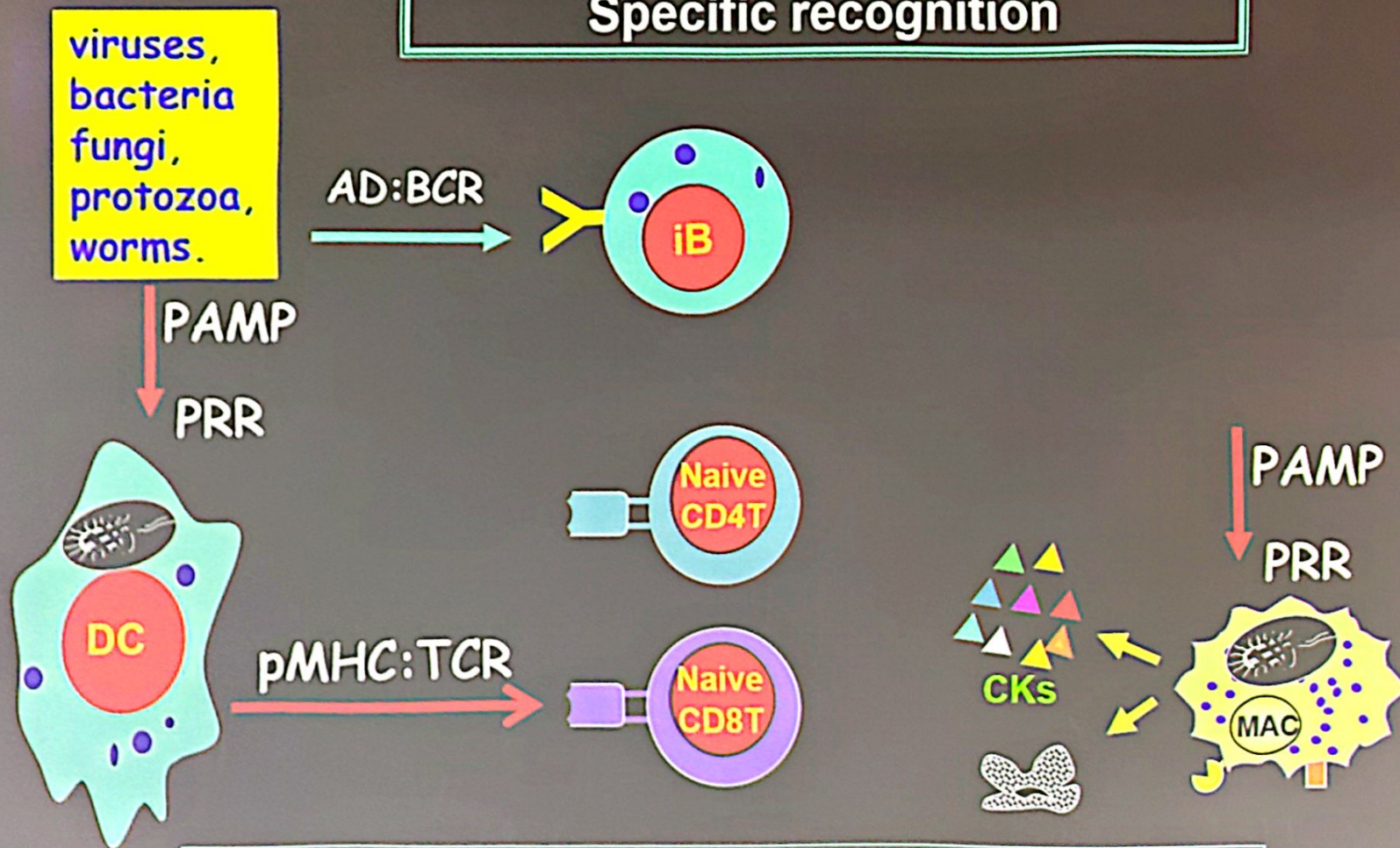
Gene conversion



class switch recombination



Gene rearrangement receptor Specific recognition



TCR ligands 是怎样产生的？

抗原加工和提呈

- **Antigen processing:** APC首先在感染或炎症局部摄取抗原，然后在细胞内降解抗原并将其加工处理成抗原多肽片段，在以抗原肽-MHC复合物形式表达于APC细胞表面。
- **Antigen presentation:** APC与TC接触时，抗原肽-MHC复合物被TC的TCR识别，从而将抗原信息传递给TC，引起TC的活化。
- APC所表达的I类和II类MHC分子是抗原多肽的载体，分别提呈内源性 (endogenous) 和外源性 (exogenous) 抗原
- APC摄取、加工和提呈抗原主要有有二条途径：
 - MHC-I途径: presented endogenous antigen
 - MHC-II途径: presented exogenous antigen
 - CD1分子途径: presented lipids antigen

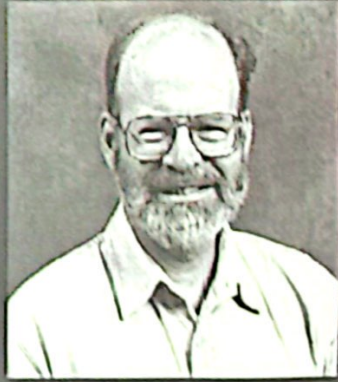
抗原提呈的两条途径

	MHC I pathway	MHC II pathway
Uptake	Intracellular	Extracellular
APCs	nucleated cells	cDC、BC、MAC
Degradated in	Cytosol (proteasome)	Endocytic vesicles (endosome-lysosomoe)
Antigenic Peptides	8-10aa	13-18aa
Peptides bind to	MHC class I	MHC class II
Peptides-MHC complex formation	ER	MIIC
Molecular chaperone	TAP1, 2, Er57, tapasin, calnexin, calreticulin	Ii, HLA-DM
Presented to	CD8 ⁺ TC	CD4 ⁺ TC

CD1分子: 提呈的脂类/糖脂类抗原

cross-presentation: MHC II \rightarrow MHC I

Autophagy: MHC I \rightarrow MHC II



Lecture-10

Kenneth Murphy, Paul Travers, Mark Walport

Immunobiology (8ed)

PART II The recognition of antigen

Chapter 6 Antigen Presentation to T Lymphocytes

Section-2 The major histocompatibility complex and its functions

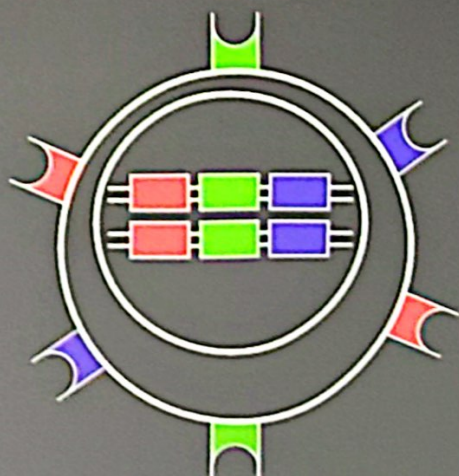


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MHC的特点

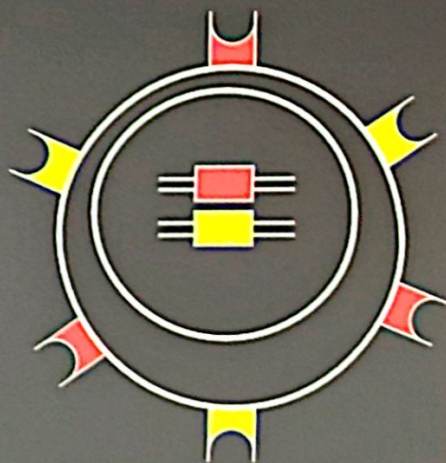
Codominance

Polygeny



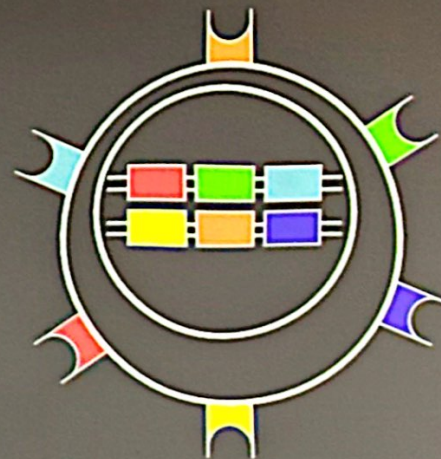
hMHC-I: HLA-A,B,C
hMHC-II: HLA-DR,DQ,DP

Polymorphism



hMHC-I: 6383 alleles
hMHC-II: 2050 alleles
2010

Polymorphism Polygeny



Diversity of
MHC molecules

1. 环境压力特别是病原压力在自然选择下，有利的遗传变异体被保留下来，是产生MHC分子高度多态性的主要因素。

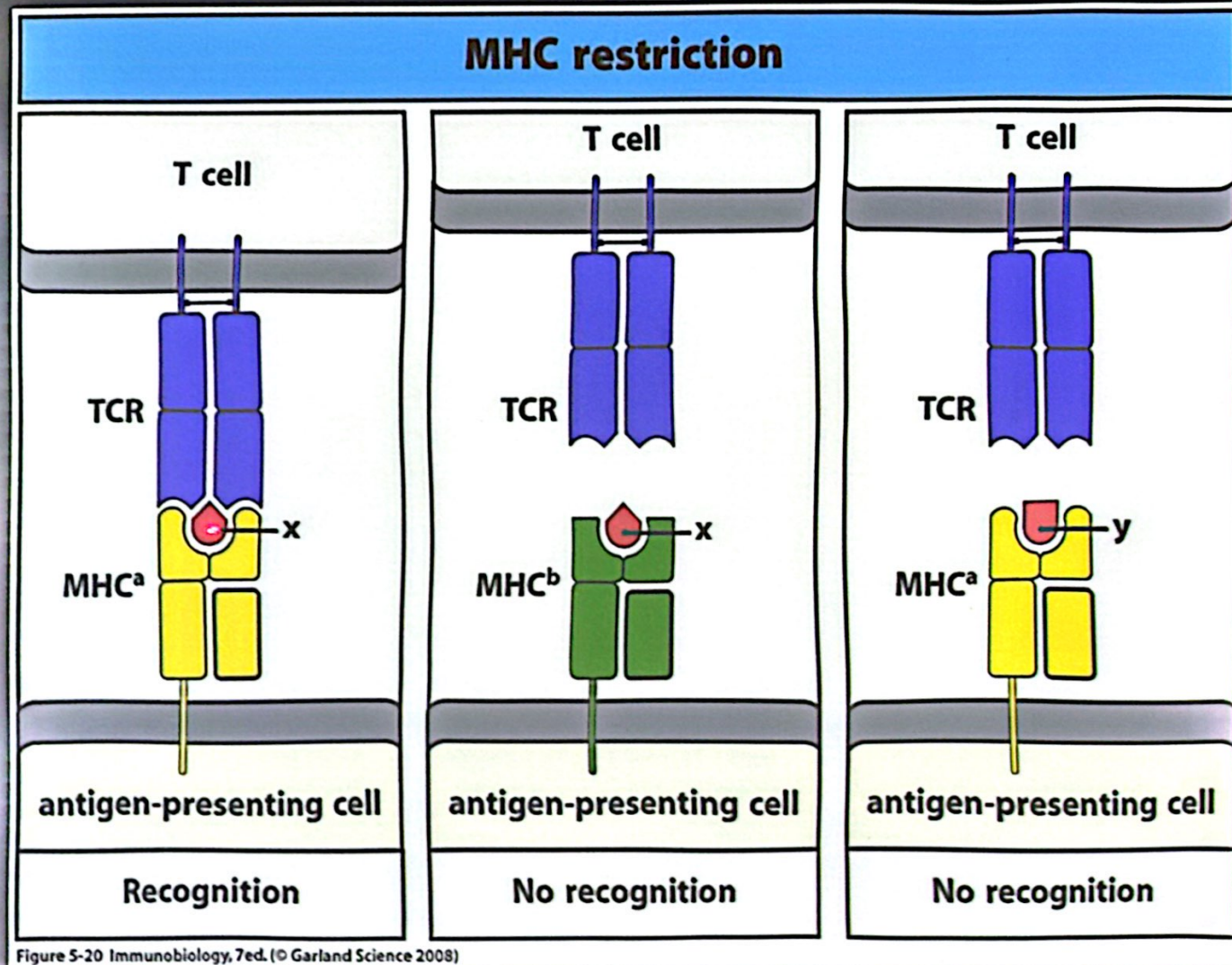
2. 多态性提高了人群整体对感染的抵抗力，避免了一个群体全体个体对病原菌易感。多基因和共显性则进一步扩大了个体免疫应答的范围。

Antigens, superantigens and Alloantigens

- Nominal antigens: 0.001% to 0.01% of T cells
- Alloantigens: 1% to 10% of T cells
- Superantigens: 2% to 20% of T cells

Specialized MHC class I molecules act as ligands for the activation and inhibition of NK cells.

T-cell recognition of antigens is MHC restricted



Questions?

