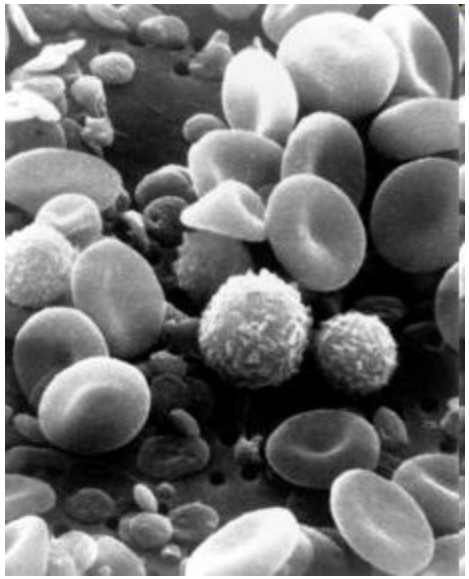
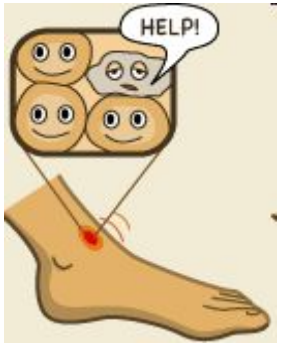
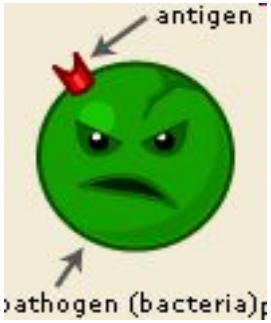
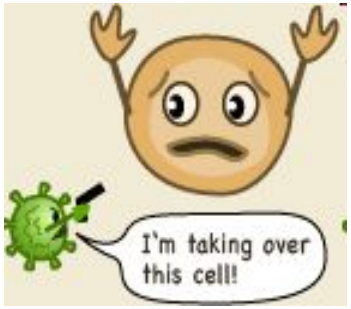
Загальна схема імунної відповіді



Потрапляння антигенів – ключовий сигнал для запуску імунної відповіді

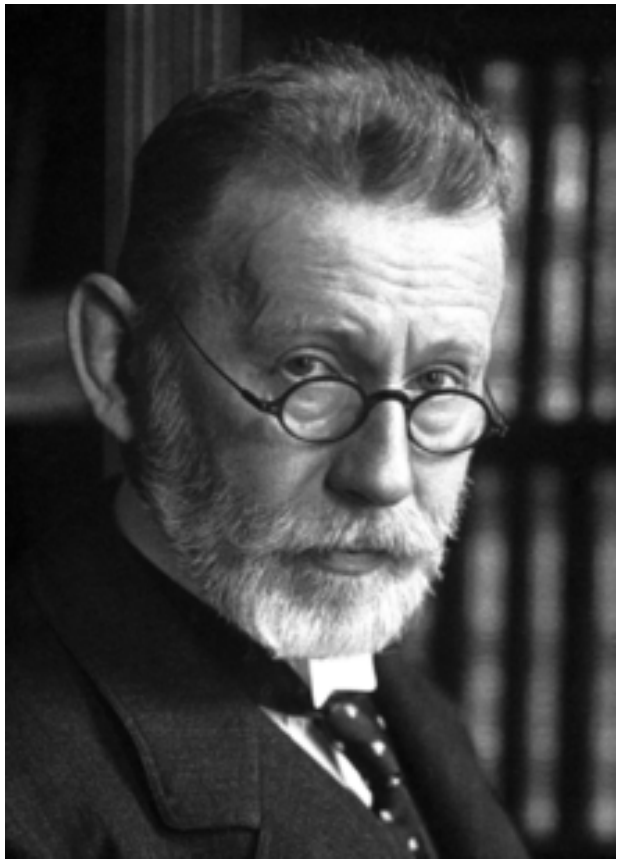




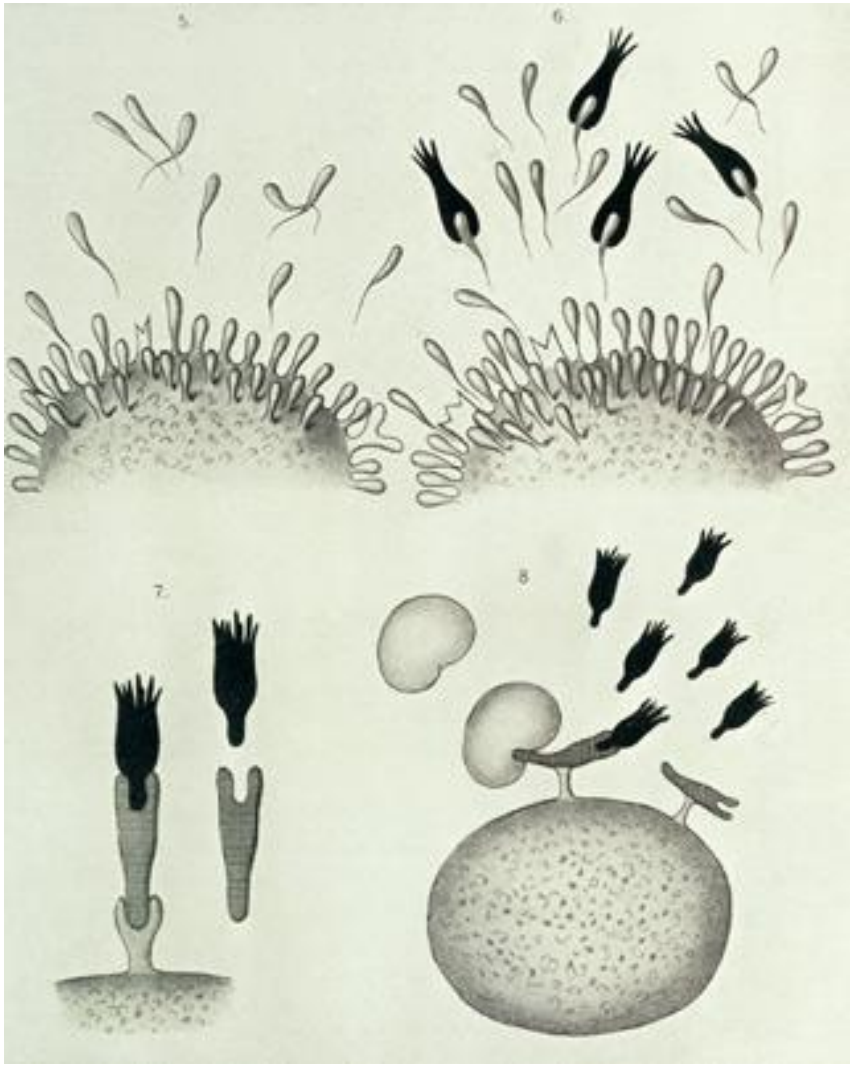


http://nobelprize.org/educational_games/medicine/immunity/immune-detail.html

- 1. Constructionist side chain theory (Ehrlich)
- 2. Instructionist antigen template theory (Pauling)
- 3. Selectionist natural selection theory (Jerne)
- 4. Accepted clonal selection theory (Burnet, Talmage, Jerne)
- 5. Seminal confirmatory experiments (Tonegawa, Nossal, Lederberg, many others)



Paul Ehrlich (1854–1915)



Lecture "On Immunity with Special Reference to Cell Life", which he gave to the Royal Society on 22 March 1900.

