Паттерн-распознающие рецепторы, их влияние на формирование адаптивного иммунитета

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План доклада:

1. Актуальность выбранной темы

2. Цель и задачи доклада

3. Строение и классификация паттерн-распознающих рецепторов
4. Формирование адаптивного иммунитета под влиянием паттерн-распознающих рецепторов
   4.1. Индукция процессинга АГ
   4.2. Презентация АГ
   4.3. Т-клеточные реакции

5.Заключение

Актуальность темы:

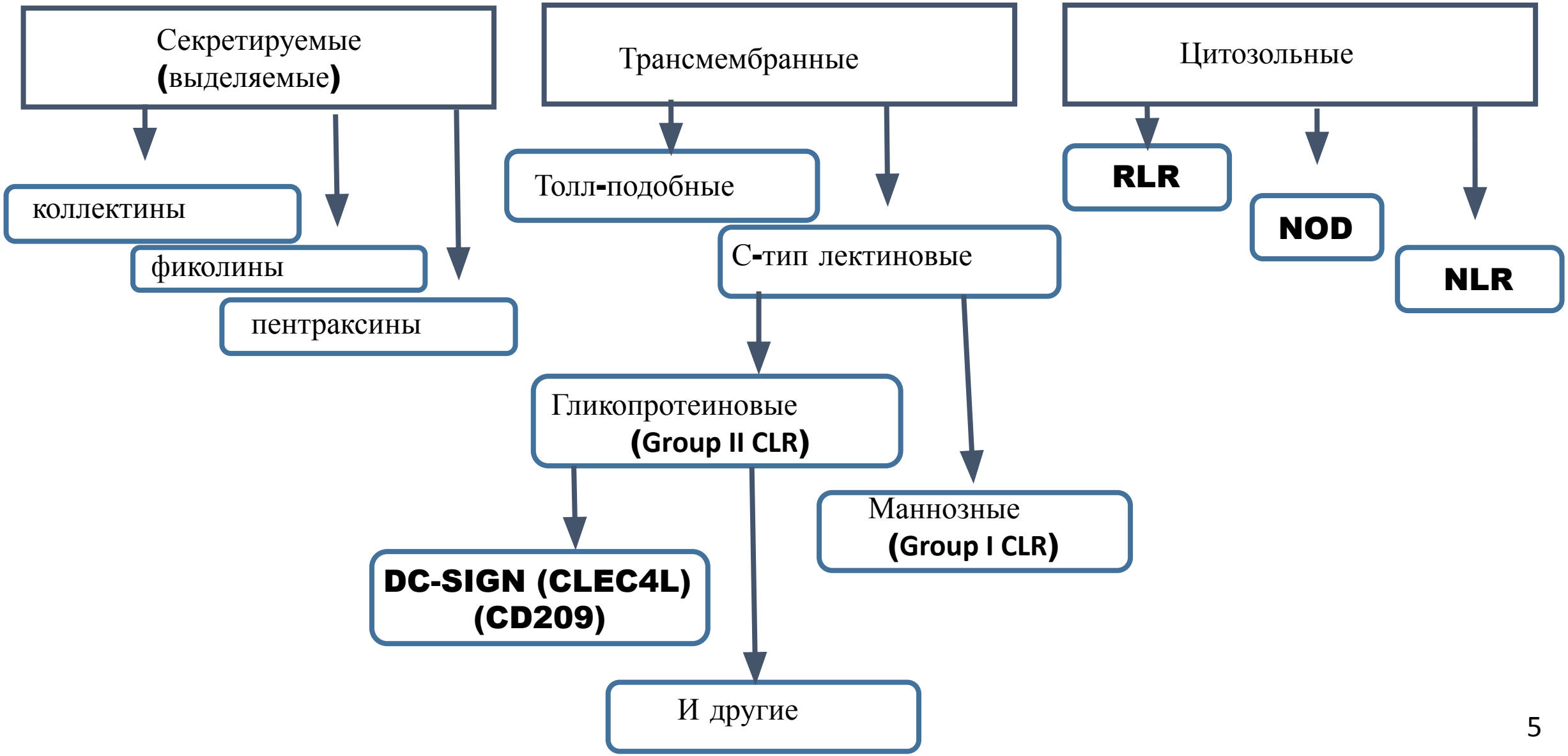
паттерн-распознающие рецепторы играют ключевую роль в функционировании иммунной системы человека, в частности
в инициации механизмов адаптивного (приобретённого) иммунитета

Цель: определить роль паттерн-распознающих рецепторов в формировании адаптивного иммунитета

Задачи:

1. Рассмотреть участие паттерн-распознающих рецепторов в реакциях адаптивного иммунитета на примере взаимодействия с:
   1.1. Бактериальными АГ
   1.2. Вирусными АГ

Классификация паттерн-распознающих рецепторов **(PRR)**



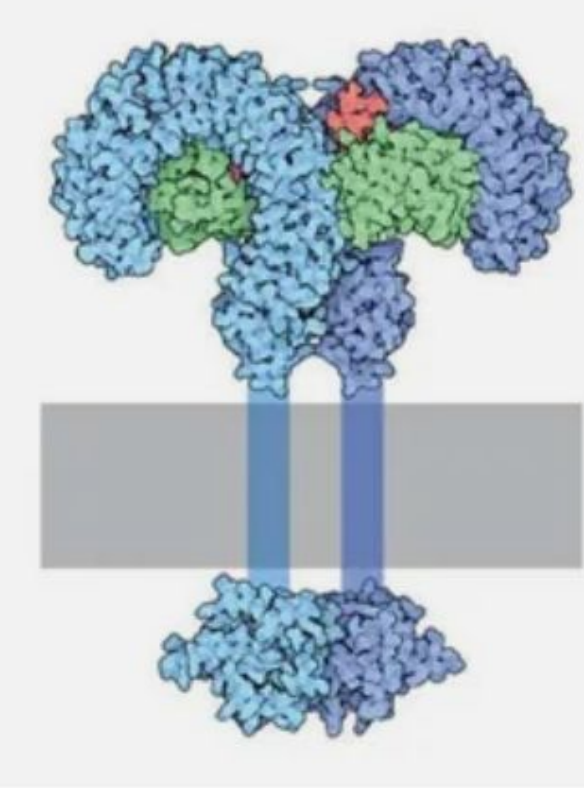
Влияние паттерн-распознающих рецепторов на адаптивный иммунитет