- ❖ ~~按照~~MHC限制性理论，若同种（异体）移植（allogeneic transplantation）供者（donor）APC与受者（recipient）TC间MHC型别不同，二者理论上不能发生相互作用。
- ❖ 无关个体间allogeneic transplantation中，宿主（host）与移植物所表达的MHC抗原型别不一致，recipient TC对移植Ag的识别是如何跨越MHC限制性而得以实现？

☎ MLR研究显示大约有占TC总数**1-10%**的TC将对从另外一个无关的、同种族的个体的刺激有反应。这种类型的TC可对异基因MHC分子等位基因**直接识别**，称为**同种反应性T细胞 (alloreactive TC)**，其应答被称为**同种反应性**。

☎ 直接识别导致的排斥反应具有两个特点：**速度快和强度大**

☎ 同一TCR可识别不同的肽-MHC分子复合物 (pMHC)。具有直接识别能力的recipient的alloreactive TC并非一个独立的群体，它们实际上是recipient体内识别外源性抗原、但同时可**交叉识别 (crossreactive recognition)** **Allogeneic Ag**的TC。其机制：

☎ 1、TCR与pMHC结合界面的结构特征

☎ 2、肽的优势结合

☎ 3、MHC分子优势结合

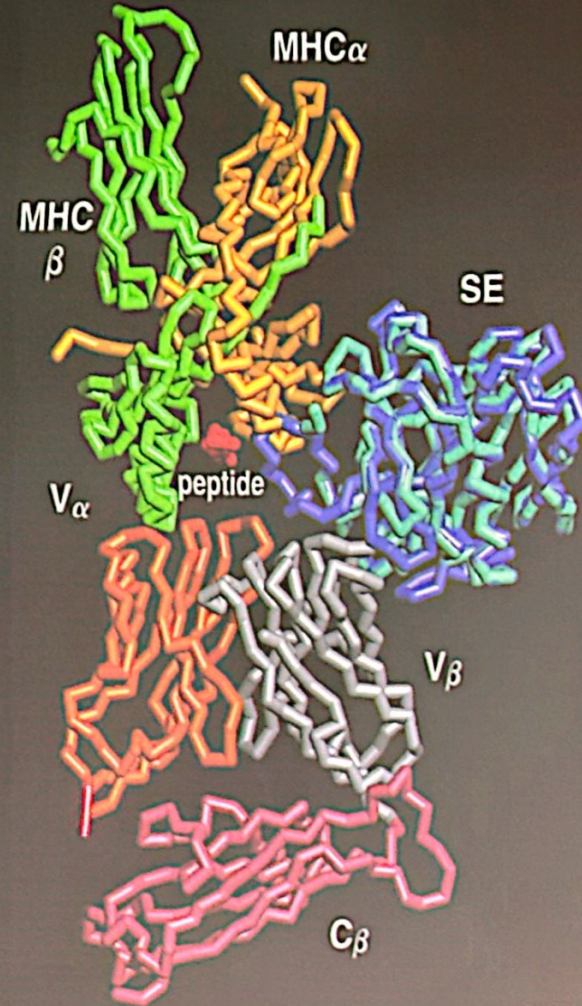
5-15. Many T cells respond to superantigens

Superantigen, SAg

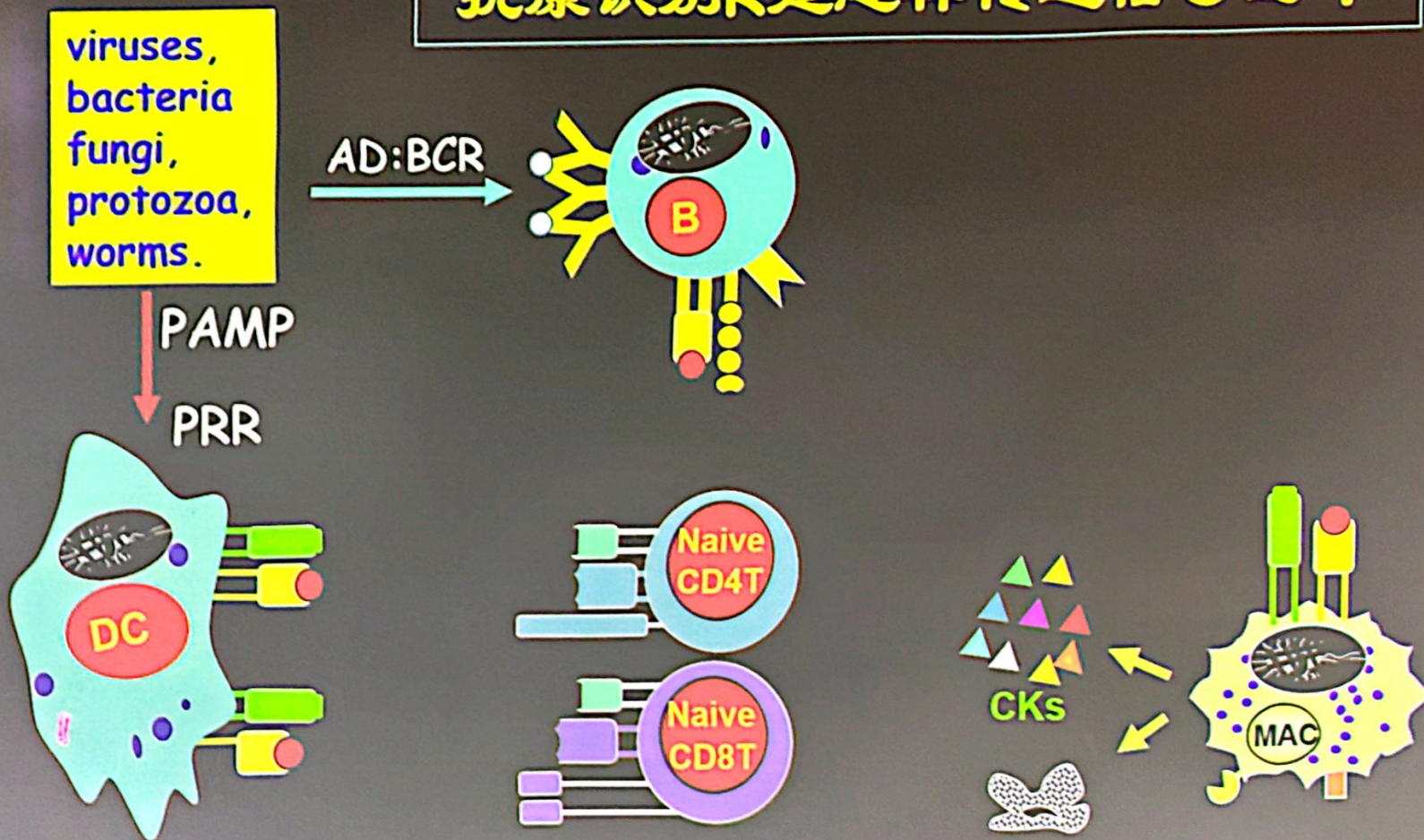
✧ SAg:指那些同时与MHC分子及TCR多肽链结合,从而非特异地激活多克隆T细胞的蛋白质大分子。

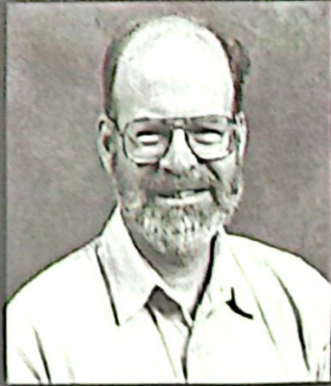
✧ Endogenous SAg: 逆转录病毒和棒状病毒编码的模型蛋白质分子。

✧ Exogenous SAg:为细菌分泌的可溶性外毒素。



抗原识别R是怎样传递信号的？





Lecture-11

Kenneth Murphy, Paul Travers, Mark Walport

Immunobiology (9ed)

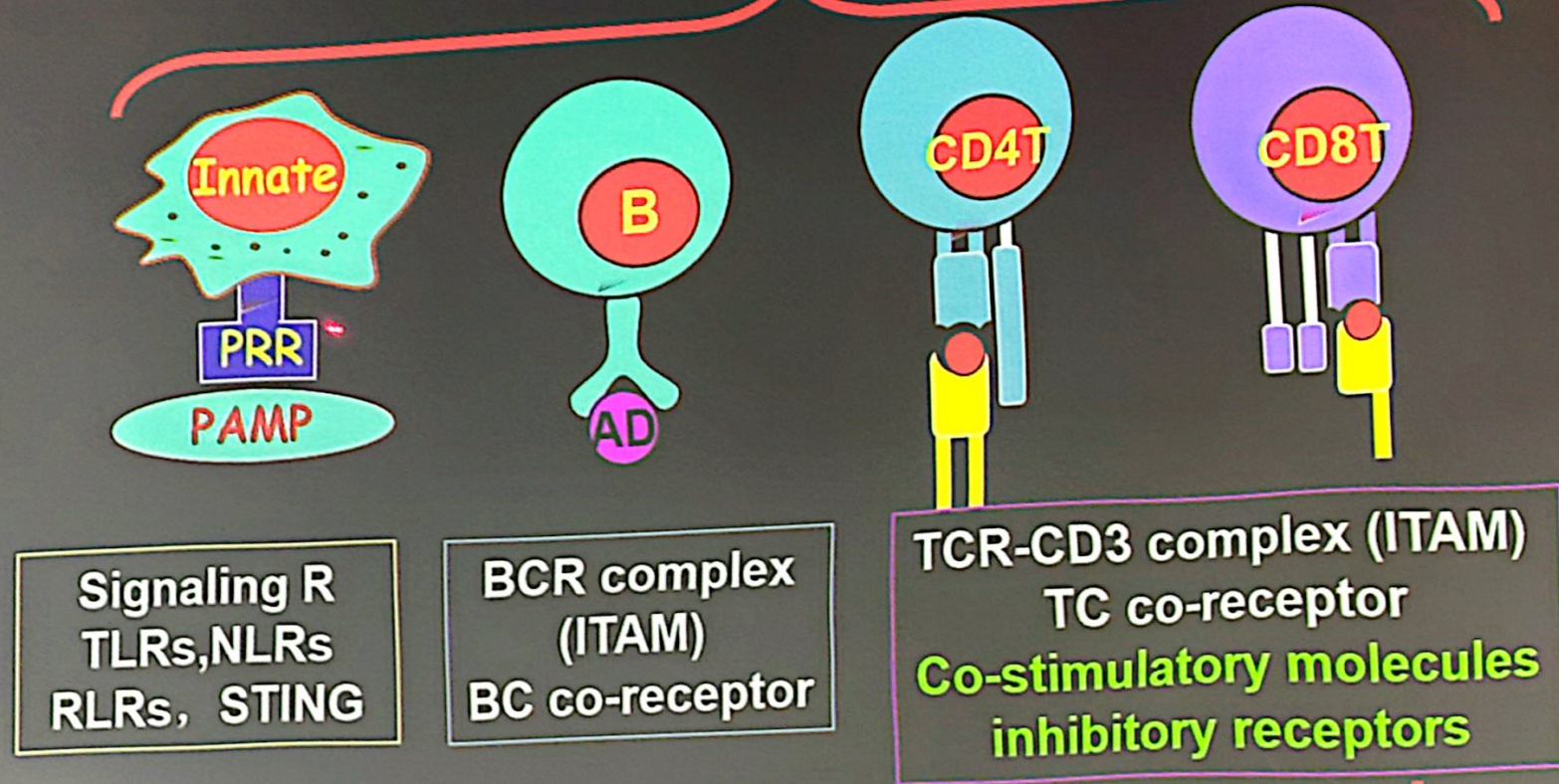
**PART III The development of mature lymphocyte
receptor repertoires**