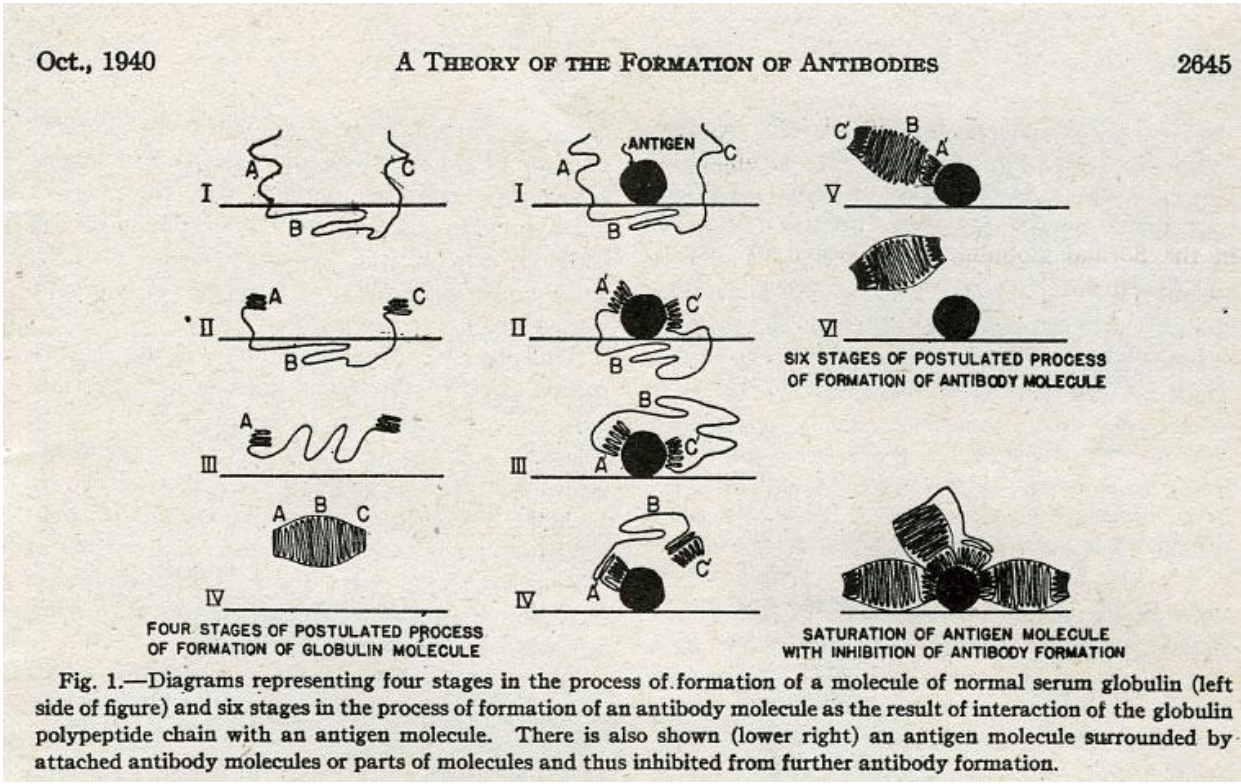
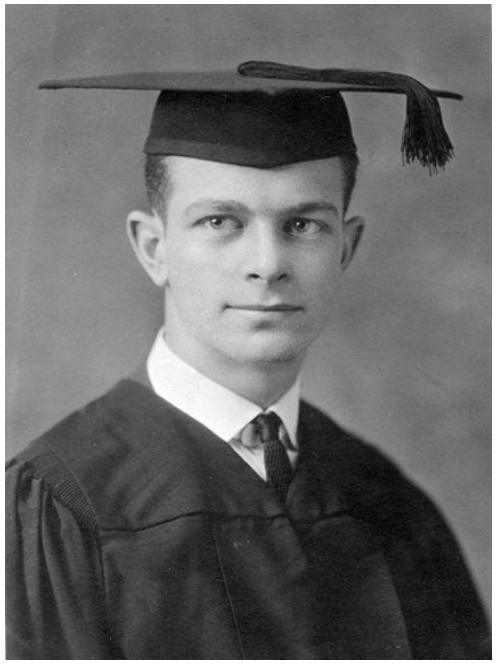


Fig. 1.—Diagrams representing four stages in the process of formation of a molecule of normal serum globulin (left side of figure) and six stages in the process of formation of an antibody molecule as the result of interaction of the globulin polypeptide chain with an antigen molecule. There is also shown (lower right) an antigen molecule surrounded by attached antibody molecules or parts of molecules and thus inhibited from further antibody formation.

Linus Pauling (1901-1994)

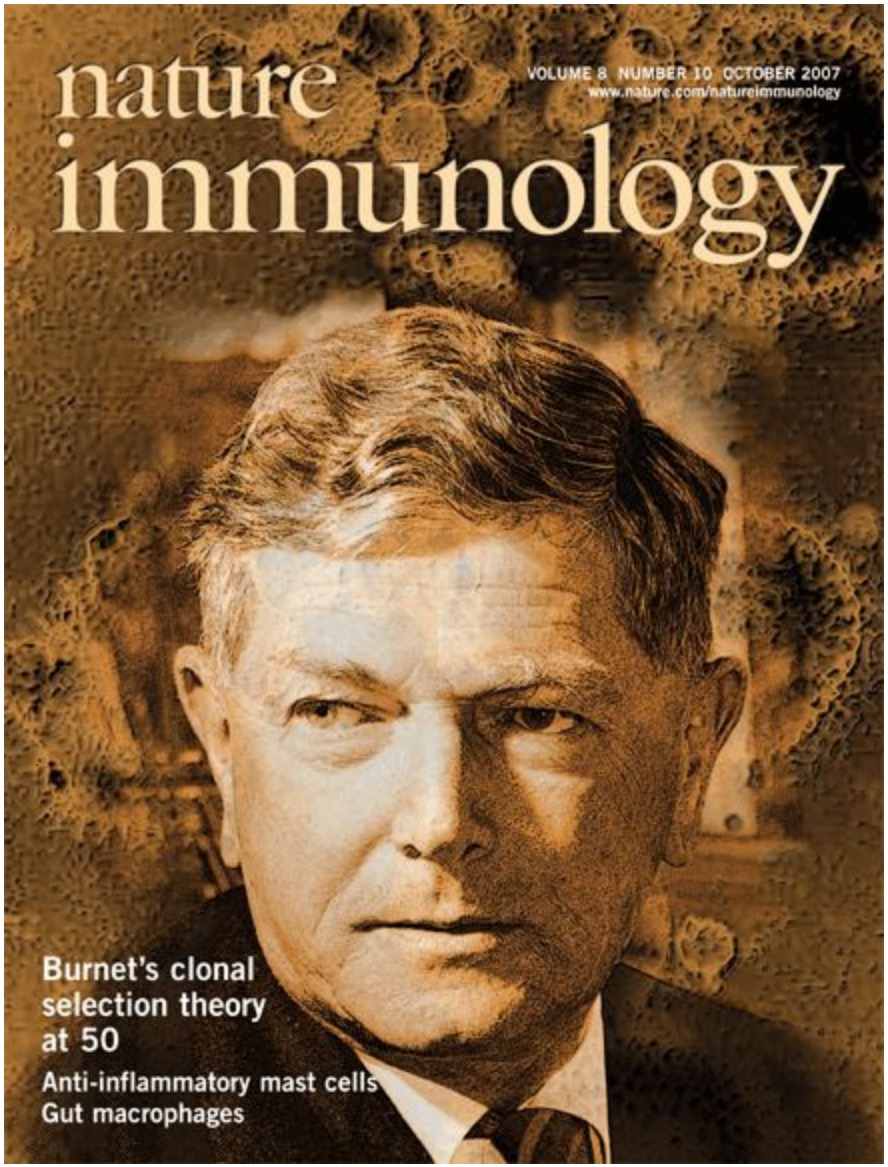
The way to get good ideas is to get lots of ideas and throw the bad ones away

- *© Linus Carl Pauling*



Сер Франк Бернет

3 September 1899 – 31 August 1985


nature
immunology
VOLUME 8 NUMBER 10 OCTOBER 2007
www.nature.com/natureimmunology
Burnet's clonal selection theory at 50
Anti-inflammatory mast cells
Gut macrophages

1st draft of clonal selection theory of antibody production
[6.9.57]

Suppose we sets out to produce a Jerne type theory from first principles.

A. The body must produce enough types of globulin to correspond to all potential antigenic determinants in and out of the body. During the pre-clinical phase all those which react with body components must be removed to account for tolerance findings. This fits with our exaggeration theory.

B.i Either the capacity to produce the removed types of globulin is eliminated i.e the clones of that pattern have no descendants –

B ii The corresponding γ globulin molecules are on being produced but circumstances are such that new contact with antigenic determinant does not result in antigenic reaction in contrast to the behaviour of a foreign determinant.

C. There is no escape from the requirement that antibody is specifically produced by cells either remotely or immediately genetically determined. One cannot assume for instance that a given antibody or globulin molecule has perhaps 100 areas over its surface corresponding to 50 antigenic determinants and averaging two of each. On second thoughts it is hard to exclude the possibility if one postulates in addition that there are 1000 different such patterns each of 50 ± a.g.ds

D If we postulate as there is some basis for, that the lymphocyte has a surface capable of reacting with appropriate antigen and that after such contact the lymphocyte has a special ability to settle into an appropriate niche and become a parent, we have a possible mechanism for Jerne's hypothesis.

