Zánět

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Definice zánětu

Souhrn reakcí na porušení integrity organismu

- Ochrana proti infikování
- Lokalizace poškození
- Regenerace, zahojení

Inzult (patogenní faktor) vyvolávající zánětlivou reakci

- Biologický (mikroorganismy, parazité)
- Fyzikální (záření, termické vlivy)
- Chemický (toxiny, žíraviny)
- Metabolický (hypoxie, poruchy metabolismu)

Rozdělení zánětu

Dle ohraničení

- lokální
- systémový

Dle dynamiky

- akutní
- chronický

Dle efektu

- obranný
- autoagresivní (deregulovaný, delokalizovaný)

Symptomy zánětu

Makroskopická úroveň

- **calor** – vyšší teplota
- **rubor** – zarudnutí, erytém
- **tumor** – zduření, otok
- **dolor** – bolest

(Celsus, De Medicina, 1. století)

- **functio laesa** – porucha funkce *(R. Virchow, 19. století)*

Mikroskopická úroveň

- alterace – změny v tkáni
- exsudace – zánětlivý exsudát (tekutina a proteiny), buňky (infiltrát)
- proliferace - tvorba granulační a vazivové tkáně (jizva)

exsudát:
serózní
nehnisavý
hnisavý
fibrinózní
gangrenózní

http://penelope.uchicago.edu/Thayer/E/Roman/Texts/Celsus/home.html

Průběh zánětu

Produkty buněk a traumatizovaných tkání vedou k:

- Zvýšení permeability cév (při poranění krátká vazokonstrikce), prostup plazmatické tekutiny do extravaskulárního prostoru
- Zvýšení přilnavosti endotelií, exprese adhezivních molekul, usnadňující migraci lymfocytů
- Změny v regulaci teploty
- Ovlivnění nervových zakončení

Souhra složek nespecifické (vrozené) a specifické imunity, v závislosti na délce trvání zánětu a intenzitě