PRR	Ligands recognized	Microbes recognized	Adaptive response induced	References
Transmembrane PRRs				
TLRs	Bacterial cell wall components, viral nucleic acids in endosomes, etc.	Gram-positive and Gram-negative bacteria, DNA and RNA viruses, fungi, protozoa	Sufficient to induce Th1, antibody (particularly IgG2), and $CD8^+$ T-cell responses	(Reviewed in 8, 20)
Dectin-1	Fungal cell wall components, β-glucan	Fungi	Sufficient to induce Th17 and antibody responses	(31, 32)
Cytosolic PRRs				
Nod1, Nod2	Cytosolic bacterial cell wall components, peptidoglycans	Intracellular bacteria	Sufficient to induce Th2 and antibody responses; potentiates Th1, Th2, Th17, and antibody responses initiated by TLR; may favor Th17 responses	(48, 50)
NALP3	Potassium efflux, LPS plus ATP, pore-forming toxins, bacterial secretion systems	Pathogenic bacteria	Required for robust T cell-dependent hypersensitivity; may potentiate Th2 driven antibody responses	(53–58)
ISD sensor	Cytosolic DNA	DNA viruses, retroviruses	Sufficient to induce $CD4^+$ T-cell and antibody responses (in hematopoietic cells); sufficient to induce $CD8^+$ T-cell responses (in non-hematopoietic cells)	(64)
RIG-I/MDA5	Cytosolic RNA	RNA viruses	Sufficient to induce $CD8^+$ T-cell responses; insufficient to induce $CD4^+$ T-cell and antibody responses	(69)

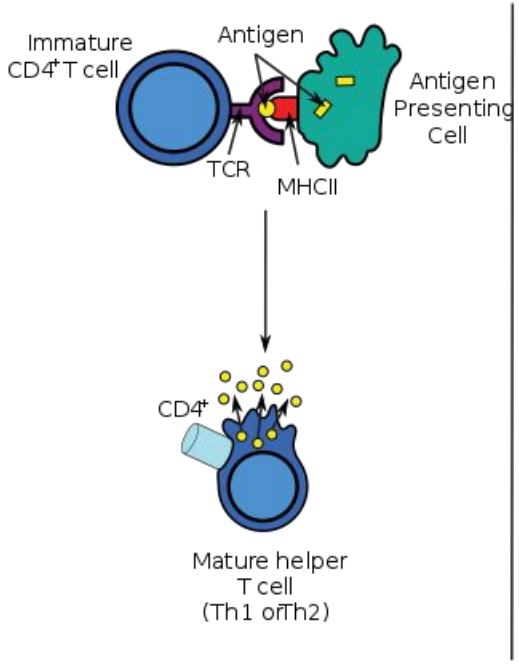
PRRs, pattern recognition receptors; TLR, Toll-like receptor; Nod, nucleotide-binding oligomerization domain; NALP3, Nacht domain-, LRR-, and PYD-containing protein 3; ISD, interferon stimulatory DNA; RIG-I, retinoic acid-inducible gene I; MDA5, melanoma differentiation-associated gene 5; LPS, lipopolysaccharide; ATP, adenosine triphosphate; Th, T-helper; IgG2, immunoglobulin G2.

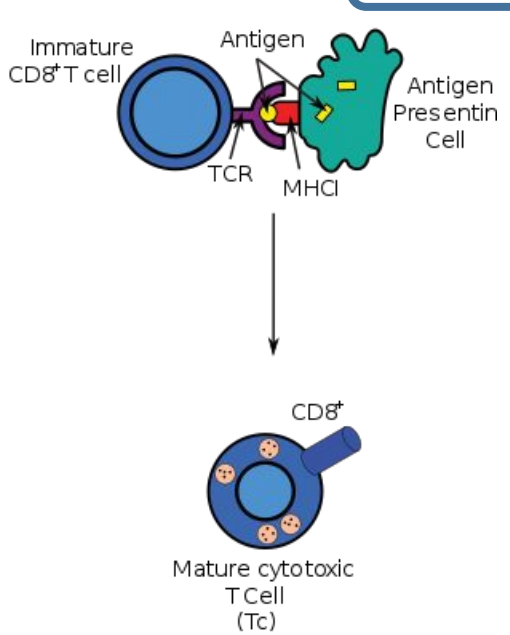
Стимуляция адаптивного иммунитета на примере **TLR**