1st insert 6.9.57.

E In the first the lymphocyte develops this capacity to proliferate only when it is 11 days post labelling.

F We must therefore postulate a period during which the lymphocytes are being moulded to tolerate self components or more simply being killed off if they do not.

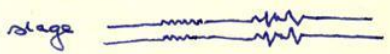
2.

F. The real problem is then in the early stage of development a randomization mechanism involves the appearance of a range of globulin patterns sufficiently wide to cover all determinants.

Suppose for instance there is some aspect of protein synthesis by which a segment or set of segments can be picked in at random – or the same thing for RNA or even the DNA blueprint.

In the ancestors of mesenchymal cells for a certain period in embryonic life DNA replication is of the nature

where — are defined codes ..... is randomized for the production of globulins.

At a later stage  stabilization of the random sequence.

The same process may occur as a result of somatic mutation in later life giving AICF reagent.

Item 06/079 from Box Number 30, Series 6 of the Records of Frank Macfarlane Burnet from University of Melbourne Archives, headed '1st draft of clonal selection theory of antibody formation.' http://www.nature.com/

Table 1. Nine propositions.

A1. The stereospecific segment of each antibody globulin is determined by a unique sequence of amino acids.

A2. The cell making a given antibody has a correspondingly unique sequence of nucleotides in a segment of its chromosomal DNA: its "gene for globulin synthesis."

A3. The genic diversity of the precursors of antibody-forming cells arises from a high rate of spontaneous mutation during their lifelong proliferation.

A4. This hypermutability consists of the random assembly of the DNA of the globulin gene during certain stages of cellular proliferation.

A5. Each cell, as it begins to mature, spontaneously produces small amounts of the antibody corresponding to its own genotype.

A6. The immature antibody-forming cell is hypersensitive to an antigen-antibody combination: it will be suppressed if it encounters the homologous antigen at this time.

A7. The mature antibody-forming cell is reactive to an antigen-antibody combination: it will be stimulated if it first encounters the homologous antigen at this time. The stimulation comprises the acceleration of protein synthesis and the cytological maturation which mark a "plasma cell."

A8. Mature cells proliferate extensively under antigenic stimulation but are genetically stable and therefore generate large clones genotypically preadapted to produce the homologous antibody.

A9. These clones tend to persist after the disappearance of the antigen, retaining their capacity to react promptly to its later reintroduction.

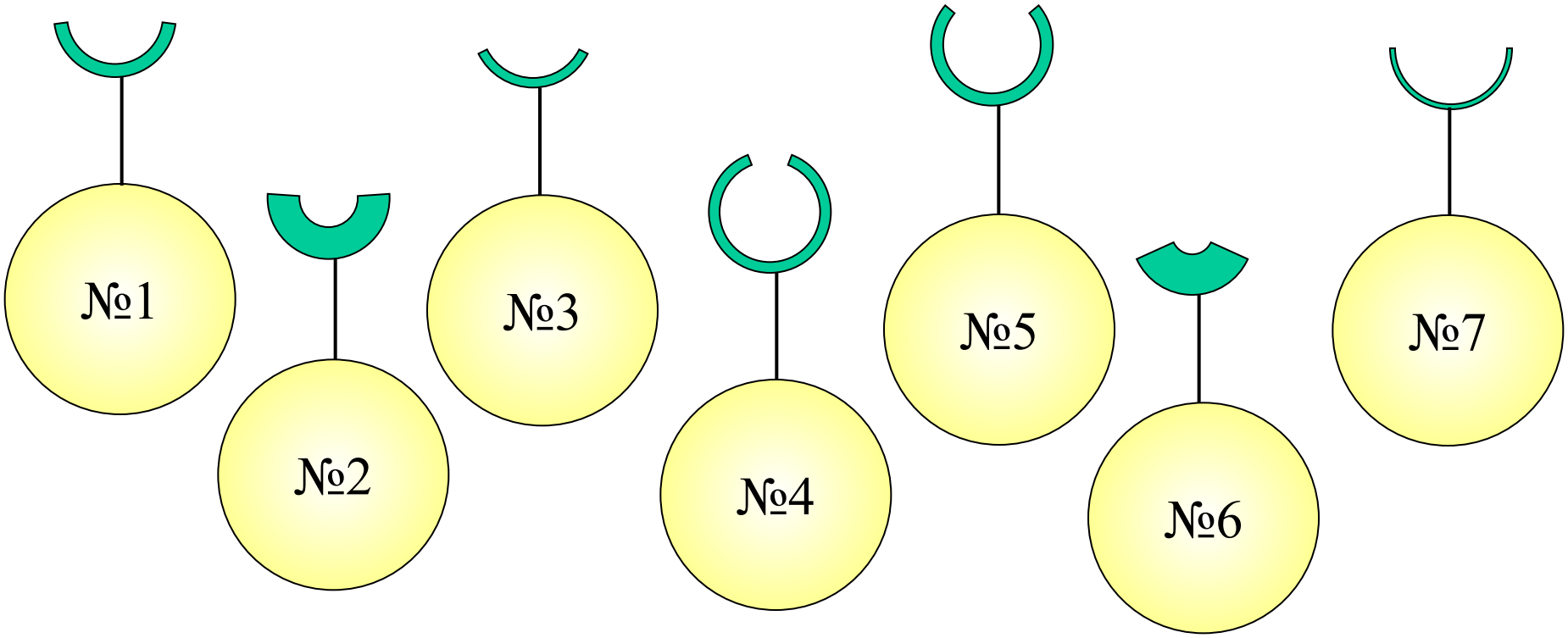
Клонально-селекційна теорія Бернета

- В організмі існують лімфоцити з рецепторами, специфічними до будь-якого антигену, ще до появи самого антигену
- Кожен лімфоцит несе рецептори лише однієї специфічності
- Зустріч з антигеном є фактором селекції для лімфоцитів

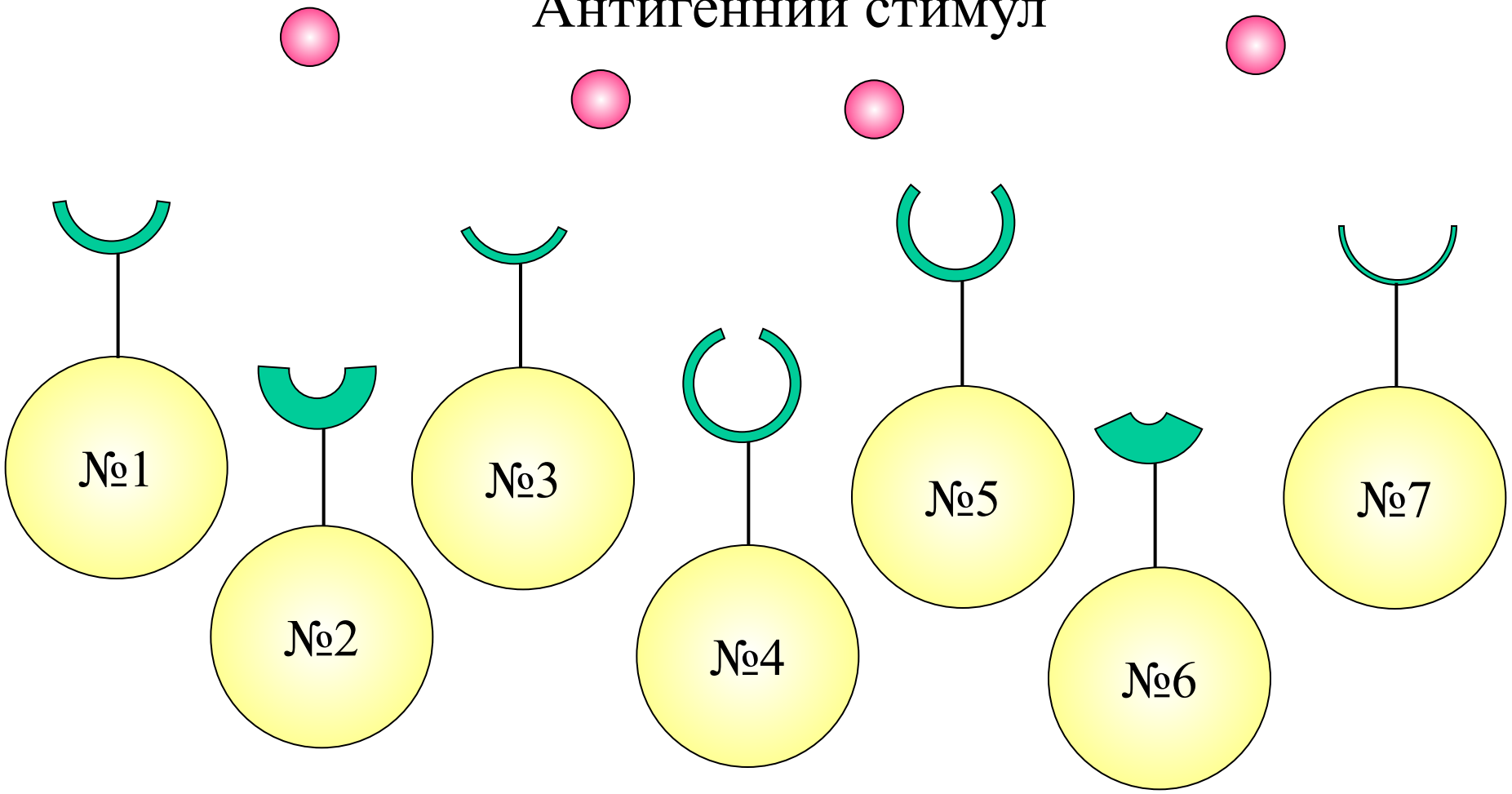
The clonal selection theory can be summarised with the following four tenets:

- Each lymphocyte bears a single type of receptor with a unique specificity (by V(D)J recombination).
- Receptor occupation is required for cell activation.
- The differentiated effector cells derived from an activated lymphocyte will bear receptors of identical specificity as the parental cell.
- Those lymphocytes bearing receptors for self molecules will be deleted at an early stage.

http://en.wikipedia.org/wiki/Clonal_selection



Наївні лімфоцити


Антигенний стимул
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№2
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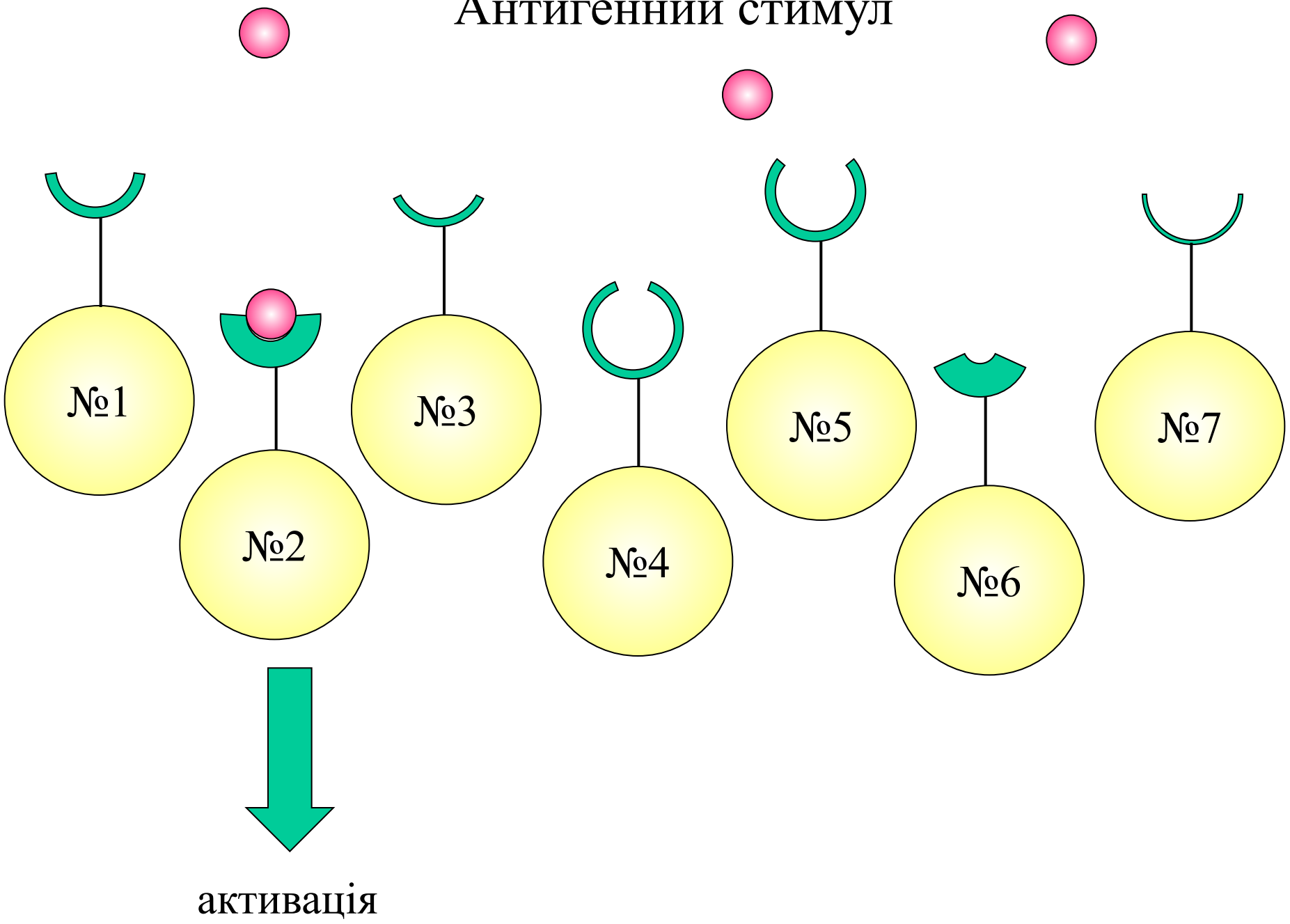
№6
№7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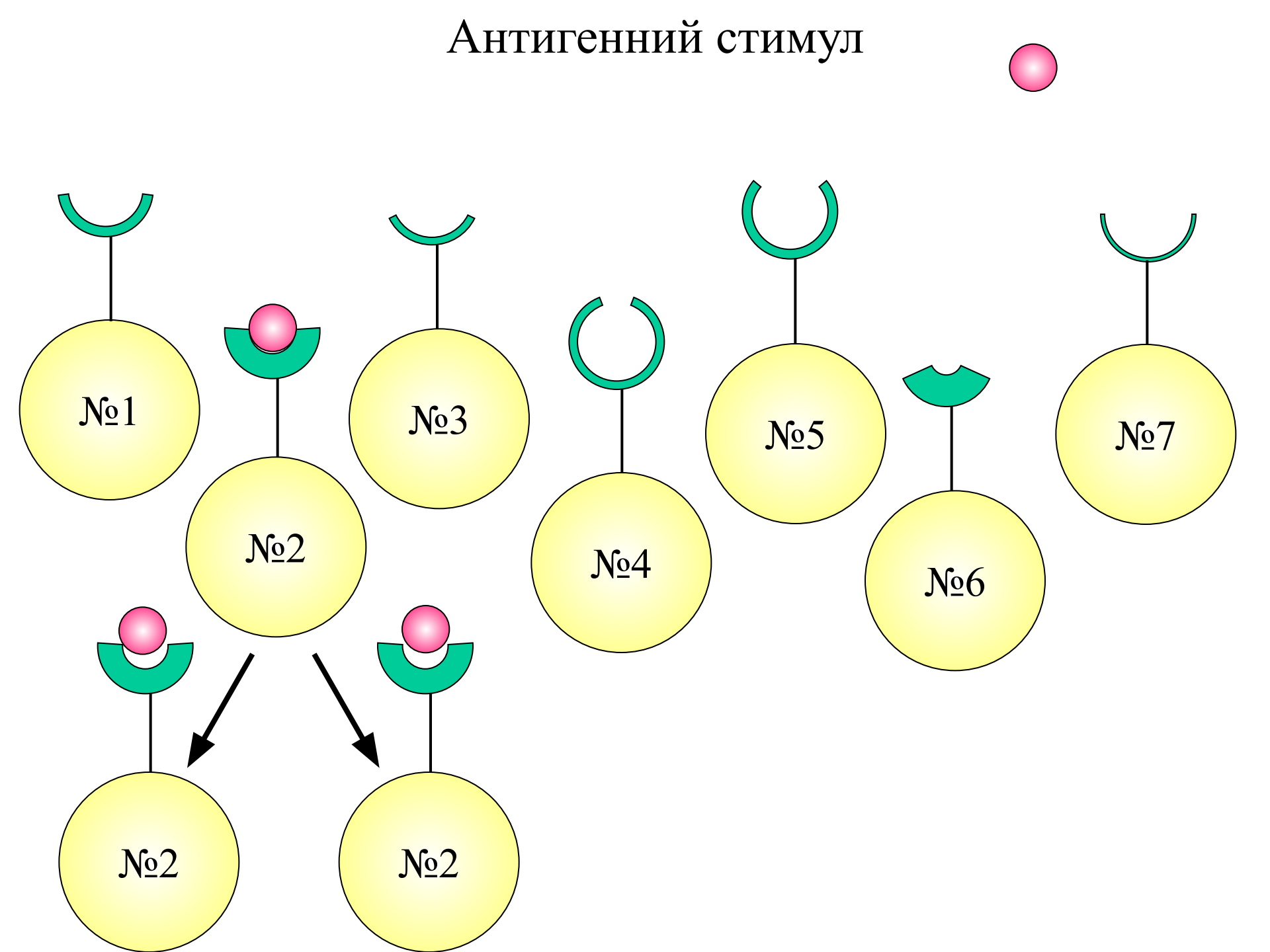
активація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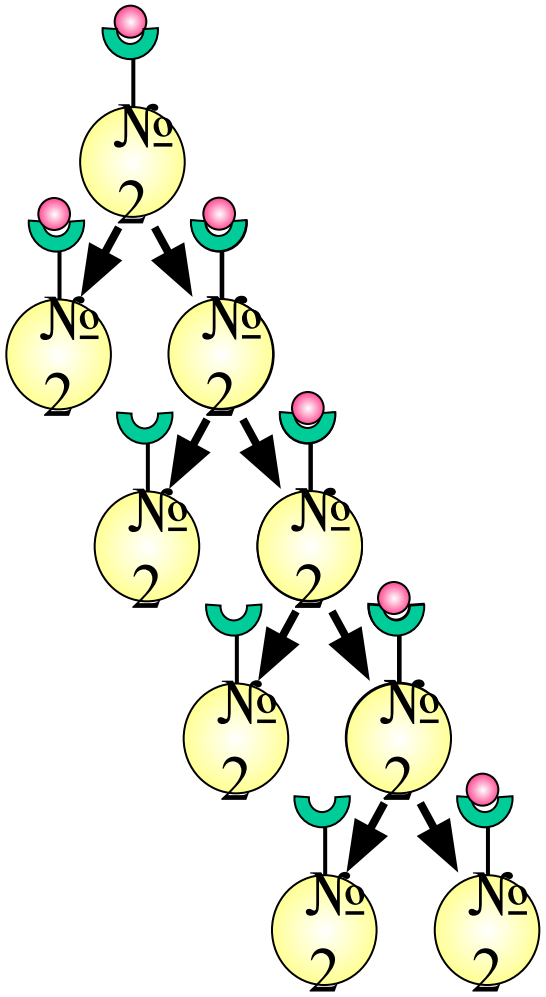
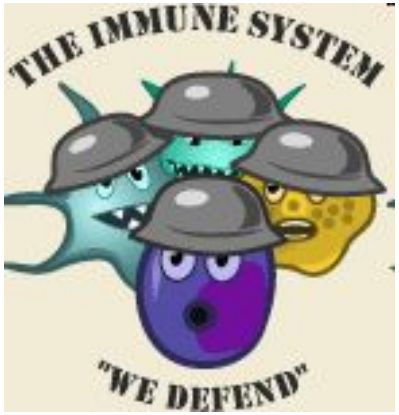
Проліферація і диференціювання антиген-специфічного клону