Chapter 7 Lymphocyte Receptor Signaling



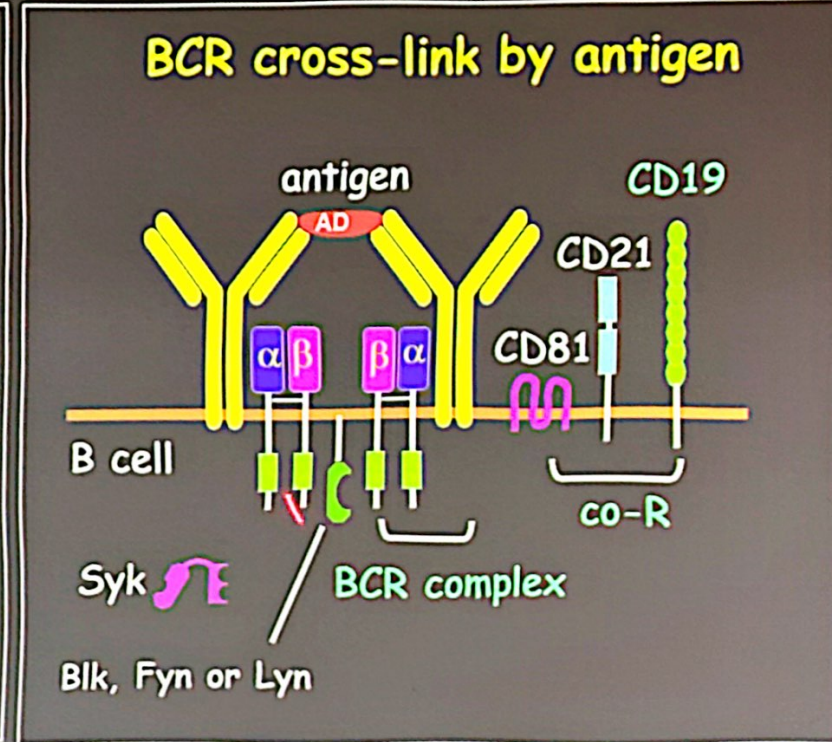
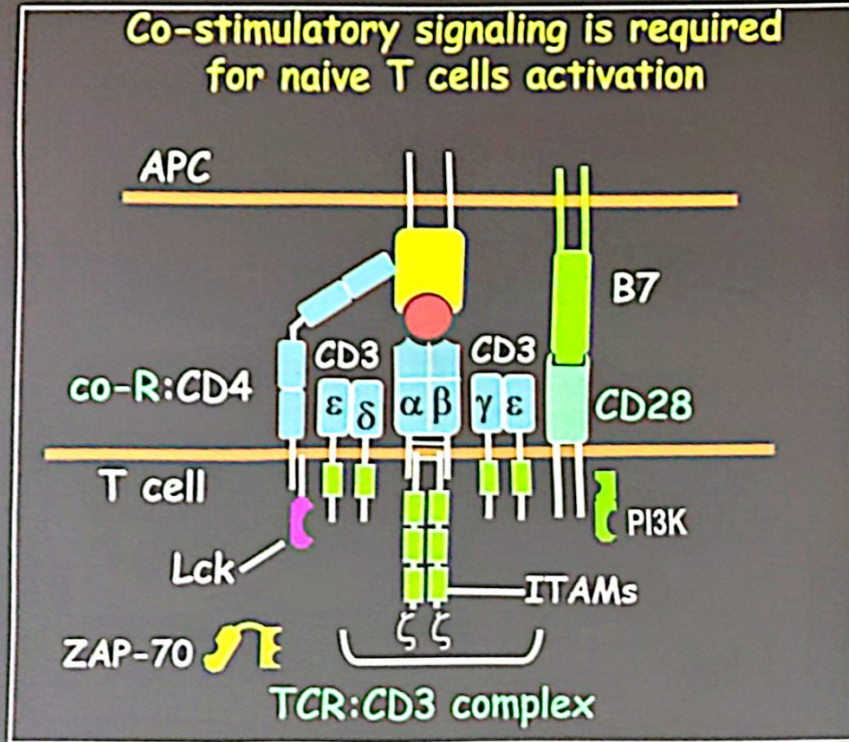
Prof. Sun Cheng
charless@ustc.edu.cn
Institute of Immunology

Immunologic Recognition



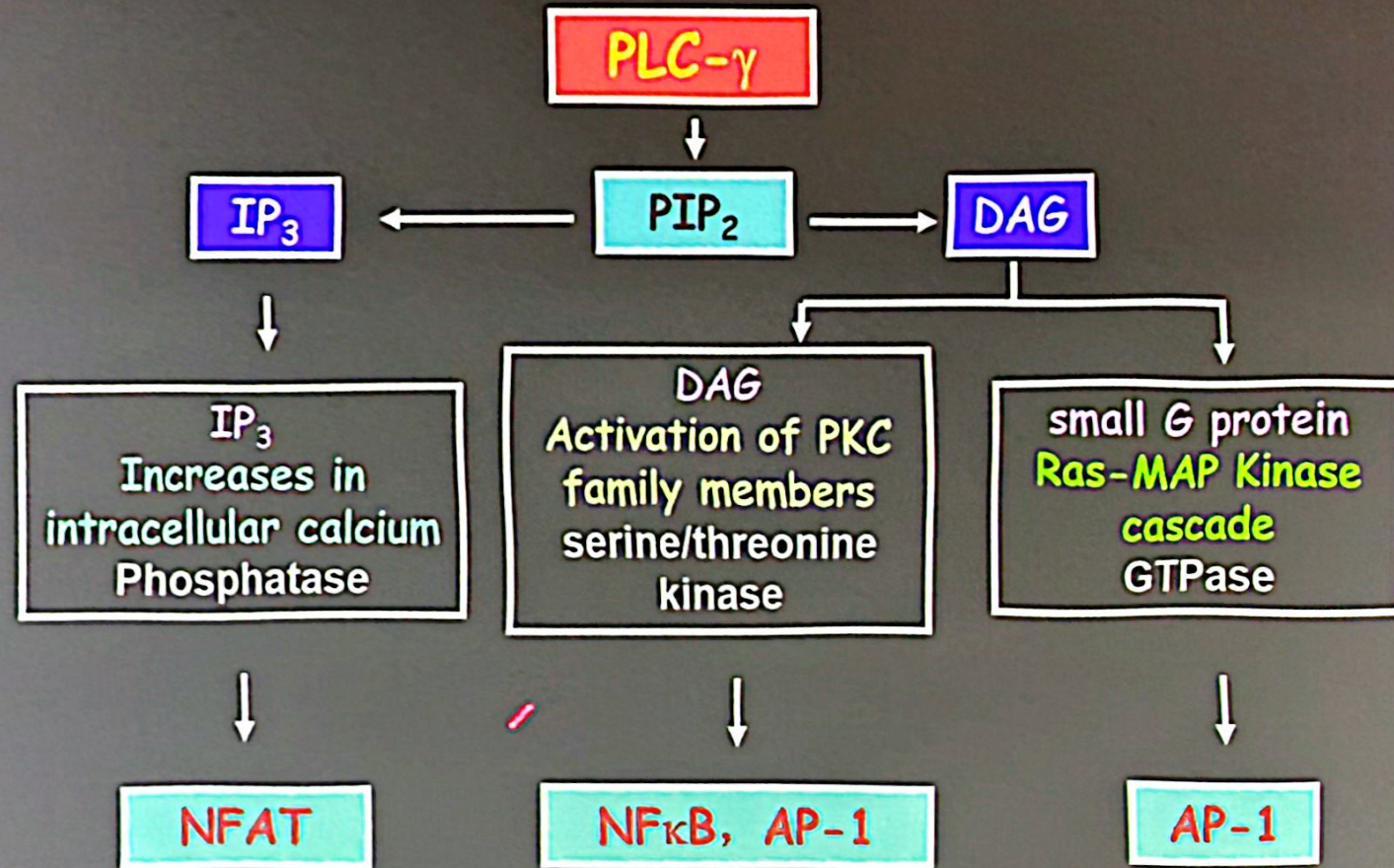
- 1.the synthesis of new proteins
- 2.induce cell division and differentiation
- 3.induce cell death

Signal transduction of TCR and BCR



PTK family	TCR	BCR	Lipid kinase
1. Src-family:	Lck	Blk, Fyn or Lyn	3. PI3K
2. Syk-family:	ZAP-70	Syk	Phospholipase
4. Tec-family:	Itk	Btk	5. PLC- γ

Signal pathway & transcription factors in T and B cells activation



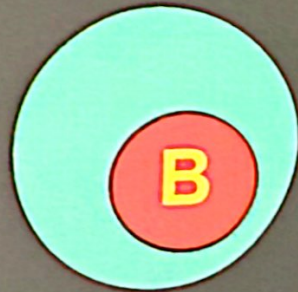
Inhibitory signaling receptor on LC downregulate immune responses

Checkpoint Blockade: Approach to tumor therapy that attempts to interfere with the normal inhibitory signals that regulate lymphocytes.⁶⁶

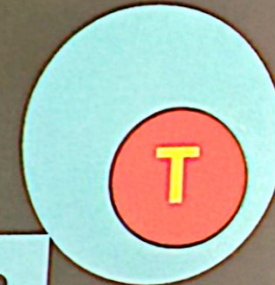
Central or primary lymphoid organs

Bone Marrow

Thymus



Self Tolerance



凡是宿主的就 tolerance

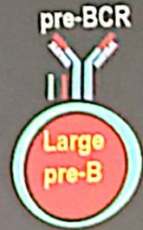
Blood and Lymph circulation

The Development and Survival of B/T cells

Development of B lymphocytes

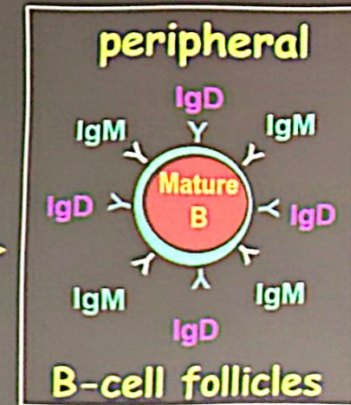
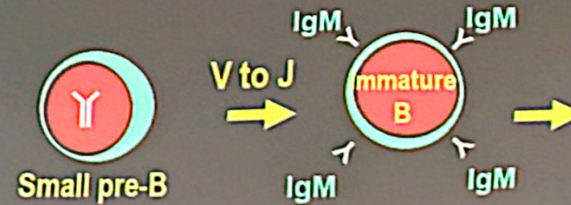


2. begins heavy-chain rearrangement



- ① inhibits further heavy-chain rearrangement
- ② enforces allelic exclusion.
- ③ cell proliferation

3. light-chain rearrangement



4. iB cells central tolerance-negative selection of B cells

- ① Deletion
- ② Receptor Editing
- ③ Anegry
- ④ Ignorant

5. B cells peripheral tolerance

- ① Apoptosis
- ② Anegry
- ③ Ignorant

6. B cells subset

- ① B-1
- ② B-2 (FBC)
- ③ MZB (B-2)



Kenneth Murphy, Paul Travers, Mark Walport

Immunobiology (9ed)

PART III **The development of mature lymphocyte
receptor repertoires**

Chapter 8 **The Development of B and T Lymphocytes**

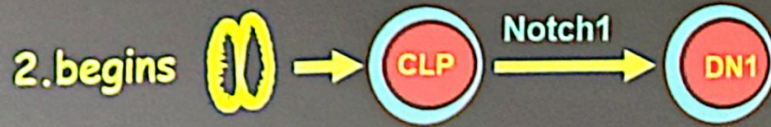
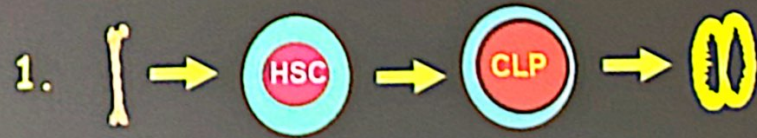
Section-2 **Development of T lymphocytes**

Section-3 **Positive and negative selection of T cells**

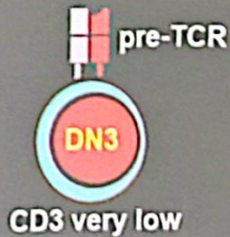
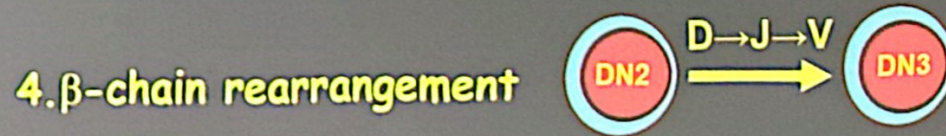
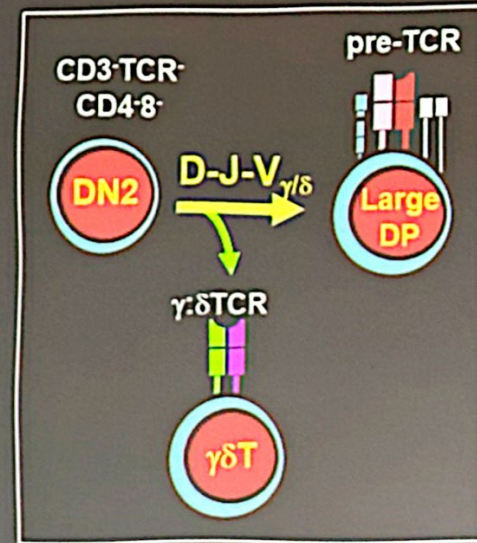


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Development of T lymphocytes



3. $\gamma\delta\text{TC}$ or $\alpha\beta\text{TC}$: a common progenitor \longrightarrow

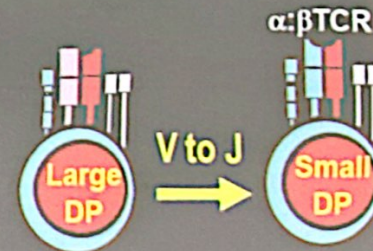


① shuts off β rearrangement on 2nd chromosome

② Ensures only one specificity of TCR expressed per cell

5. DN4: cell proliferation 

6. CD4/8 and α -chain rearrangement



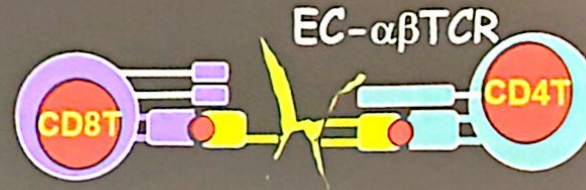
selective
events begin

Development T lymphocytes

7. T cells-Positive selection

① Thymic cortex

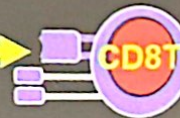
② MHC-restricted:



③ TF: ThPOK →



Runx3 →



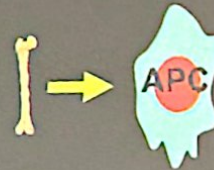
FoxP3 →



8. T cells-negative selection

① Thymocytes: cortex or medulla

② SP T cells : BM-derived APC



③ Central tolerance: Deletion

9. Final T cells maturation: Thymic medulla T cells-S1PR1 ↑ → peripheral

10. T cells peripheral tolerance: ① AICD ② Anegry

11. T cells subset: ① αβT ② γδT, dETCs (γδT) ③ NKT

Peripheral or secondary lymphoid organs

Spleen

Mucosal
Immune System

Lymph
Nodes

B

Ag Specific

T

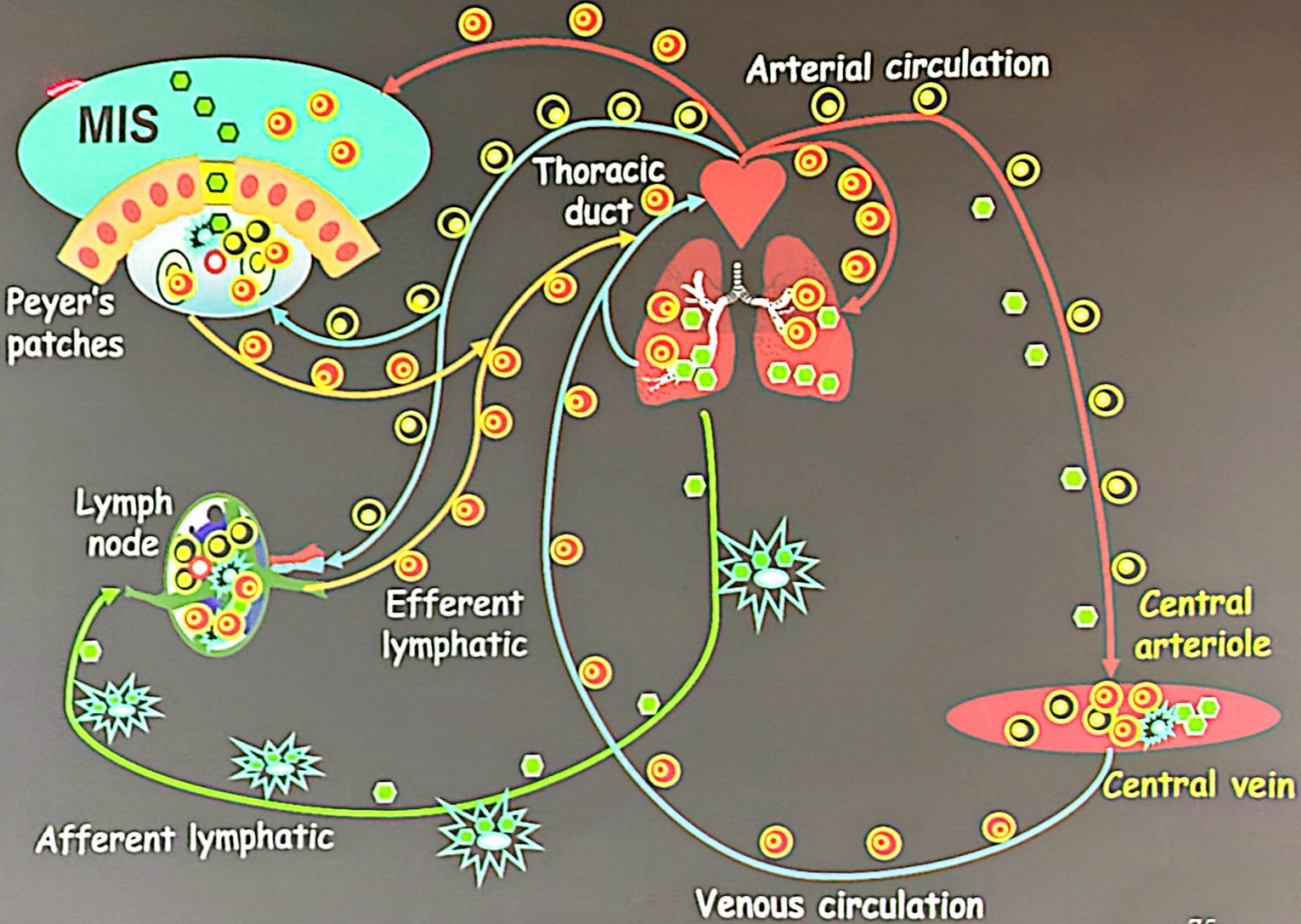
凡是外来的就response

Blood and Lymph circulation

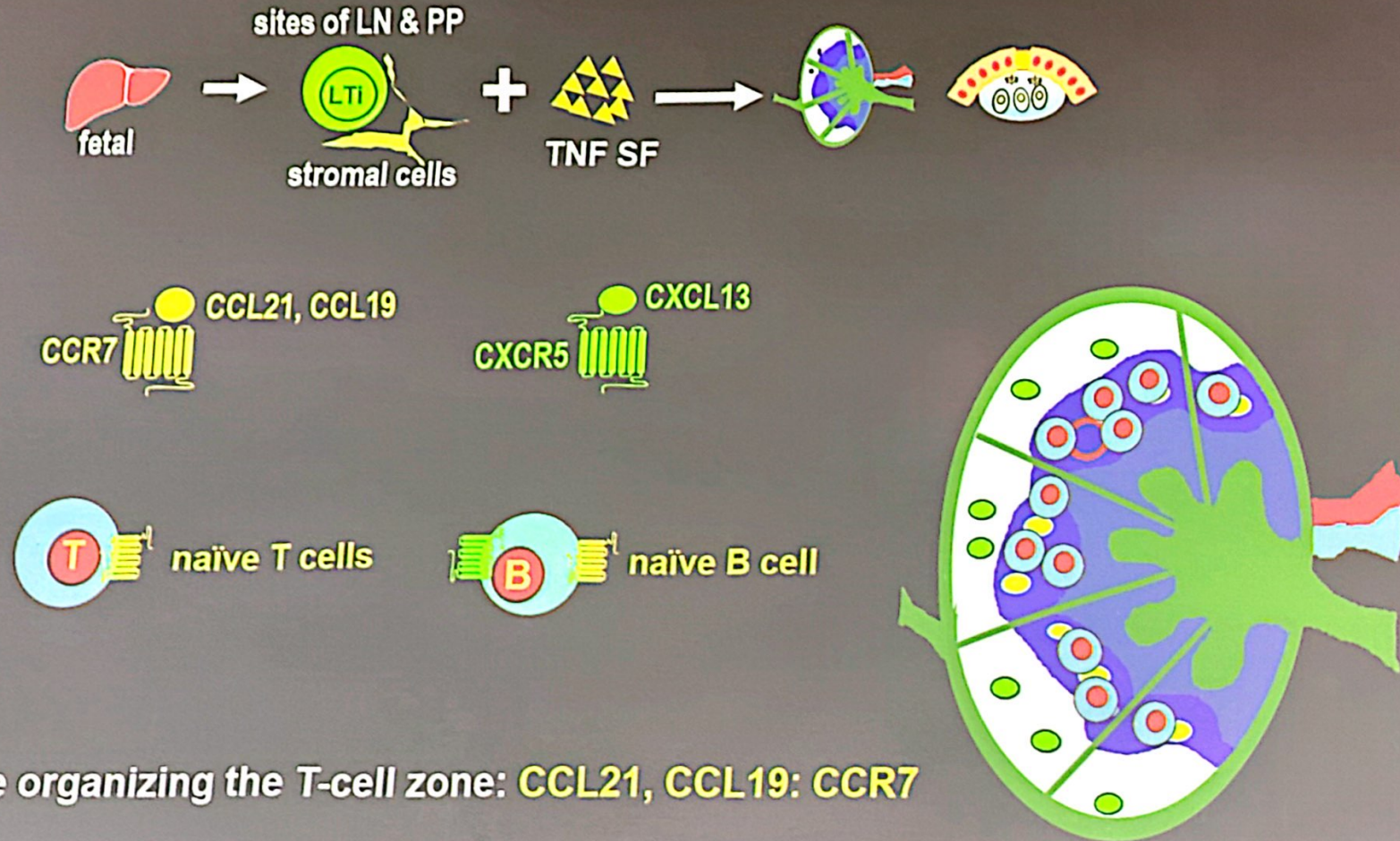
Inflammatory Site

Immune defense, Immune surveillance, Homeostasis

LYMPHOCYTE RECIRCULATION

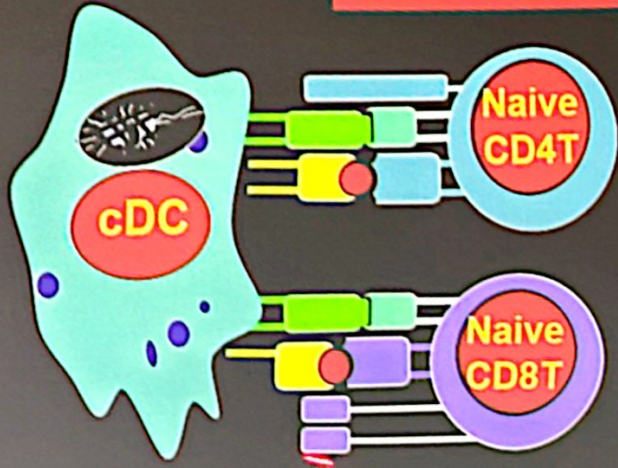


Development and function of secondary lymphoid organs

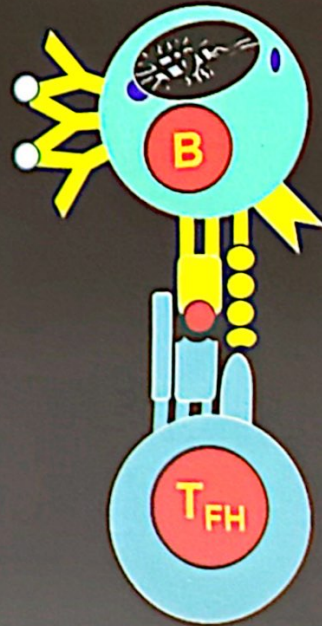


The organizing the T-cell zone: **CCL21, CCL19: CCR7**

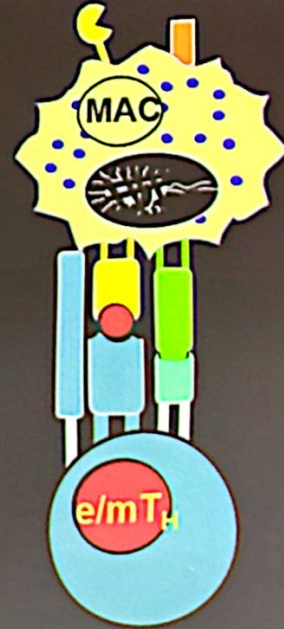
APCs



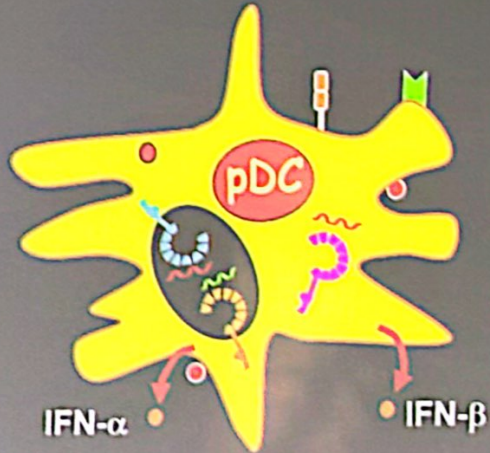
cDC: activation of naïve T cells



B cells are presenting antigens to T_{FH}

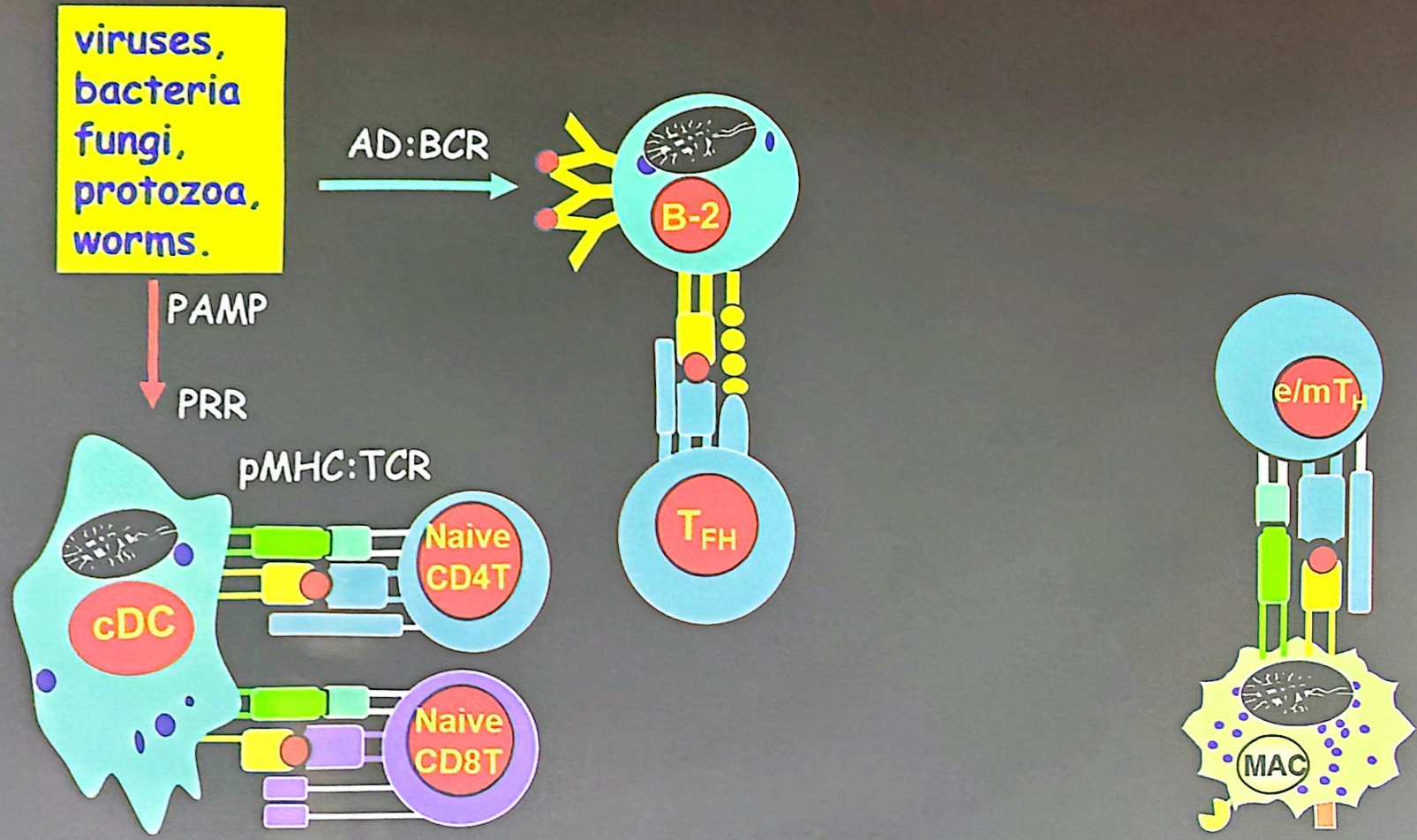


MAC are scavenger cells and is important for the maintenance and functioning of effector or memory T cells.