Toll-подобные рецепторы → Активация эффекторов адаптивного иммунитета → Ответ

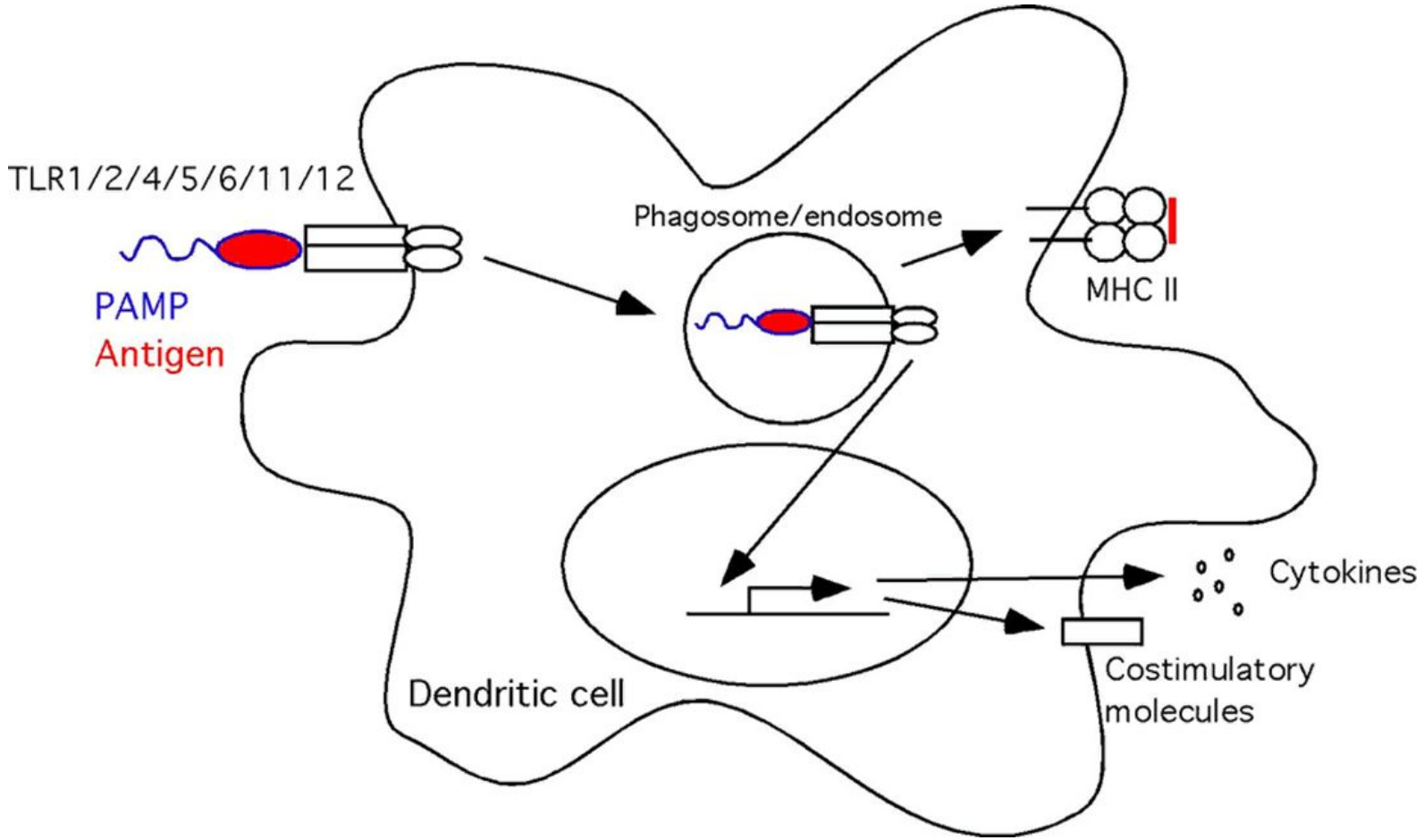


- Ответ
  - T helper (Th)1