Франк Бернет і Пітер Медавар

Нобелевська премія (1960 р)

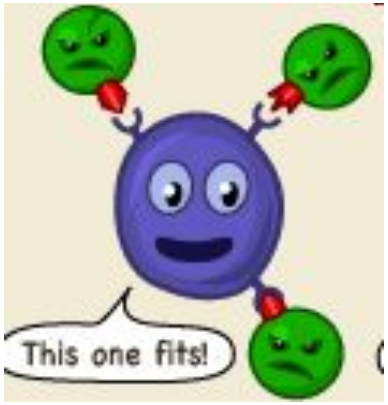
за відкриття набутої імунологічної толерантності



http://nobelprize.org/educational_games/medicine/immunity/immune-detail.html

Розпізнавання “чужого”

Т-лімфоцит



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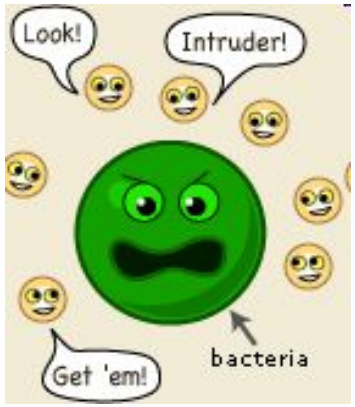
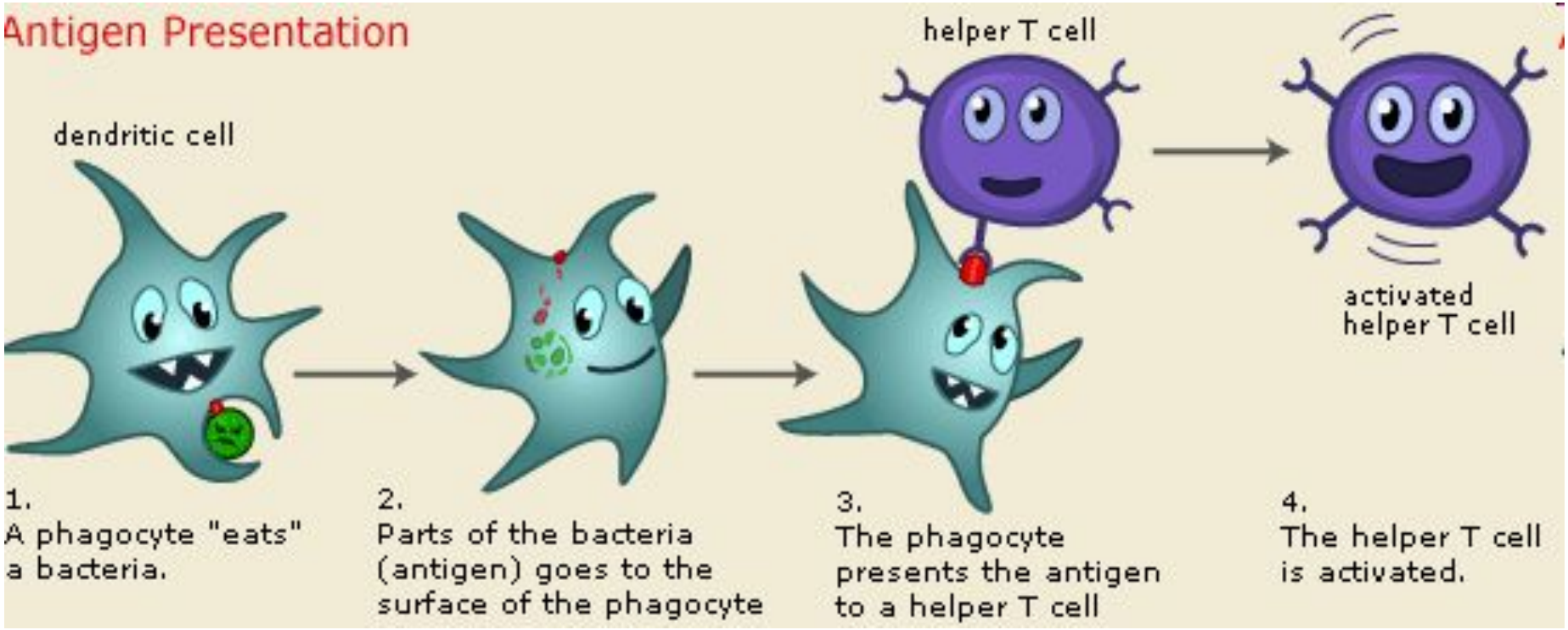