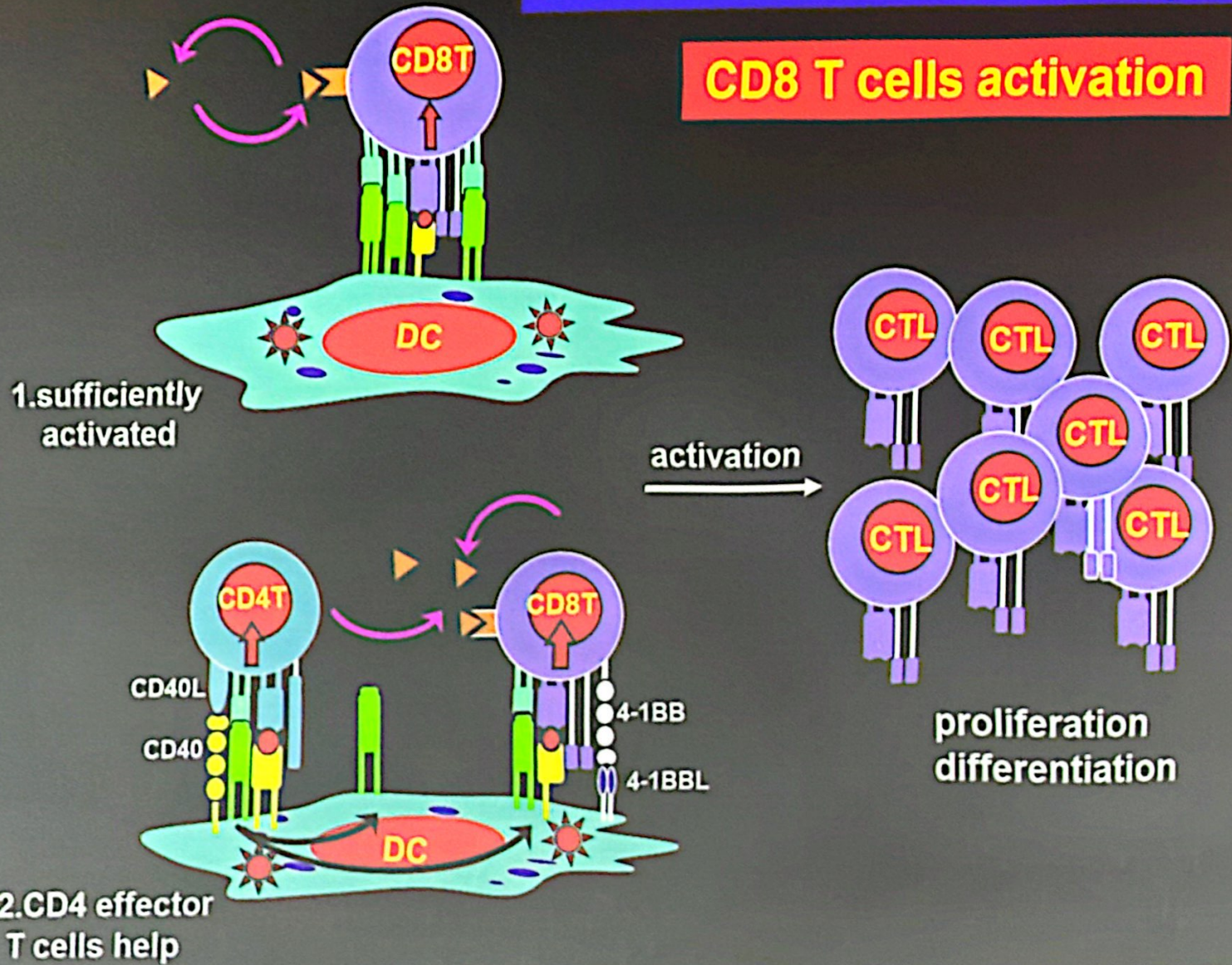
pDC: produce abundant IFN-I and against viral infection