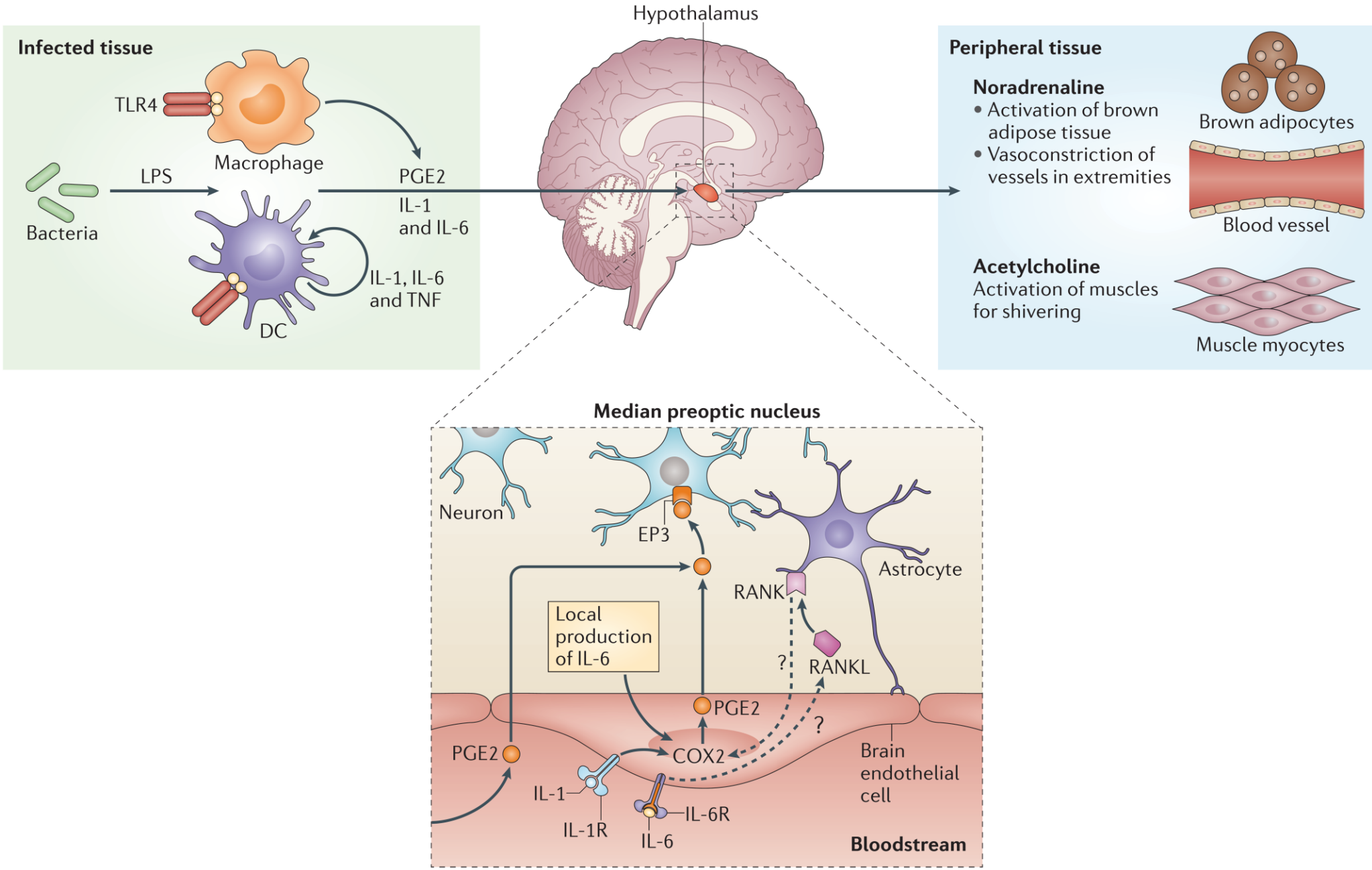
Horečka

Zvýšení tělesné teploty v klidu účinkem patogenního podnětu

- Infekční agens, trauma, inkompatibilní transfuze
- Zvýšená produkce prozánětlivých cytokinů (**IL-1, TNF, IL-6**), prostaglandiny (pyrogeny)
- Působení na hypotalamické termoregulační centrum

Účinky (mediátorů) horečky na funkce organismu

- Nervový systém (bolest, únava, spavost)
- Kardiovaskulární systém (zvýšený tep, +1 °C => +10 tepů za minutu)
- Metabolismu (urychlení látkové přeměny, 40 °C => 50% navíc)
- Respirační systém (zrychlené dýchání)
- Trávicí systém (snížená činnost, porušena resorpce živin)
- Ledviny (snížená tvorba moči, bílkovina v moči)