  - Th17 CD4+ T cell
  - CD8+ T cell

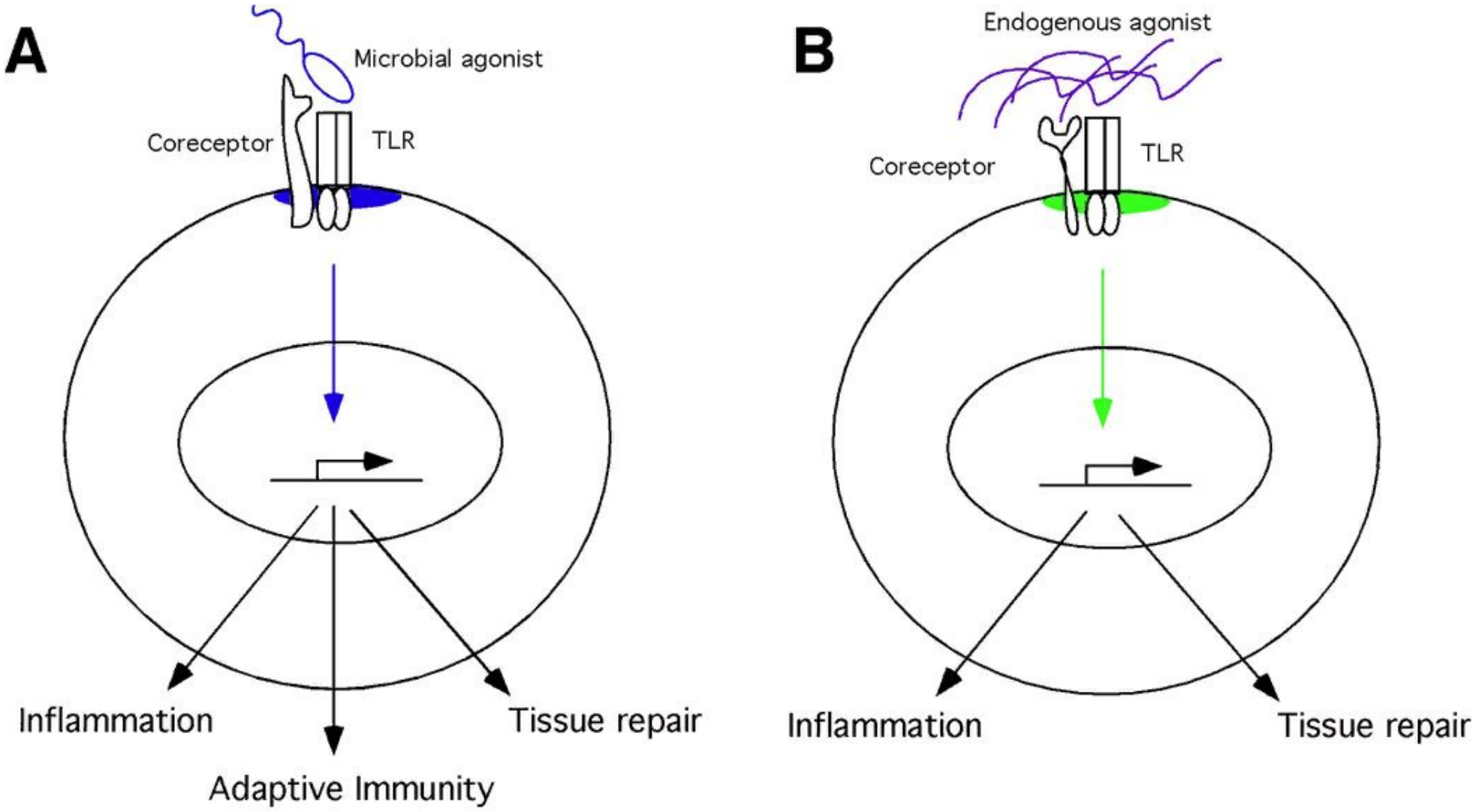




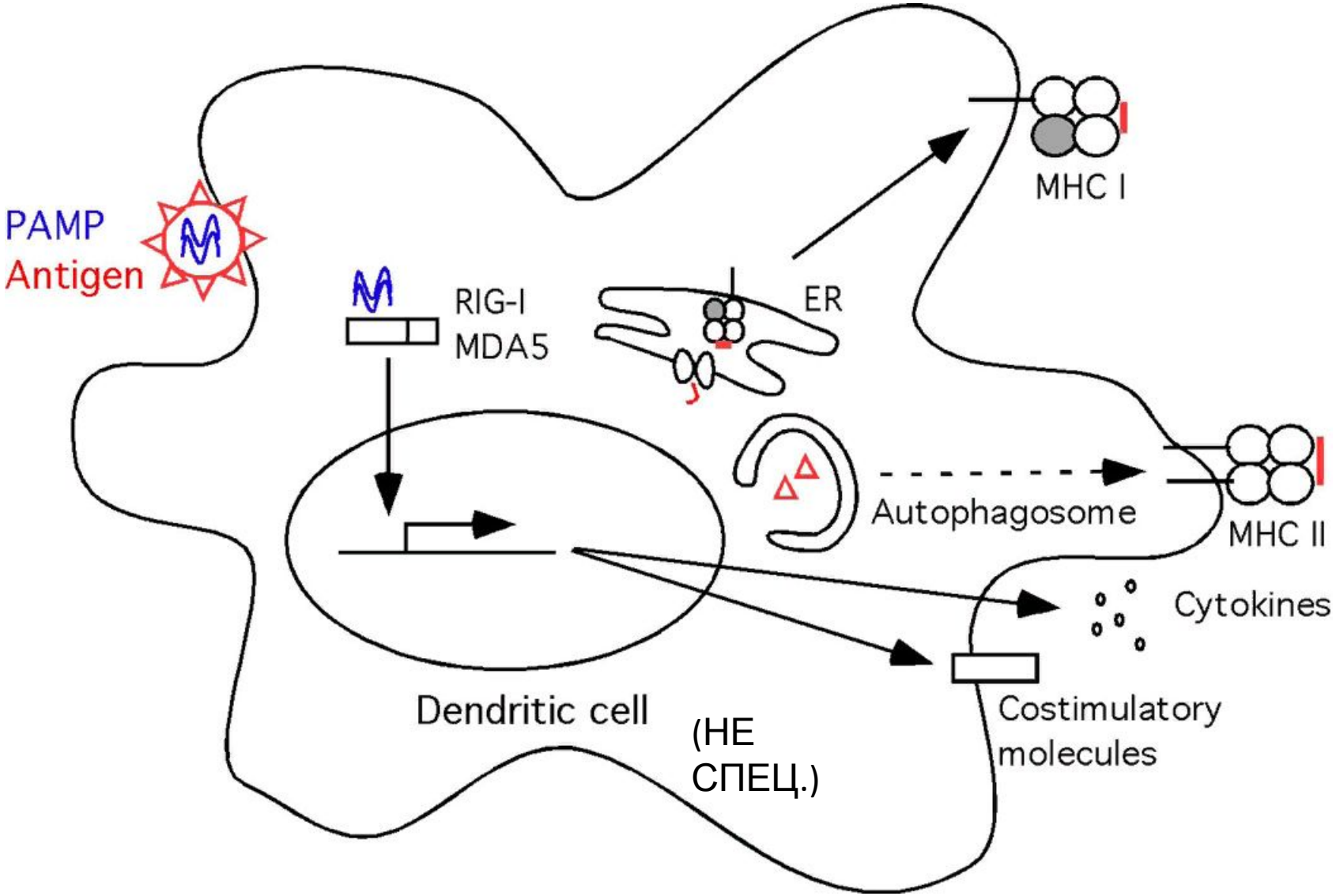
Взаимодействие **TLR** с бактериальными АГ