Activation, proliferation and differentiation of T cell



Cell-mediated immune response

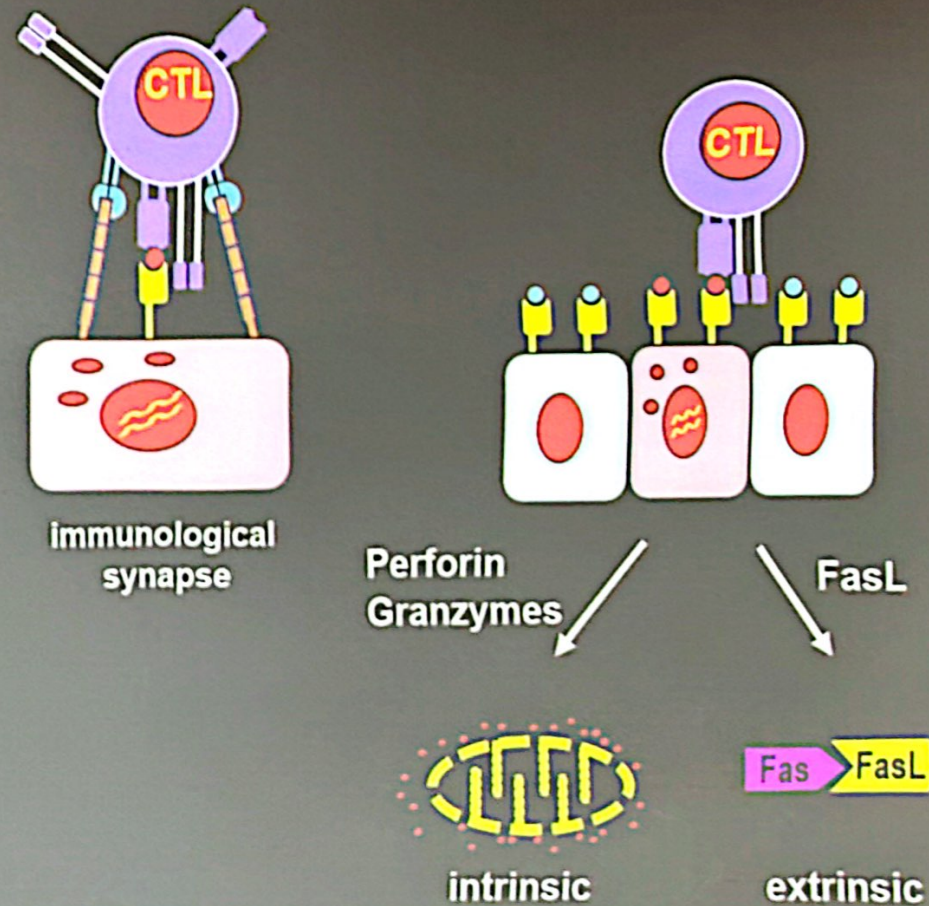
CD8 T cells activation



Three signals of T cells activation, proliferation and differentiation⁷⁹

Cell-mediated immune response

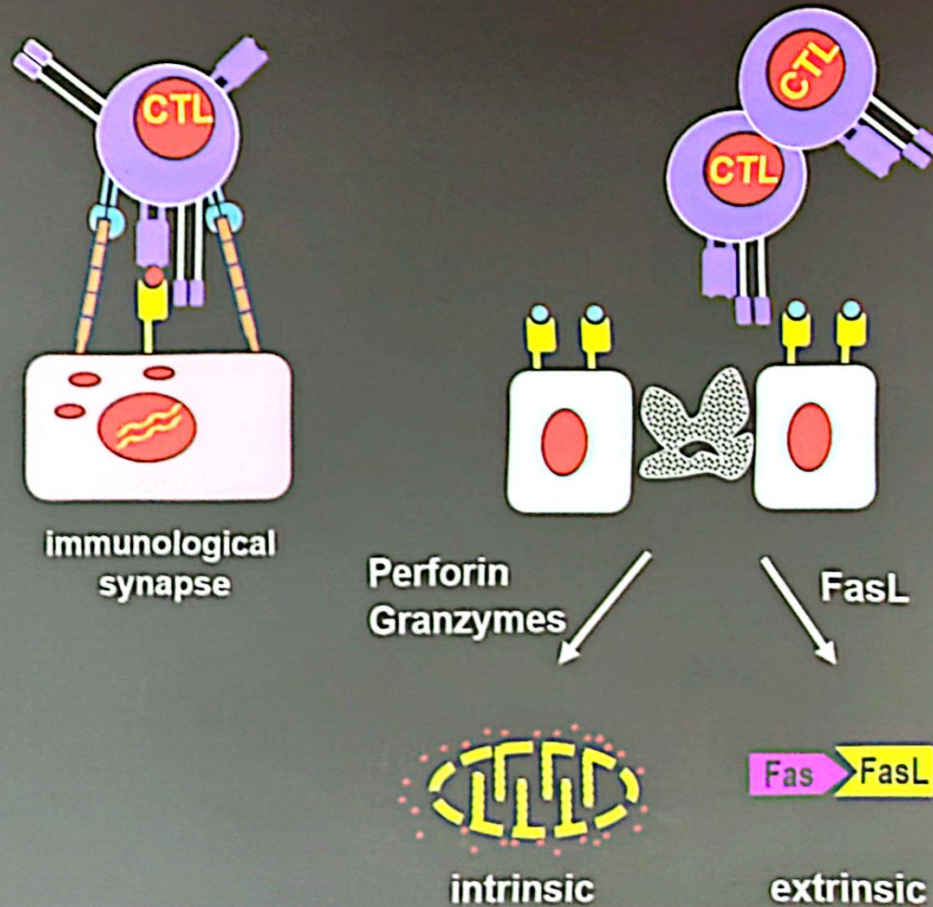
CD8 T cells function



Effector CD8 T cells can respond to their target cells without co-stimulation

Cell-mediated immune response

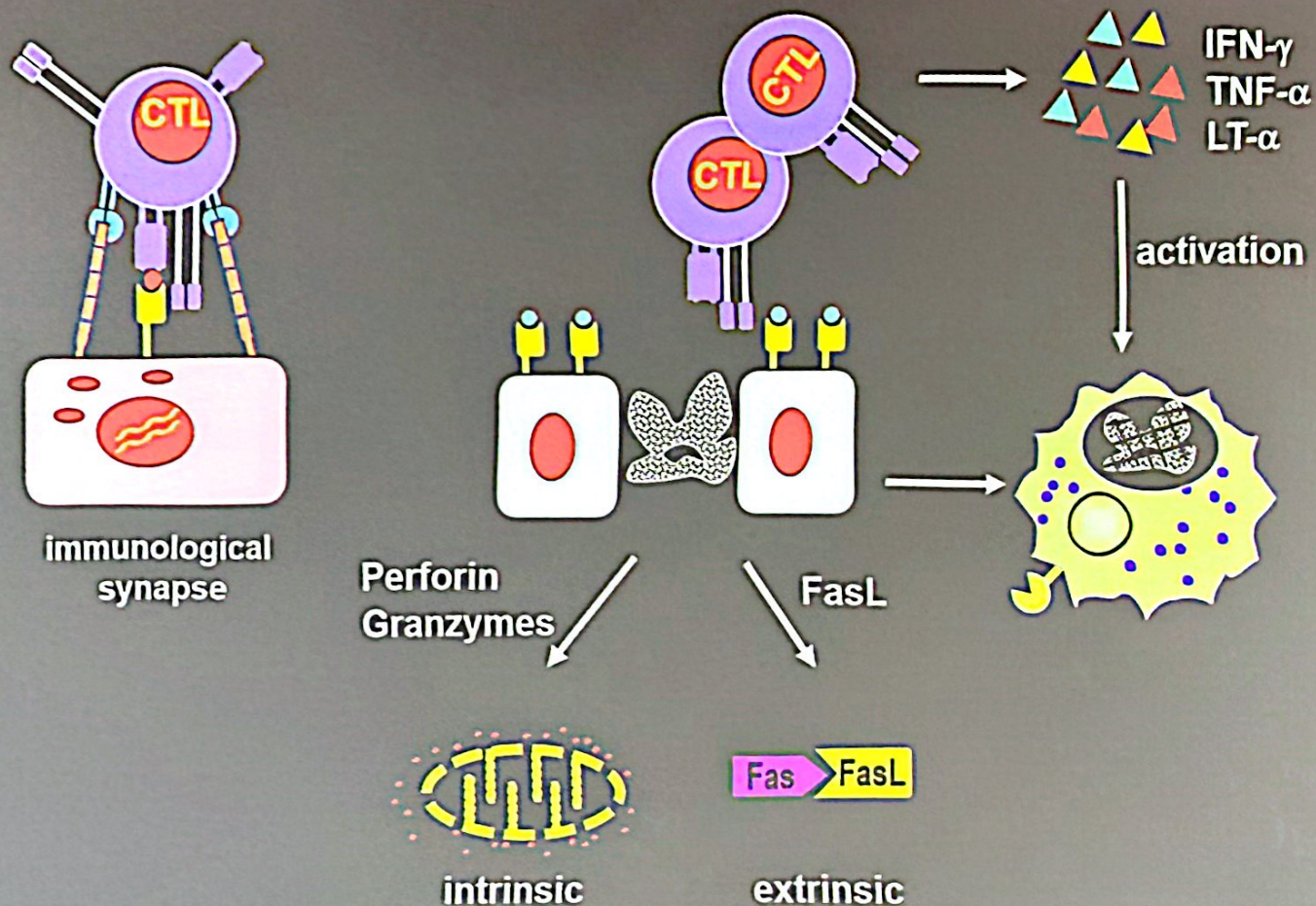
CD8 T cells function



Effector CD8 T cells can respond to their target cells without co-stimulation

Cell-mediated immune response

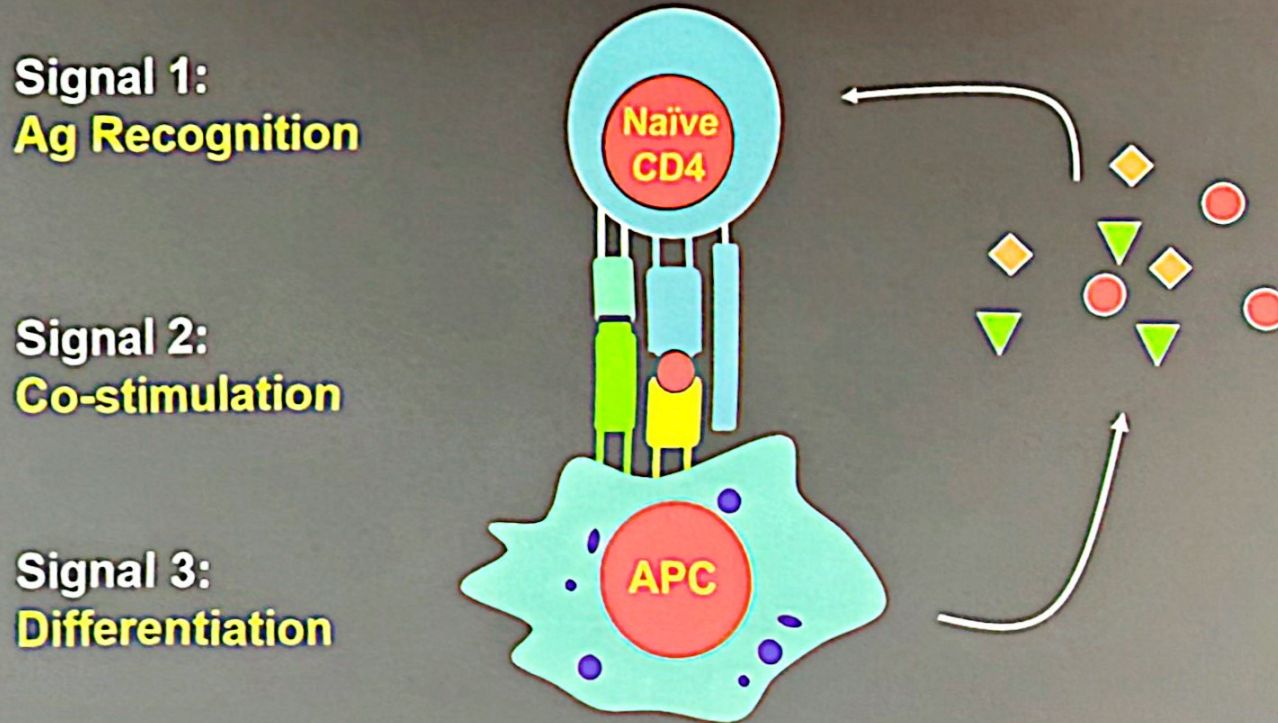
CD8 T cells function



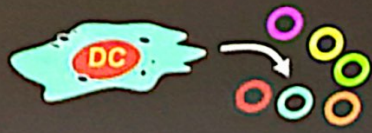
Effector CD8 T cells can respond to their target cells without co-stimulation