комплемент

http://nobelprize.org/educational_games/medicine/immunity/immune-detail.html

Презентація антигенів



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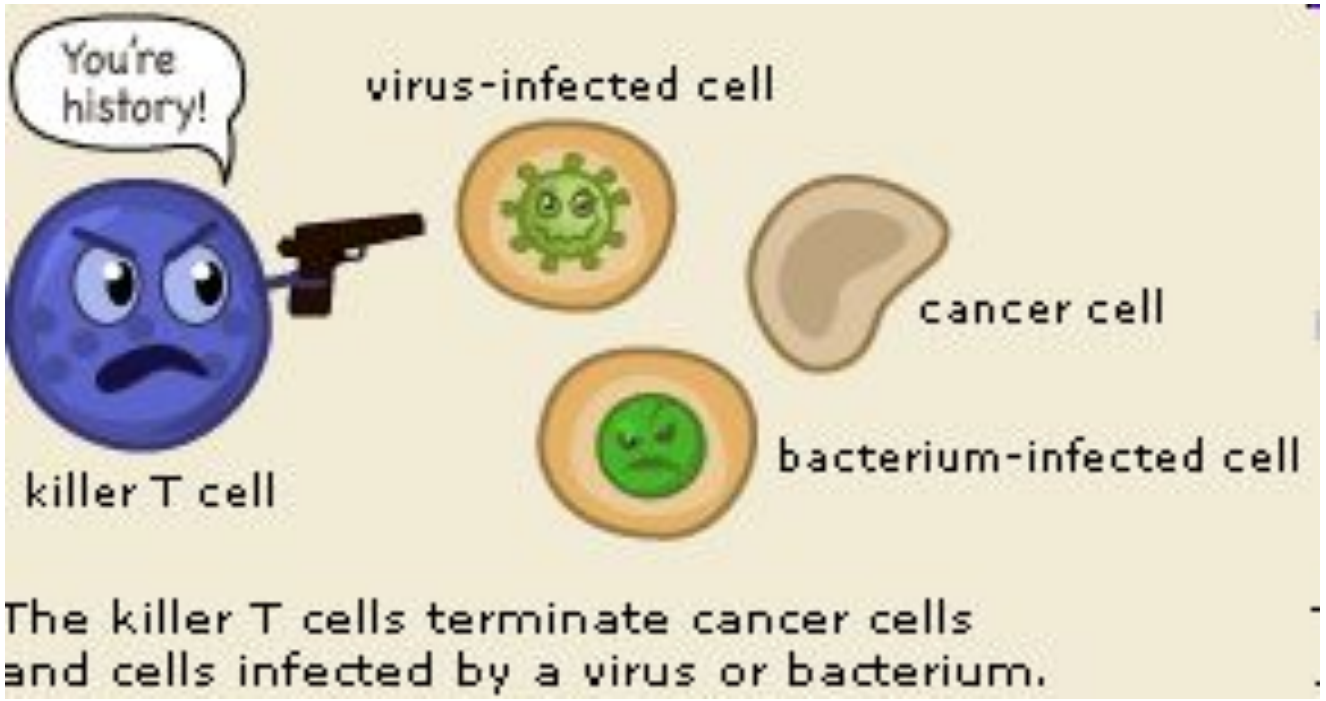
Вбивство уражених клітин Т-кілерами



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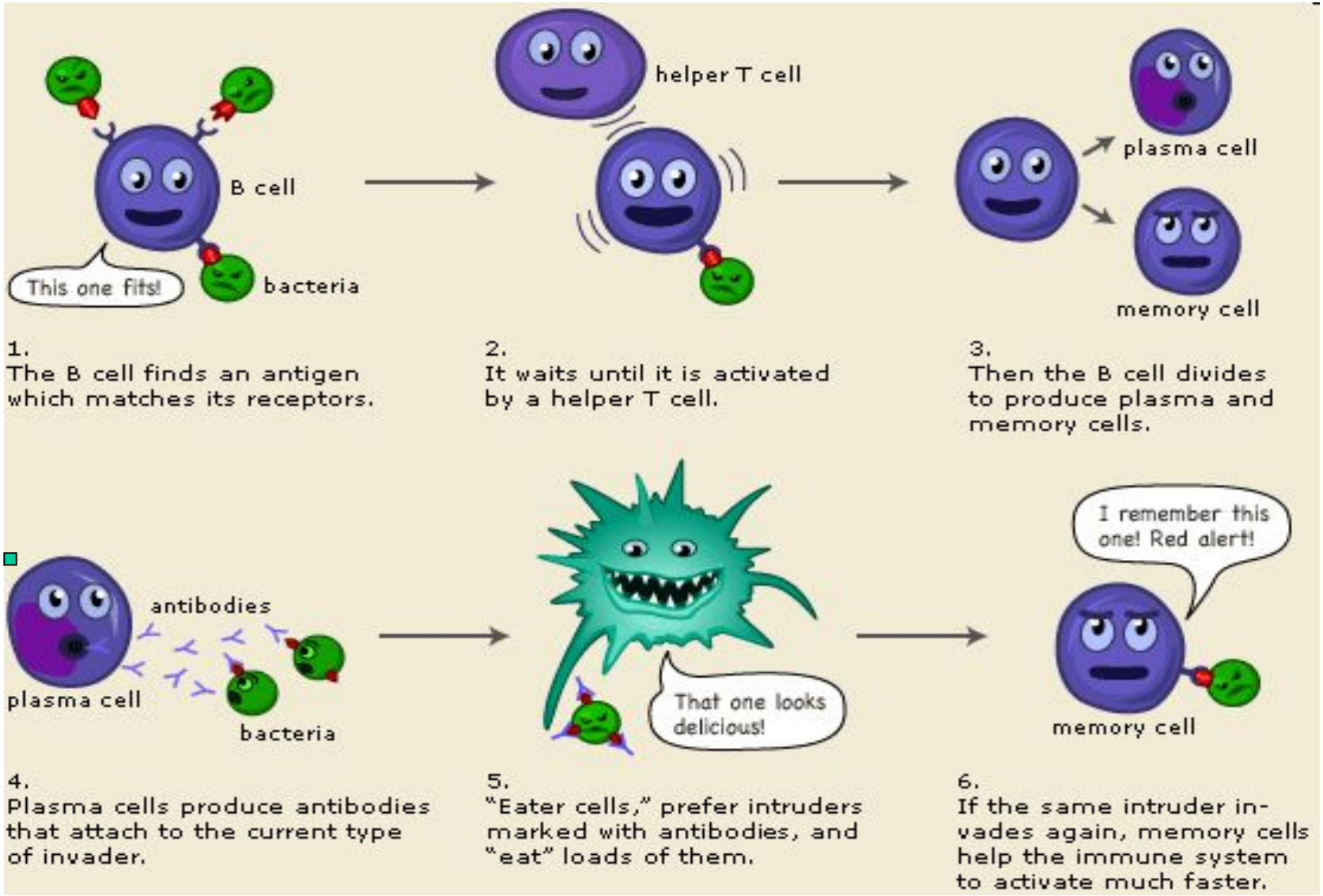
Активація В-лімфоцитів і синтез антитіл