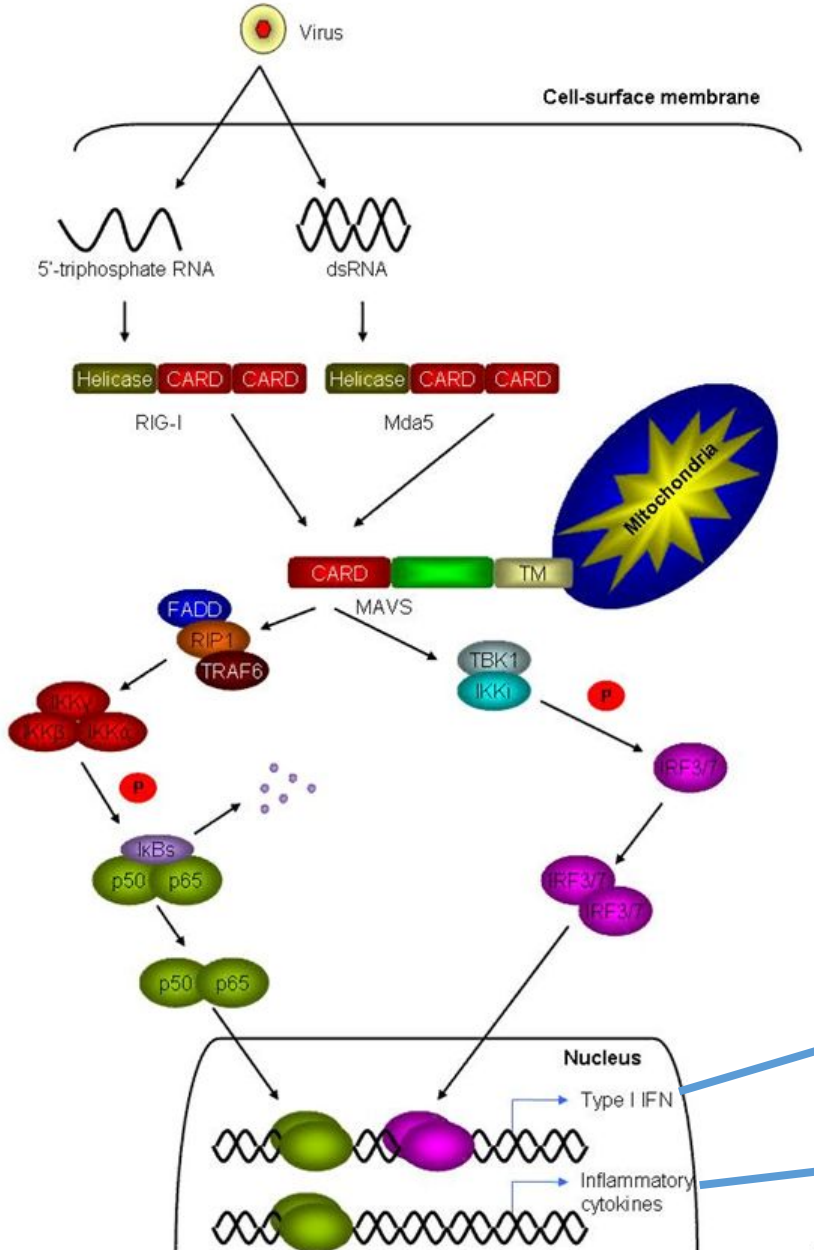
Исходы взаимодействия **TLR** с экзо- и эндо- АГ



Стимуляция адаптивного иммунитета на примере **RLR**



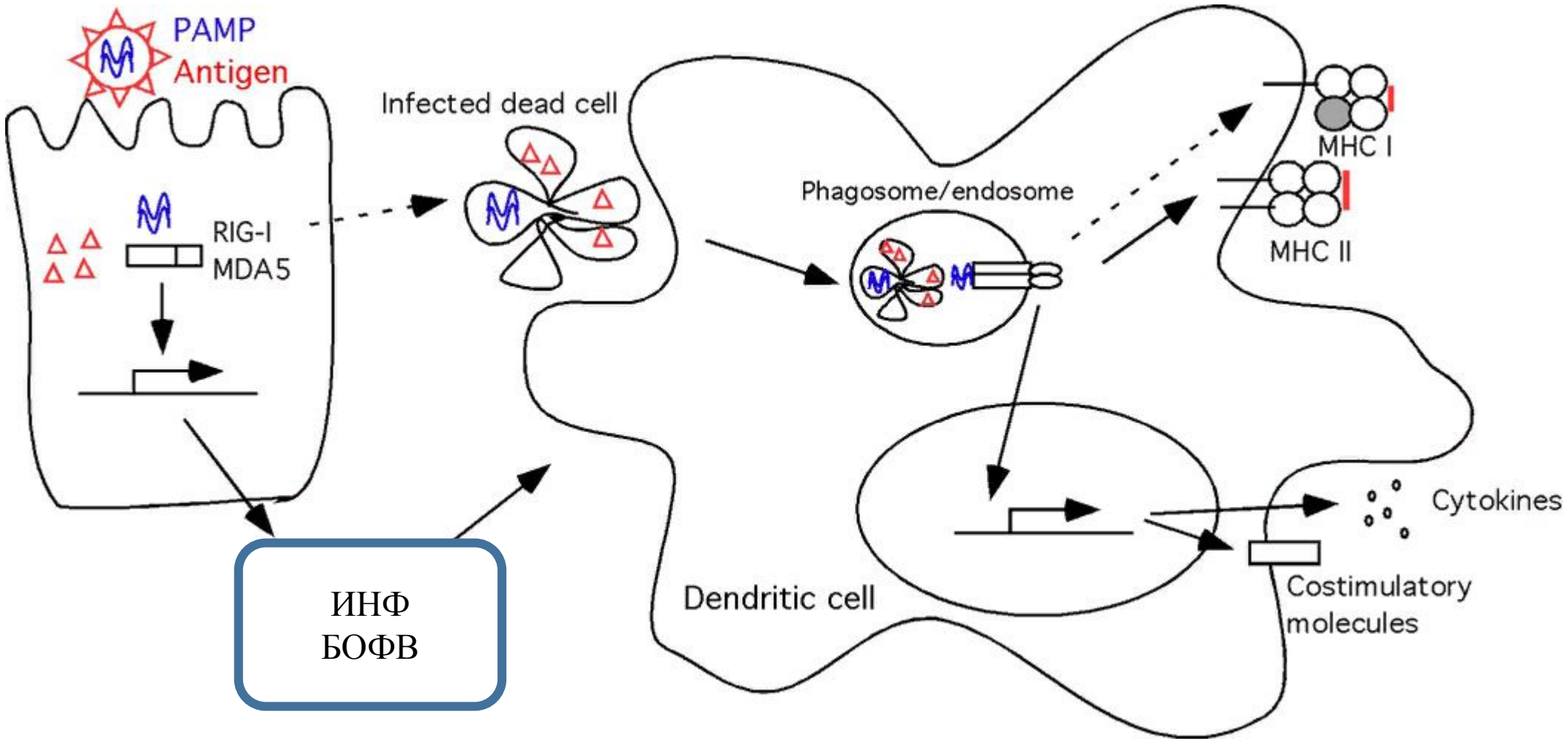
Каскад БХ превращений, запущенный **RIG-I** рецептором