Cell-mediated immune response

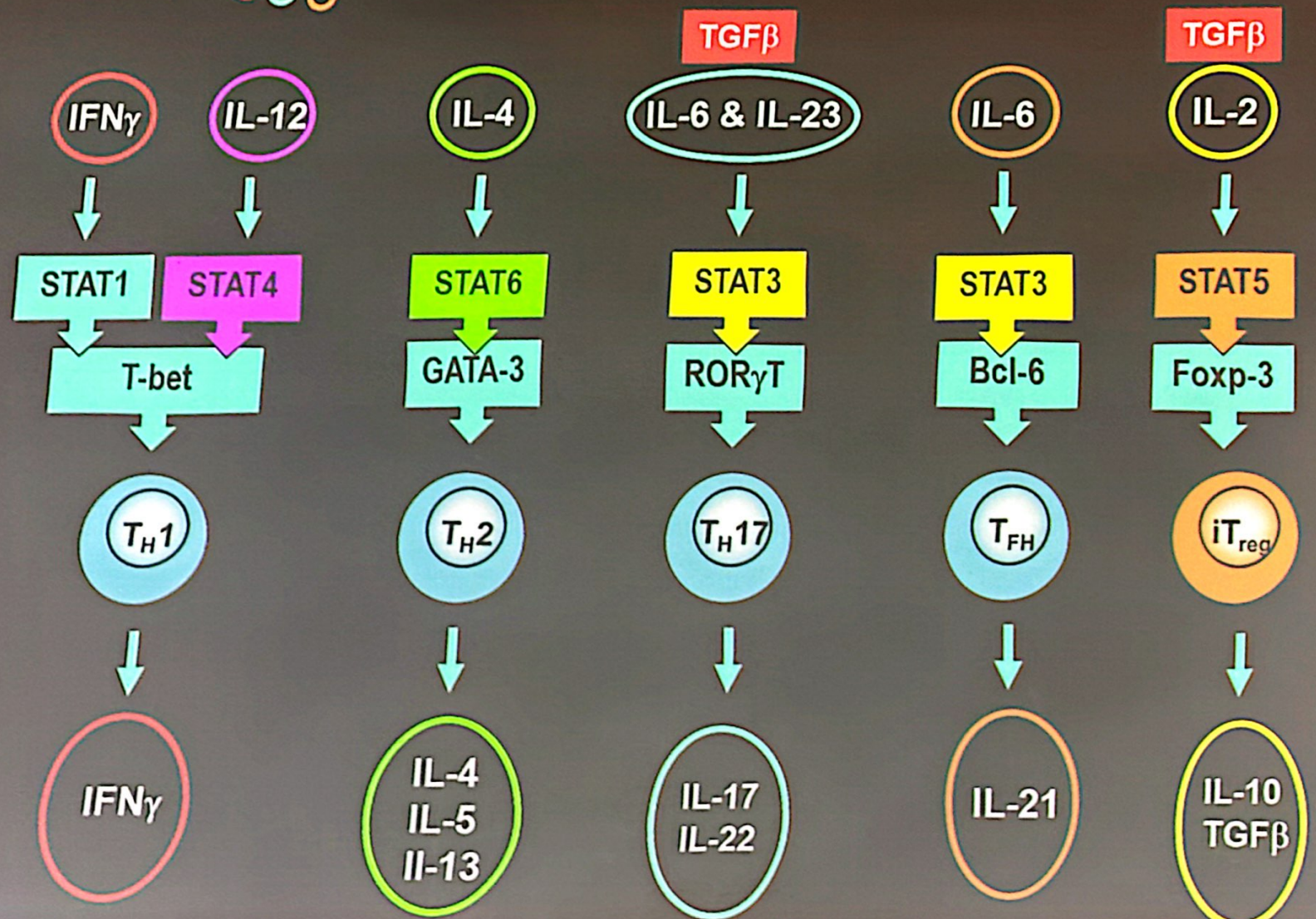
CD4 T cells activation



Three signals of T cells activation, proliferation and differentiation

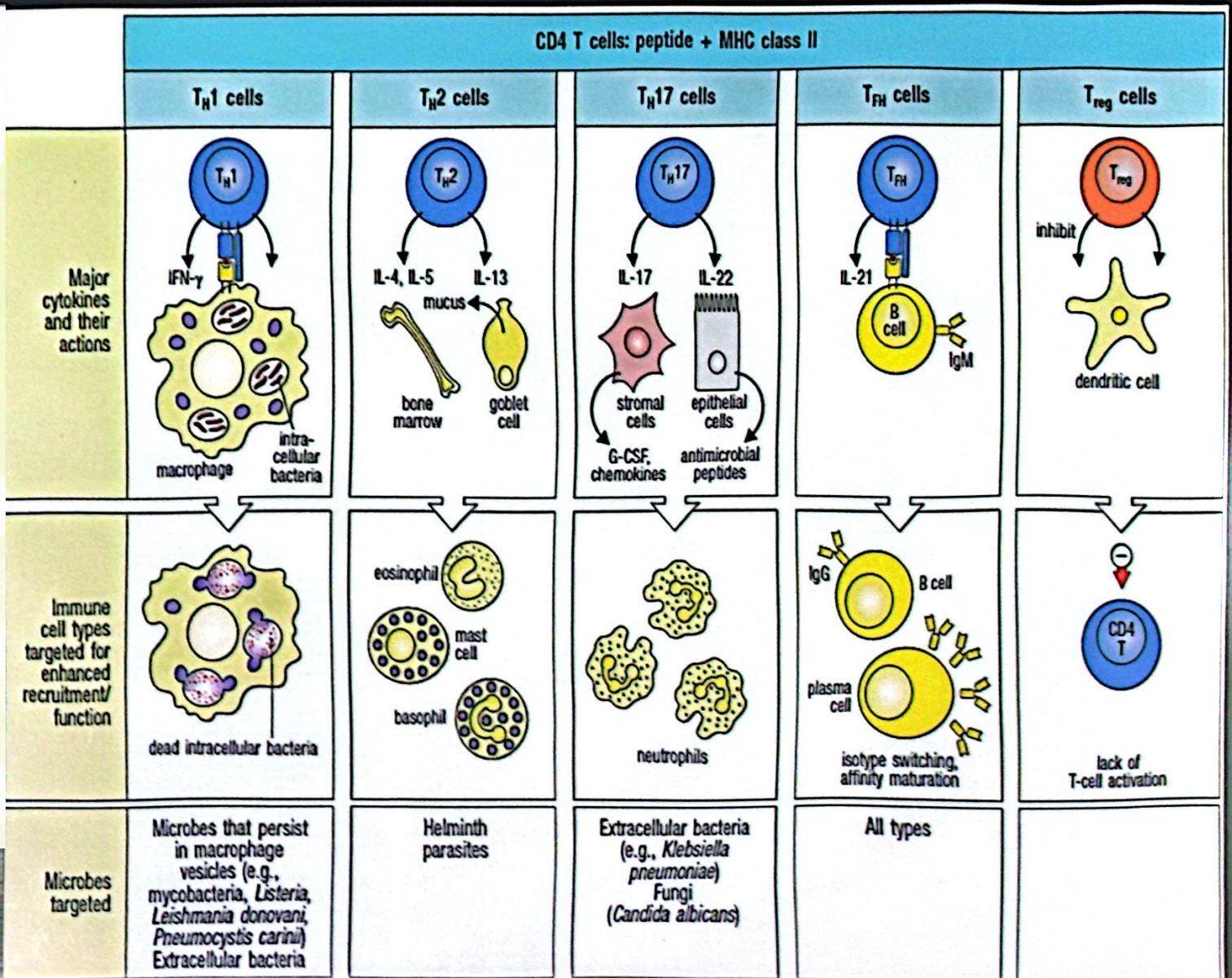


CD4 T cell differentiation



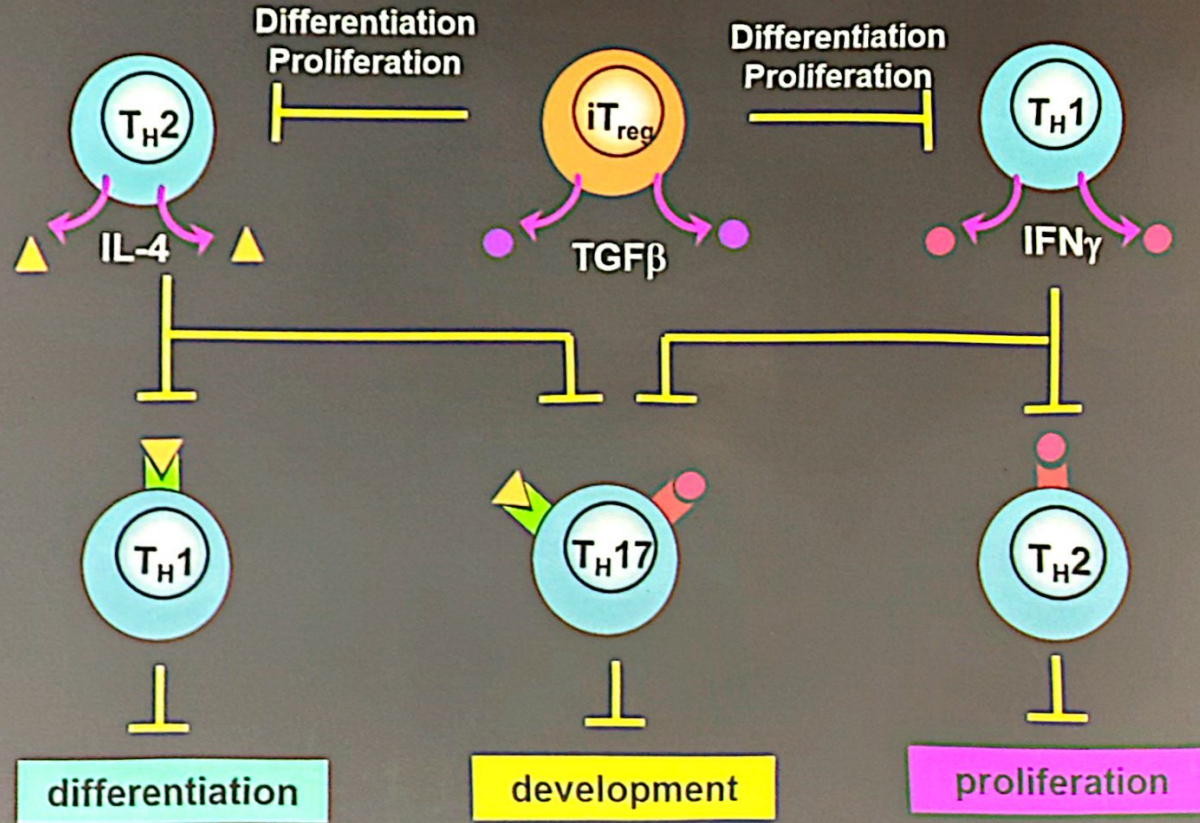
Cell-mediated immune response

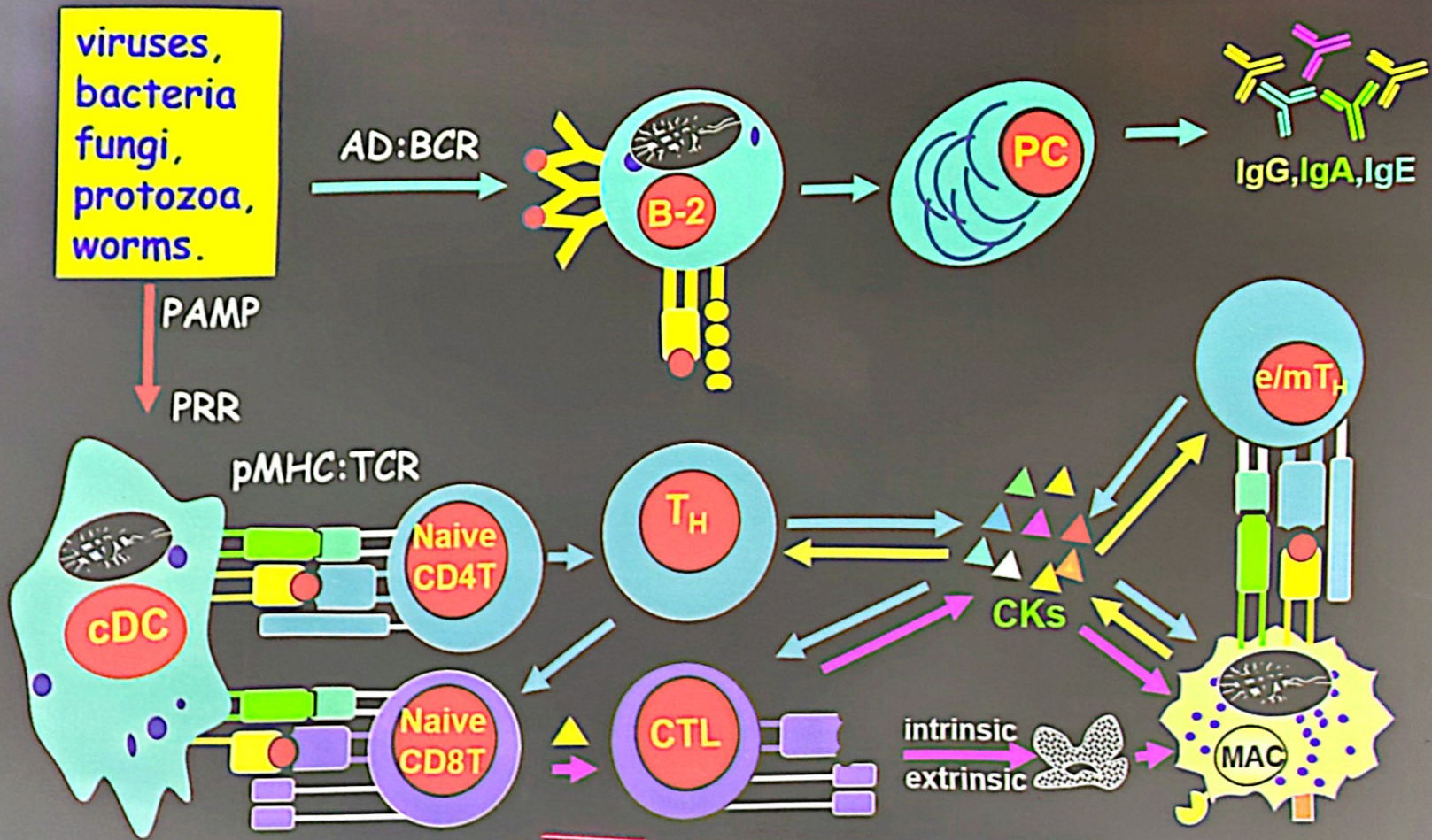
CD4 T cell function



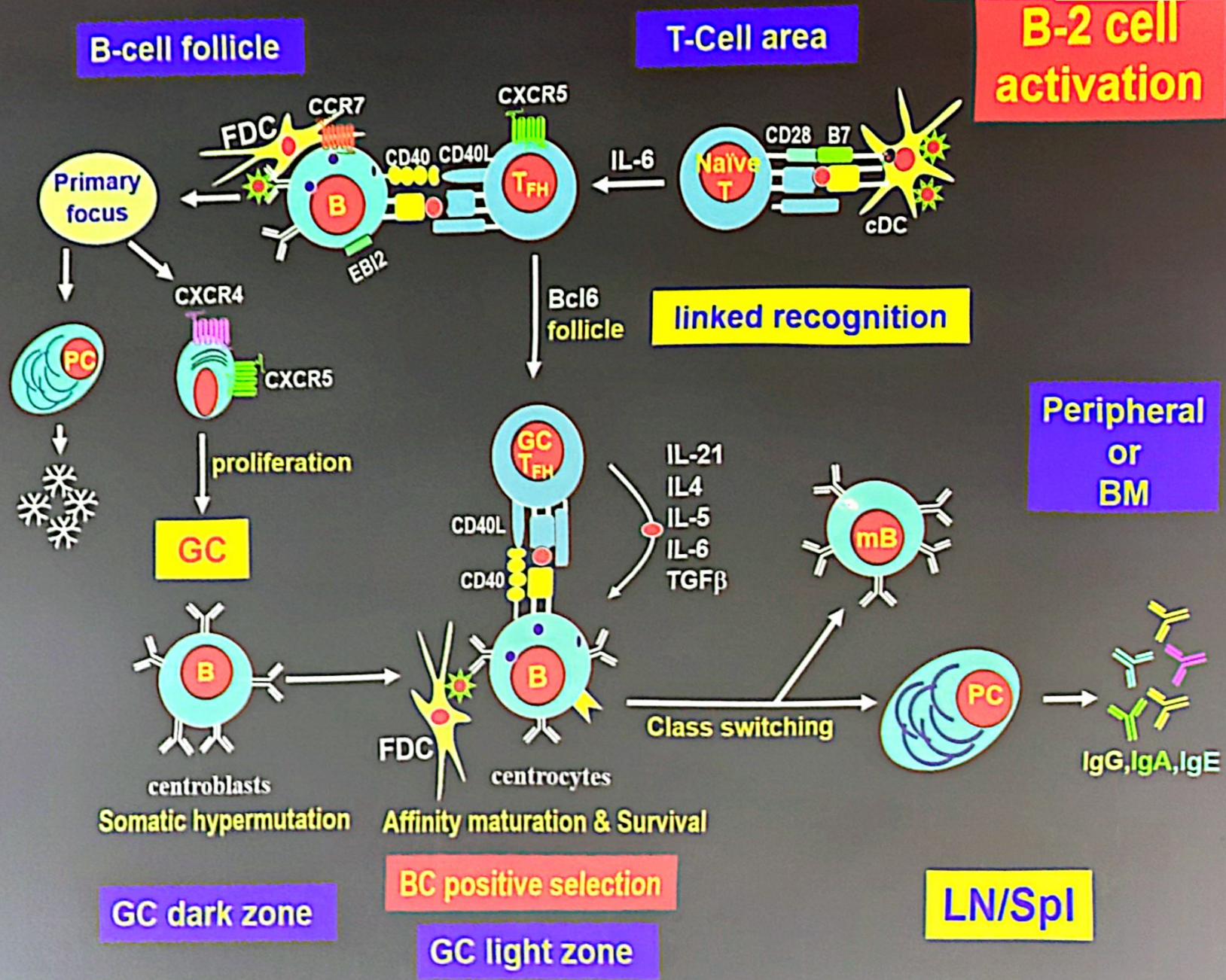
Cell-mediated immune response

CD4 T cell regulation





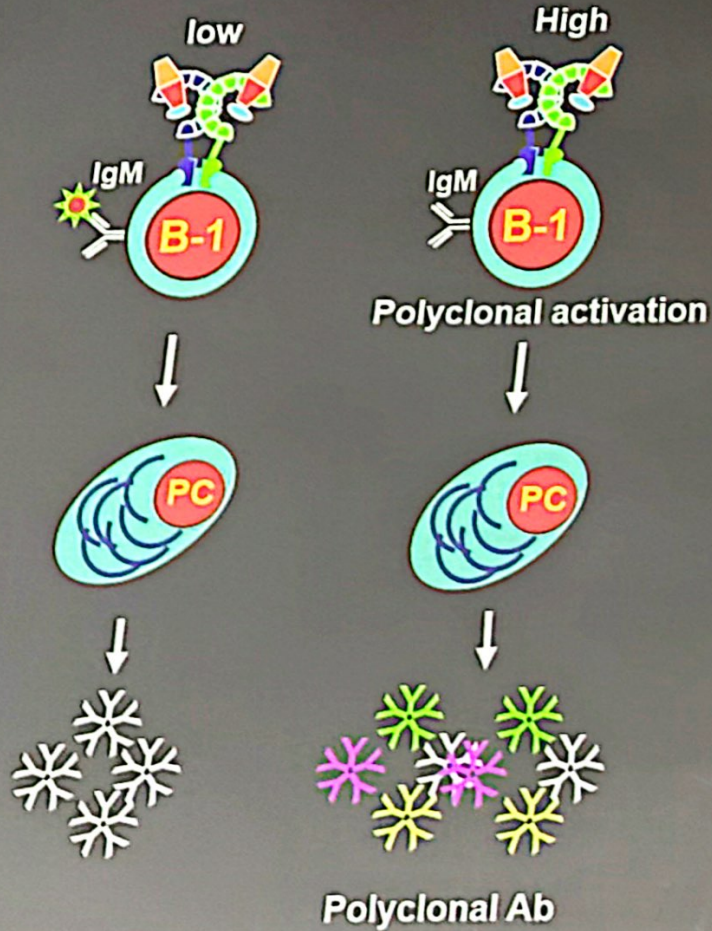
Cell-mediated immune response