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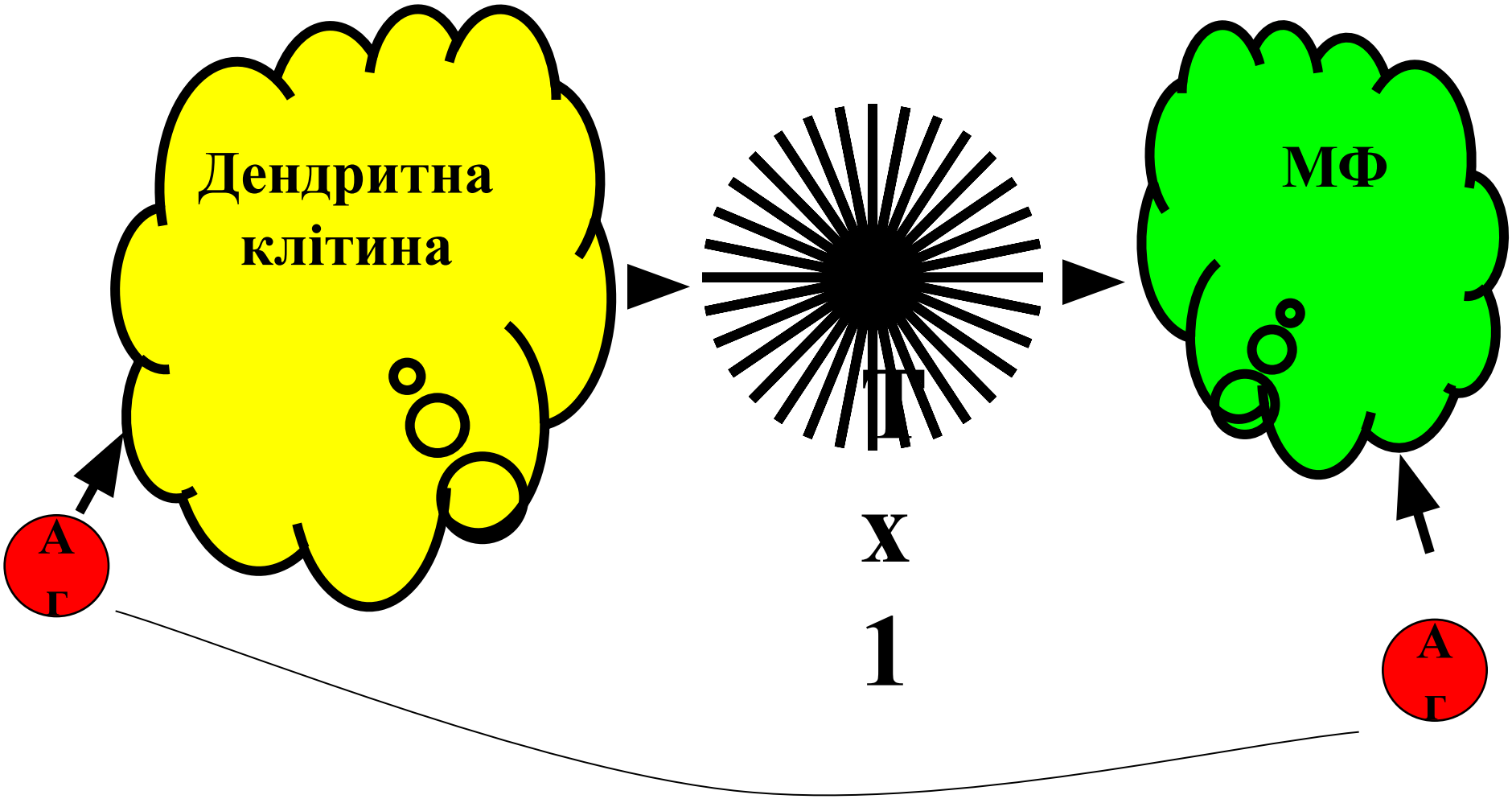
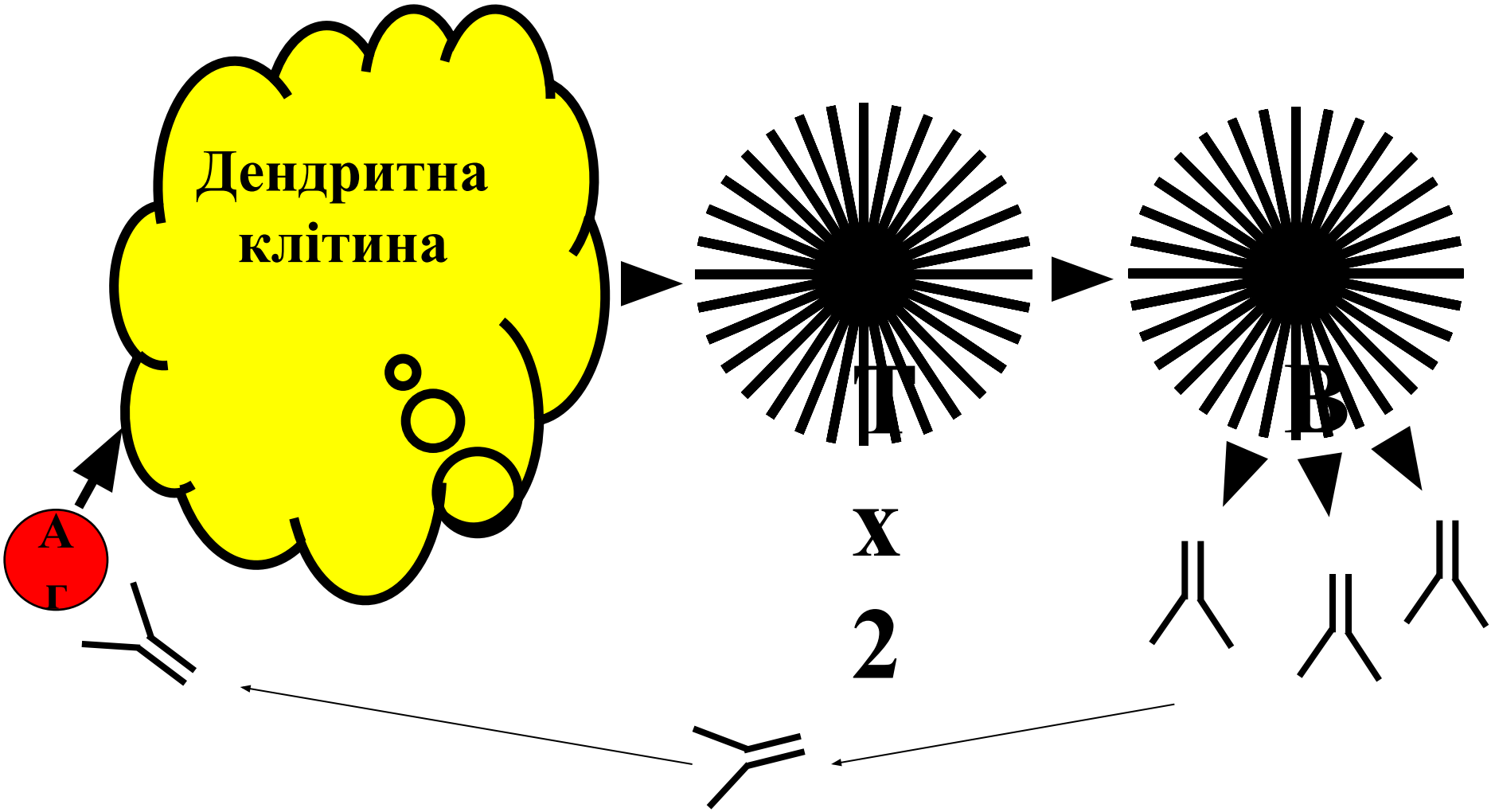