ИНФ

Белки острой фазы воспаления

Исход действия **RLR**



Заключение:

1. Участие паттерн-распознающих рецепторов в формировании адаптивного иммунитета бесспорно

2. По средствам паттерн-распознающих рецепторов осуществляется взаимодействие врождённого иммунитета и приобретённого

3. Паттерн-распознающие рецепторы действуют как механизмы выбора в активации иммунных реакций

4. Механизмы активации разных паттерн-распознающих рецепторов зависят от типа антигена

Список литературы:

1. **Palm N. W., Medzhitov R. Pattern recognition receptors and control of adaptive immunity. Immunol Rev. 2009; 227 (1): 221-233.**

2.Iwasaki A., Medzhitov R. Regulation of adaptive immunity by the innate immune system. Science 2010; 327 (5963): 291-295.

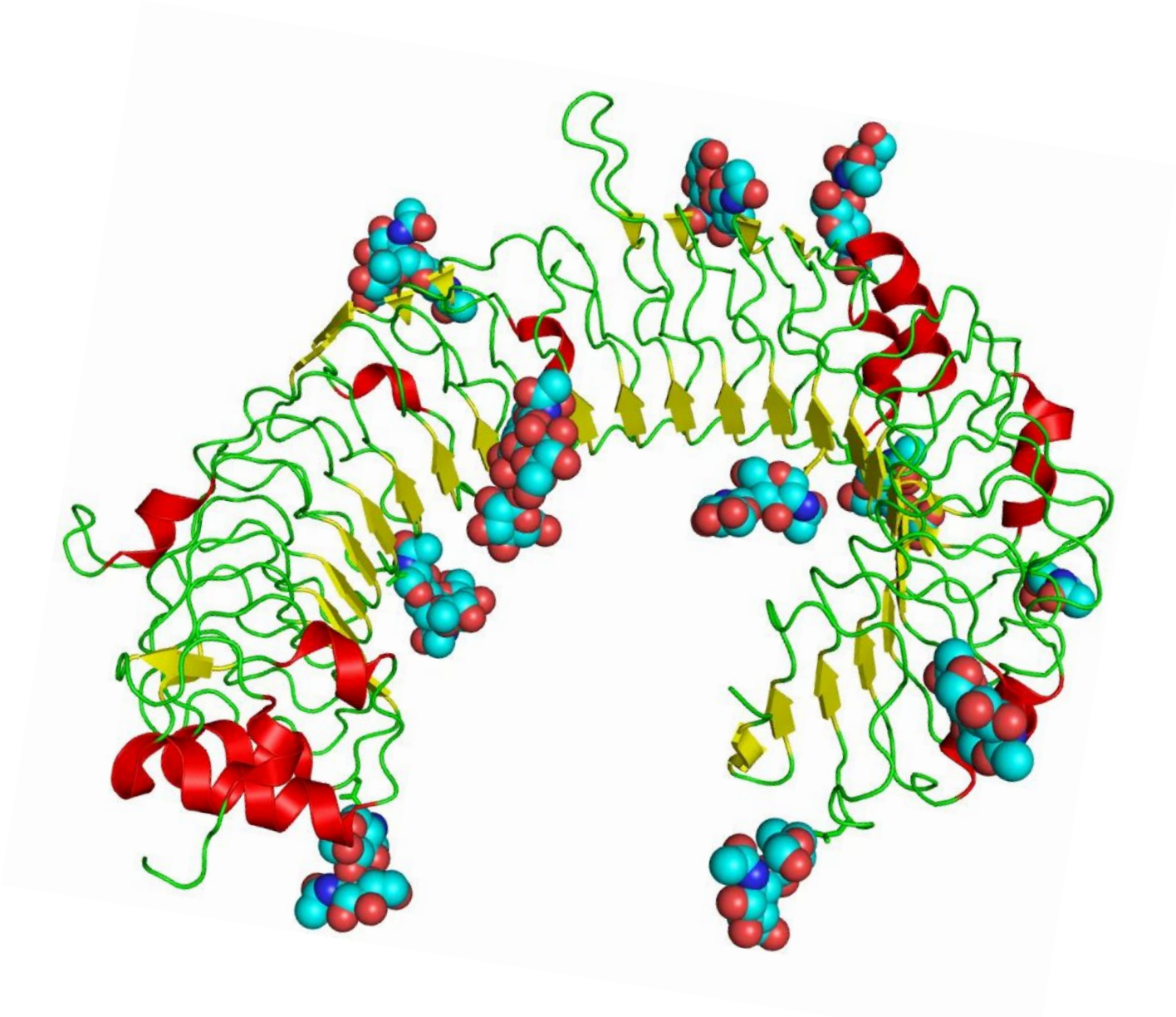
3. van Vliet S. J., Garcia-Vallejo J. J., van Kooyk Y. Dendritic cells and C-type lectin receptors: coupling innate to adaptive immune responses. Immunol. Cell Biol. 2008; 86 (7): 580-587.