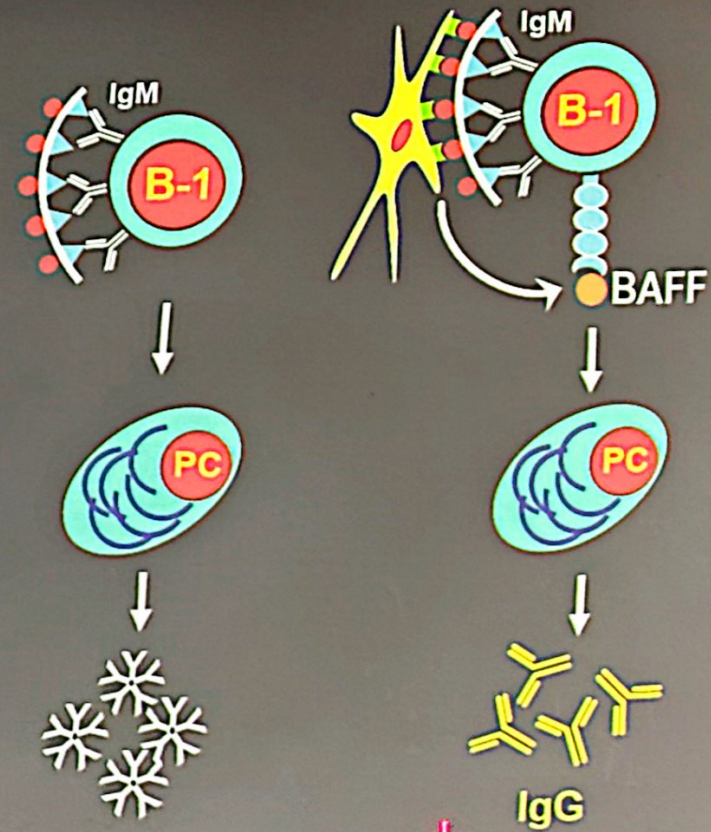
Humoral immune responses

B-1 cells activation

TI-1 Antigen

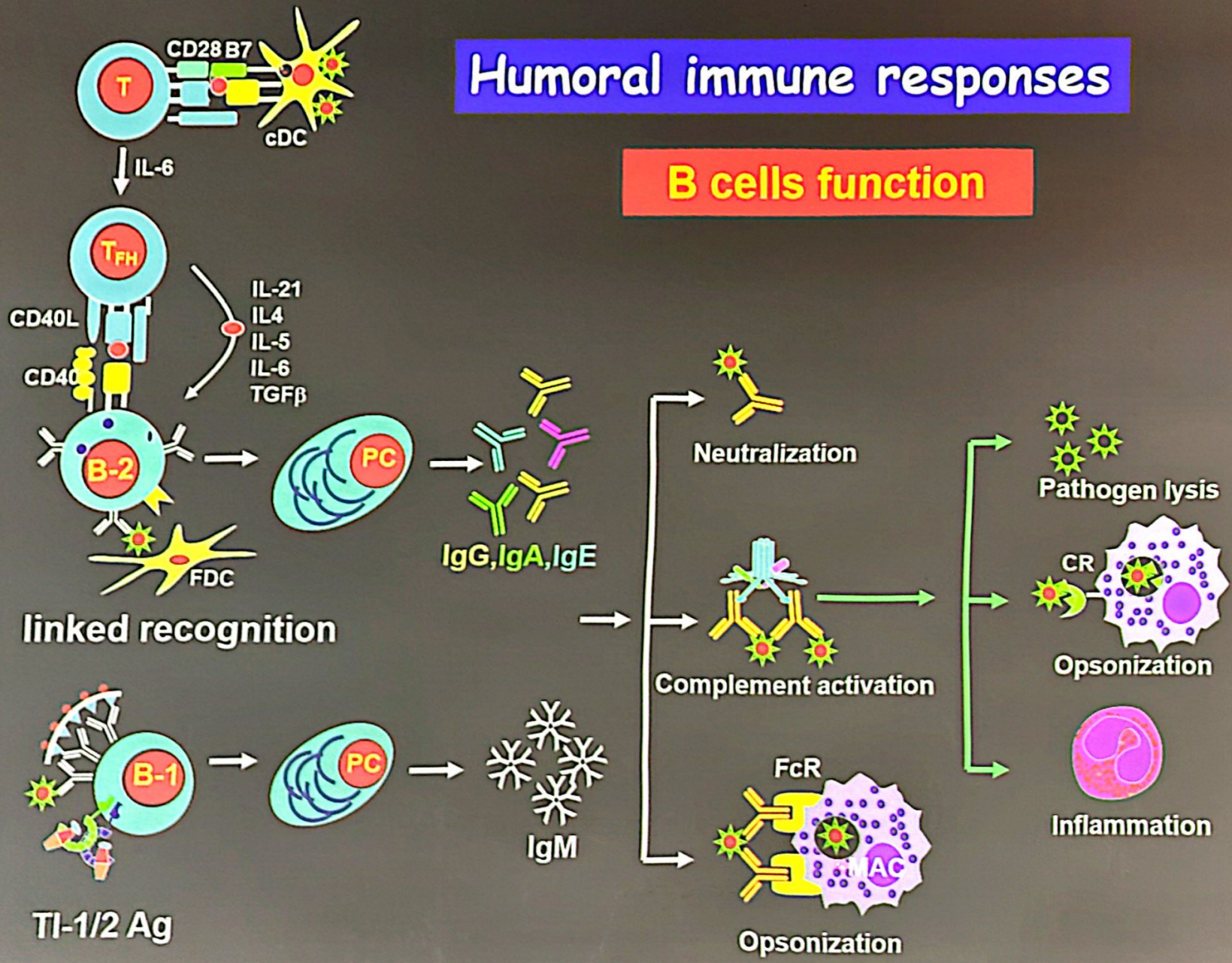


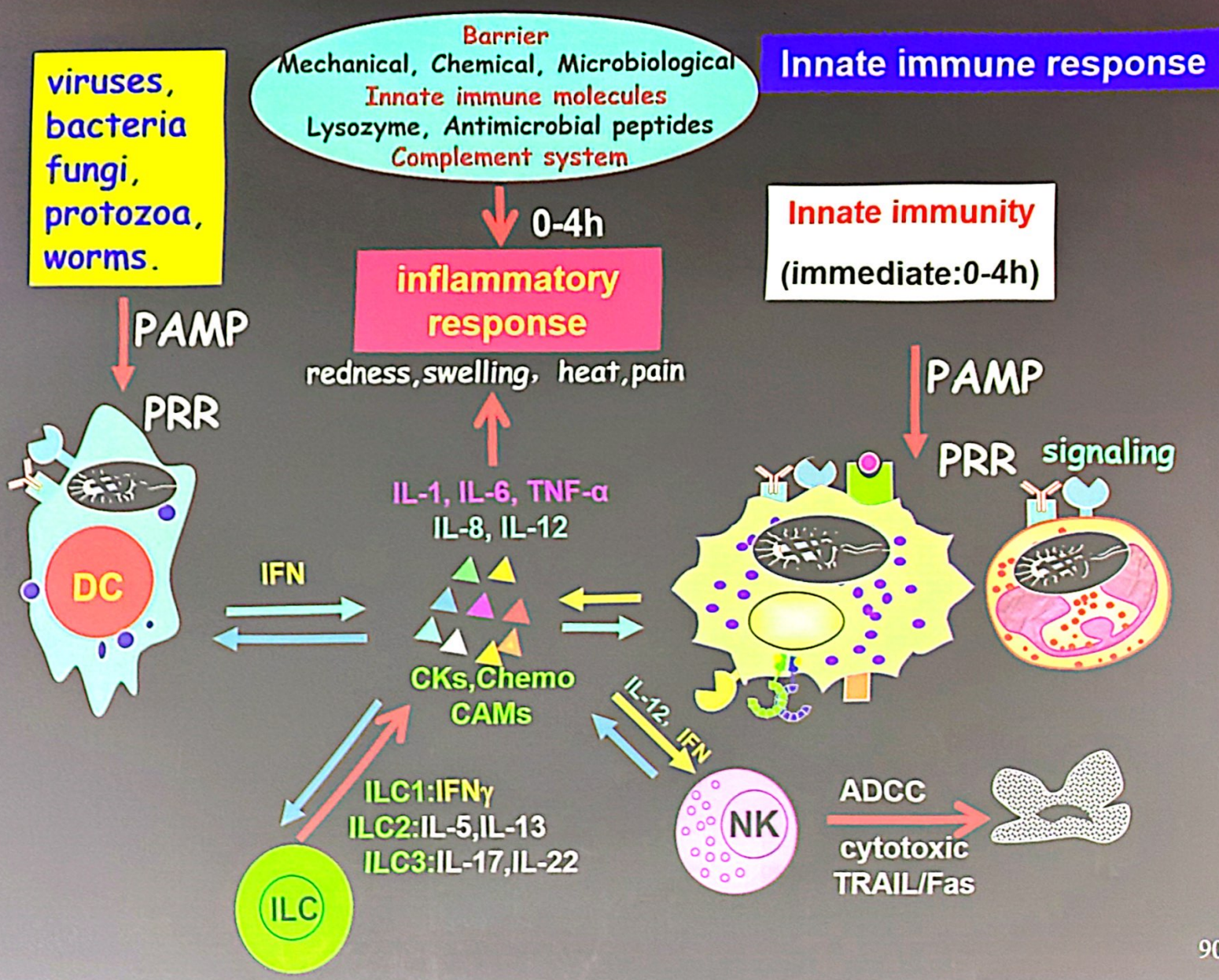
TI-2 Antigen



Humoral immune responses

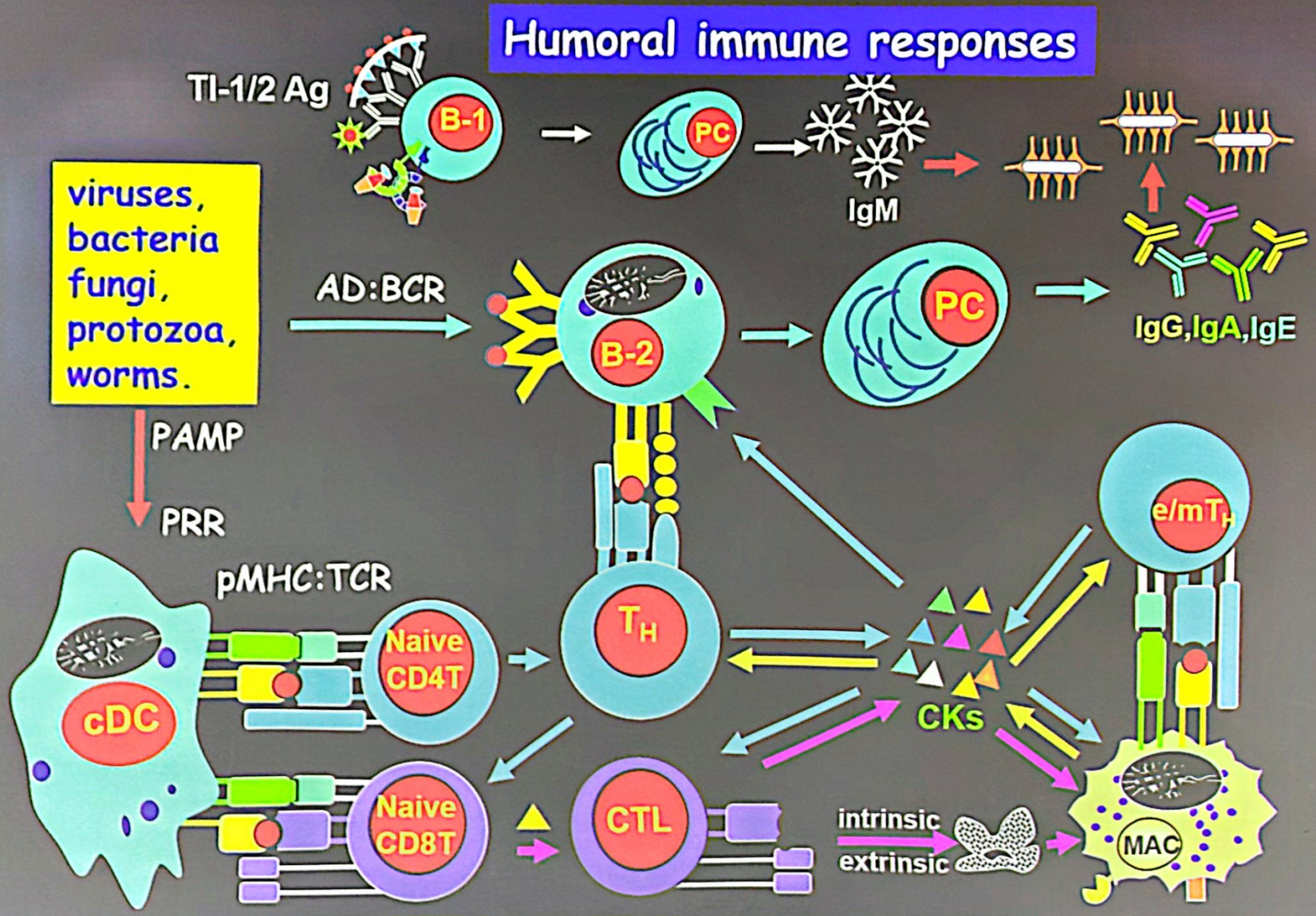
B cells function





Humoral immune responses

viruses,
bacteria
fungi,
protozoa,
worms.



Cell-mediated immune response

A scenic view of a fjord with steep, snow-capped mountains and a small boat on the water. The text "The End" is overlaid in a large, bold, orange font.

The End

2024-12-29