Гуморальна імунна відповідь



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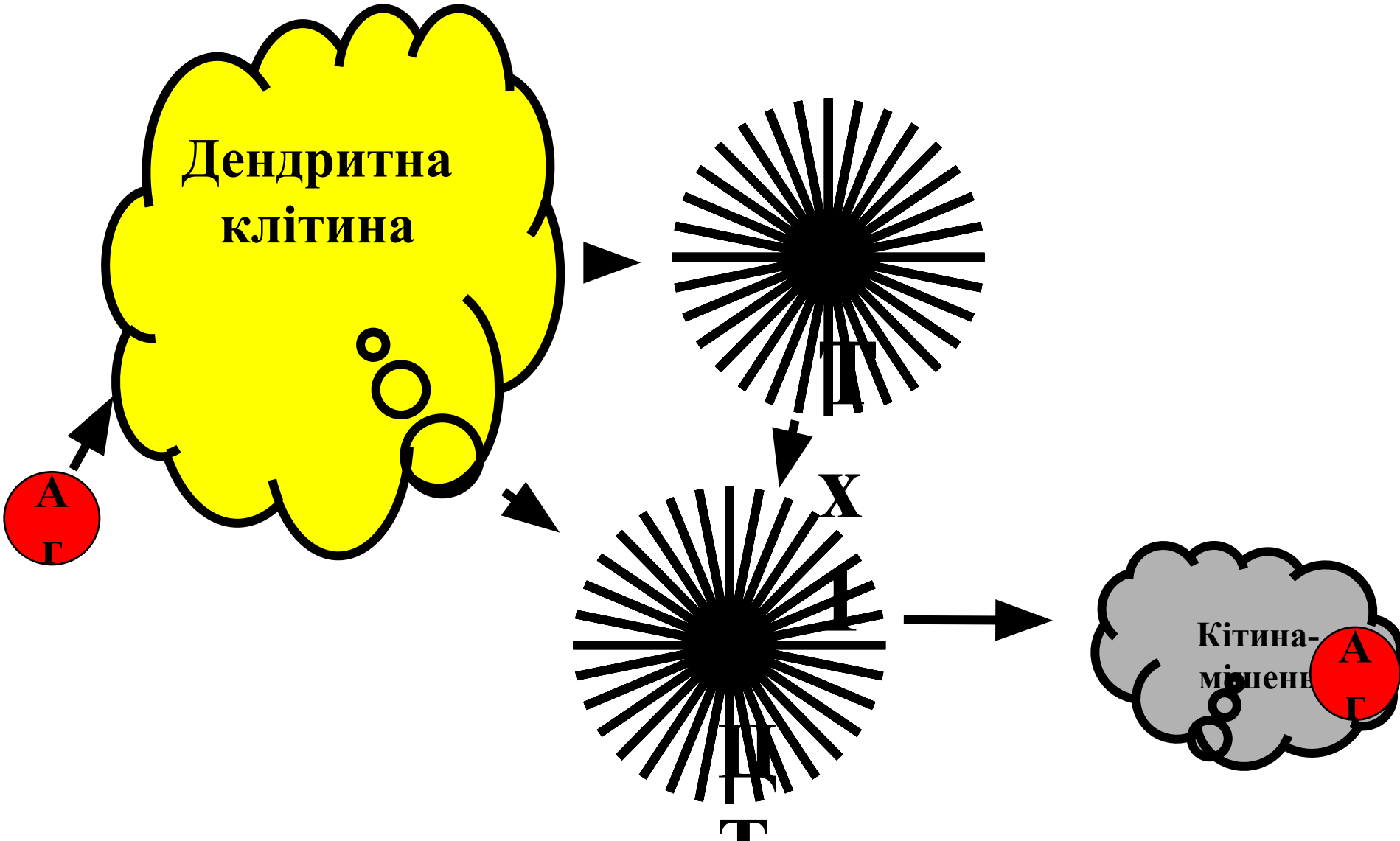
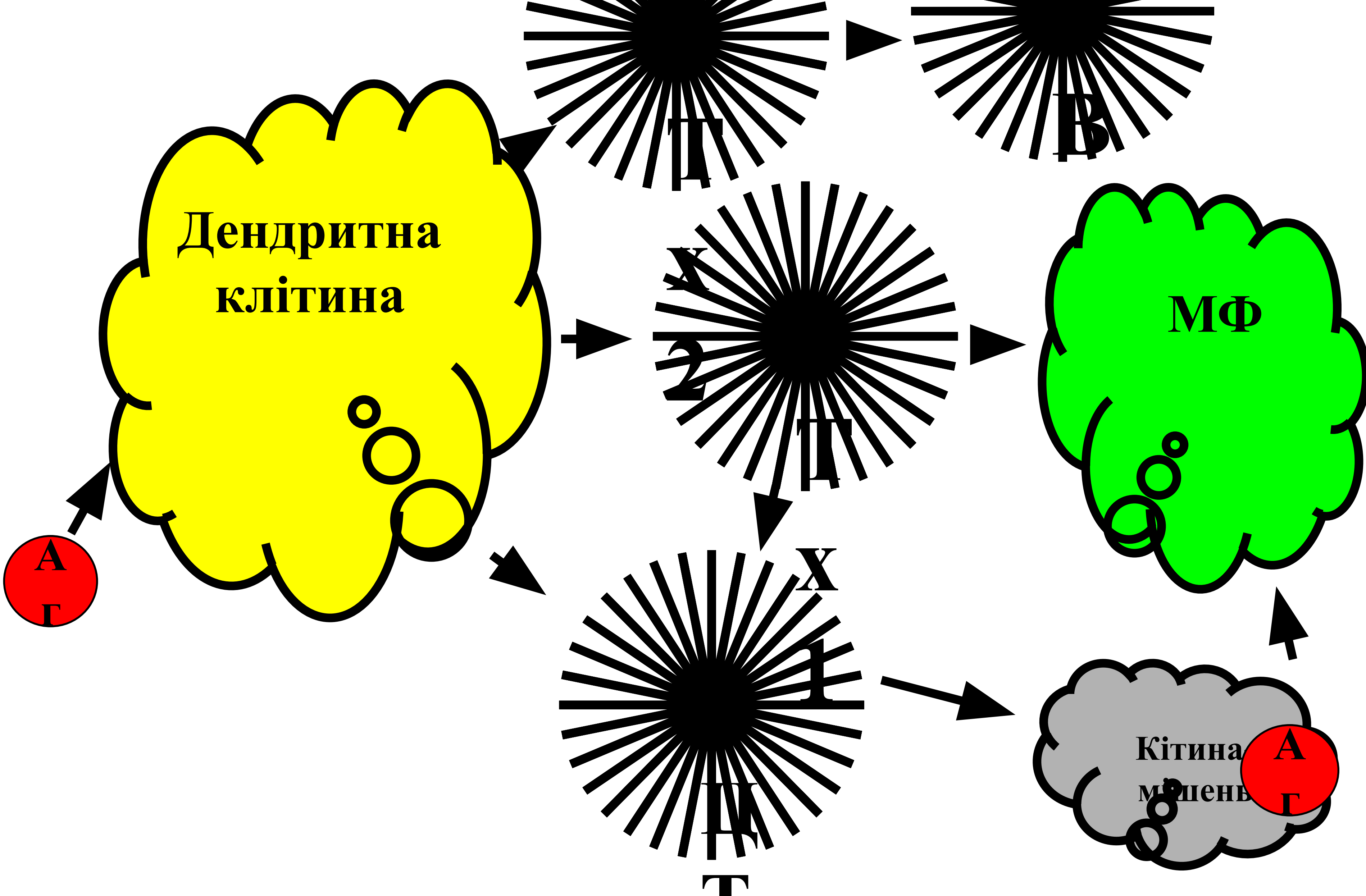
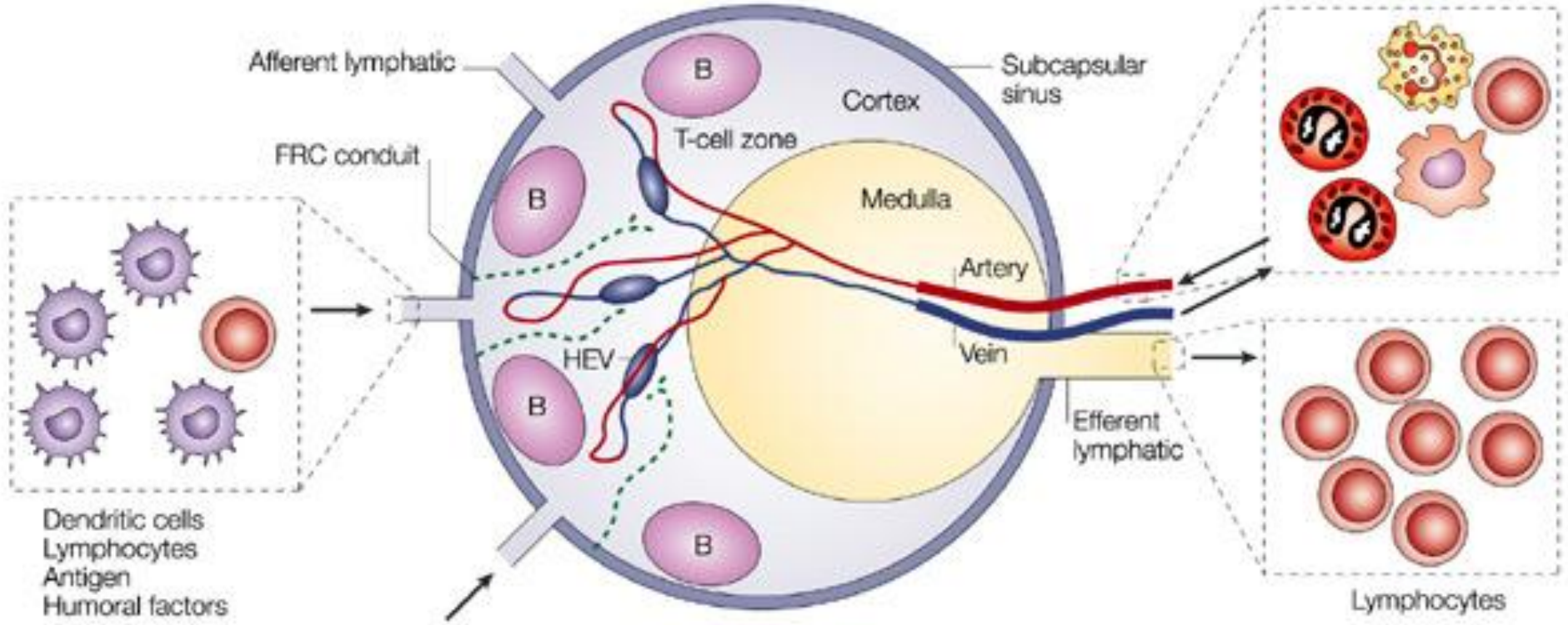


Загальна схема імунної відповіді





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