4. Svajger U., Anderluh M., Jeras M., Obermajer N. C-type lectin DC-SIGN: an adhesion, signalling and antigen-uptake molecule that guides dendritic cells in immunity. Cell Signal. 2010; 22 (10): 1397-1405.

5. Beutler B, Jiang Z, Georgel P, Crozat K, Croker B, Rutschmann S, Du X, Hoebe K (2006). "Genetic analysis of host resistance: Toll-like receptor signaling and immunity at large". Annual Review of Immunology. 24: 353–89.

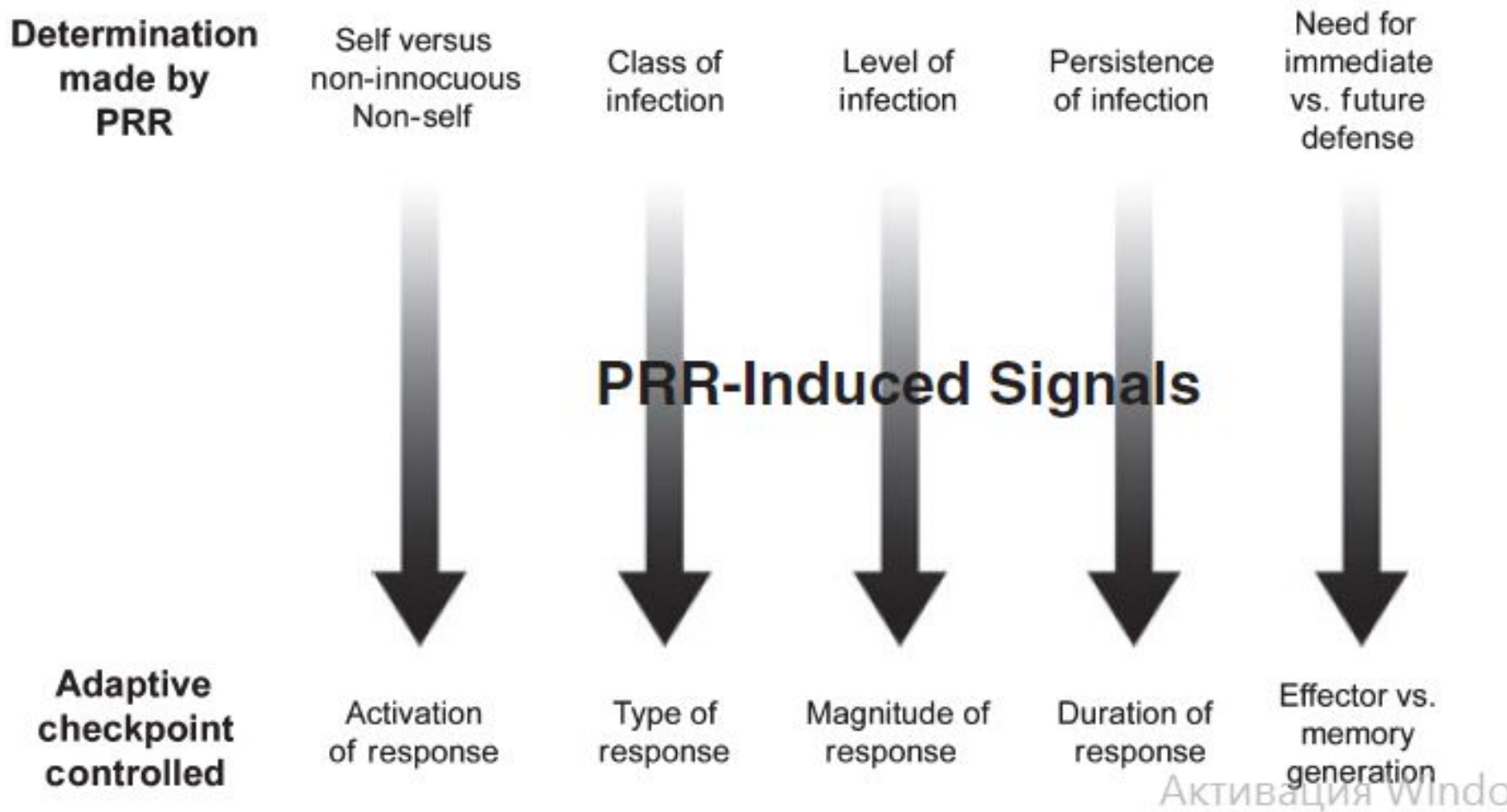
6. East L, Isacke CM (September 2002). "The mannose receptor family". Biochimica et Biophysica Acta. 1572 (2–3): 364–86.

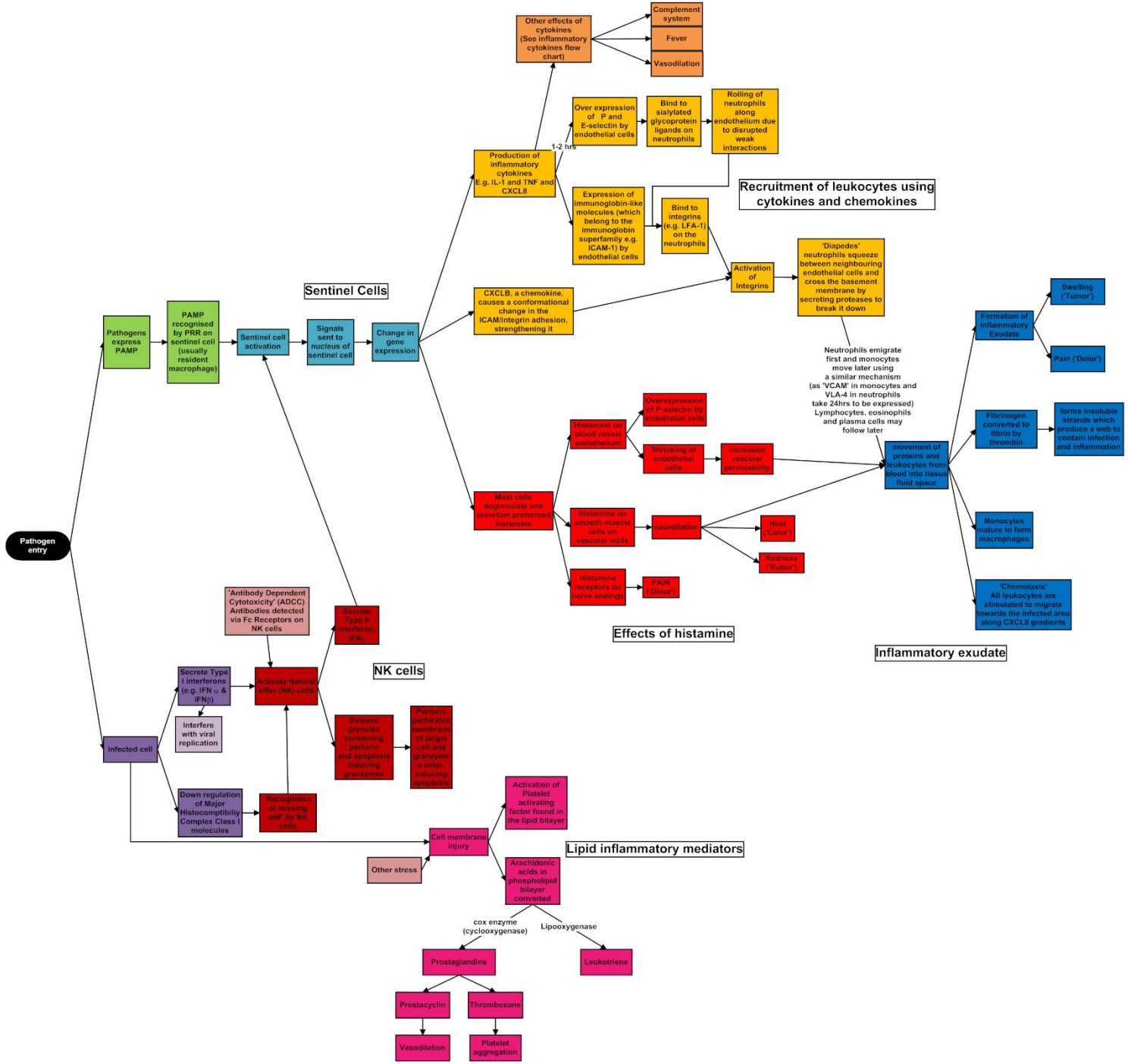
Благодарю за внимание



Приложение:

Момент определения механизма действия ПРР




Pathogen entry
Pathogens express PAMP
PAMP recognised by PRR on sentinel cell (usually resident macrophage)
Sentinel cell activation
Signals sent to nucleus of sentinel cell
Change in gene expression
Sentinel Cells
Production of inflammatory cytokines E.g. IL-1 and TNF and CXCL8
1-2 hrs
Other effects of cytokines (See inflammatory cytokines flow chart)
Complement system
Fever
Vasodilation
Over expression of P and E-selectin by endothelial cells
Bind to sialylated glycoprotein ligands on neutrophils
Rolling of neutrophils along endothelium due to disrupted weak interactions
Expression of immunoglobin-like molecules (which belong to the immunoglobin superfamily e.g. ICAM-1) by endothelial cells
Bind to integrins (e.g. LFA-1) on the neutrophils
Recruitment of leukocytes using cytokines and chemokines
CXCL8, a chemokine, causes a conformational change in the ICAM/integrin adhesion, strengthening it
Activation of Integrins
'Diapedes' neutrophils squeeze between neighbouring endothelial cells and cross the basement membrane by secreting proteases to break it down
Neutrophils emigrate first and monocytes move later using a similar mechanism (as 'VCAM' in monocytes and VLA-4 in neutrophils take 24hrs to be expressed) Lymphocytes, eosinophils and plasma cells may follow later
Mast cells degranulate and secretion preformed histamine
Histamine on blood vessel endothelium
Overexpression of P-selectin by endothelial cells
Shrinking of endothelial cells
Increased vascular permeability
Histamine on smooth muscle cells on vascular walls
vasodilation
Heat ('Calor')
Redness ('Rubor')
Histamine receptors on nerve endings
PAIN ('Dolor')
Effects of histamine
movement of proteins and leukocytes from blood into tissue fluid space
Formation of inflammatory Exudate
Swelling ('Tumor')
Pain ('Dolor')
Fibrinogen converted to fibrin by thrombin
forms insoluble strands which produce a web to contain infection and inflammation
Monocytes mature to form macrophages
'Chemotaxis' All leukocytes are stimulated to migrate towards the infected area along CXCL8 gradients
Inflammatory exudate
'Antibody Dependent Cytotoxicity' (ADCC) Antibodies detected via Fc Receptors on NK cells
Secrete Type II interferon IFNγ
Secrete Type I interferons (e.g. IFN α & IFNβ)
Activate Natural killer (NK) cells
NK cells
Interfere with viral replication
Release granules containing perforin and apoptosis inducing granzymes
Perforin perforates membrane of target cell and granzyme enter, inducing apoptosis
Infected cell
Down regulation of Major Histocomptibiliy Complex Class I molecules
'Recognition of missing self' by NK cells
Cell membrane injury
Other stress
Activation of Platelet activating factor found in the lipid bilayer
Arachidonic acids in phospholipid bilayer converted
Lipid inflammatory mediators
cox enzyme (cyclooxygenase)
Lipooxygenase
Prostaglandins
Leukotriene
Prostacyclin
Thromboxane
Vasodilation
Platelet aggregation

Классификация паттерн-распознающих рецепторов **(PRR)**