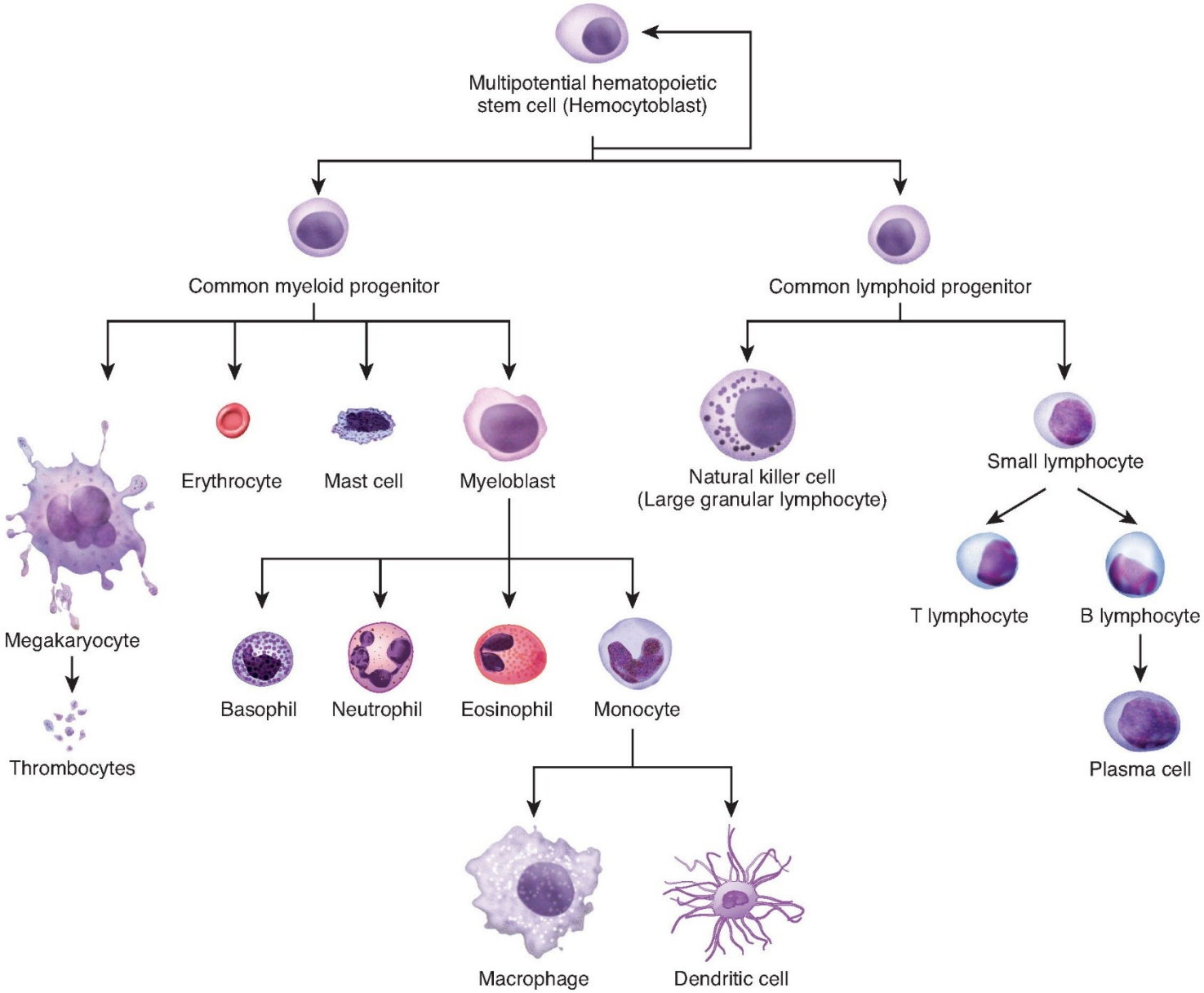


https://www.semanticscholar.org/paper/Fever-and-the-thermal-regulation-of-immunity%3A-the-Evans-Repasky/1f6af26441b91283fa996849daba93b073c3d200

Systémy realizující zánětovou odpověď

- Leukocyty
- Endotel
- Destičky
- Plazmatický koagulační systém
- Komplement
- Proteiny akutní fáze

Leukocyty


Multipotential hematopoietic stem cell (Hemocytoblast)
Common myeloid progenitor
Common lymphoid progenitor
Erythrocyte
Mast cell
Myeloblast
Natural killer cell (Large granular lymphocyte)
Small lymphocyte
Megakaryocyte
Thrombocytes
Basophil
Neutrophil
Eosinophil
Monocyte
T lymphocyte
B lymphocyte
Plasma cell
Macrophage
Dendritic cell

Vrozená imunita

ne až tak úplně nespecifická… rozeznávání:

- **Pathogen-associated molecular patterns (PAMPs)**
  - pocházejí z mikroorganismu, evolučně konzervované molekuly typické pro patogeny
  - bakteriální sacharidy (lipopolysacharidy, také LPS, manóza), nukleové kyseliny (bakteriální nebo virální DNA nebo RNA), bakteriální peptidy (flagelin), peptidoglykany a lipoteichoická kyselina (gram pozitivní bakterie), N-formylmethionin, lipoproteiny a glukany, chitin

- **Damage (danger)-associated molecular patterns (DAMPs)**
  - pocházejí ze stresovaných nebo poškozených buněk hostitele, záleží často na kontextu
  - HSPs, HMBG1, hyaluronan, ATP, adenosin, kyselina močová, heparin sulfát, DNA, RNA, TNF-α, IL-1β, IFNα

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3443751/

Annu. Rev. Immunol. 1994. 12:991–1045

TOLERANCE, DANGER, AND THE EXTENDED FAMILY*

Polly Matzinger

Laboratory of Cellular and Molecular Immunology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Building 10, Room 111, Bethesda, Maryland 20892

KEY WORDS: antigen presentation, immunity, T cells, dendritic cells, viruses

Abstract

For many years immunologists have been well served by the viewpoint that the immune system's primary goal is to discriminate between self and non-self. I believe that it is time to change viewpoints and, in this essay, I discuss the possibility that the immune system does not care about self and non-self, that its primary driving force is the need to detect and protect against danger, and that it does not do the job alone, but receives positive and negative communications from an extended network of other bodily tissues.

IN A FULLY H-2 INCOMPATIBLE CHIMERA, T CELLS OF DONOR ORIGIN CAN RESPOND TO MINOR HISTOCOMPATIBILITY ANTIGENS IN ASSOCIATION WITH EITHER DONOR OR HOST H-2 TYPE*

BY POLLY MATZINGER AND GALADRIEL MIRKWOOD

(From the Department of Biology, University of California San Diego, La Jolla, California 92093)

Despite much recent interest and effort, the role played by major histocompatibility complex products in the regulation of T-cell responses remains perplexing. In 1972 it was observed that mouse T and B cells would only cooperate in an antibody reponse if they shared certain regions of H-2 (1). Subsequently, H-2 gene products were also found to be involved in cytotoxic T-cell reactions, and it was postulated that the killer T cell must bear H-2 molecules in common with those of its target in order to effect lysis (2–6). Later studies with radiation chimeras showed that this is not the case, but that the H-2 region must be shared between the cells used to stimulate the response and the targets; a killer T cell that was itself H-2 type A, after having grown up in an (A × B)F_1 could be stimulated to lyse H-2 type B virus-infected or trinitrophenyl-modified targets (7–9). Such chimeras were also found to contain A type helper T cells which can cooperate with B type B cells (10). It was then postulated that T-cell precursors "learn" to recognize the H-2 type of the host as self (11). Recent evidence shows that the host H-2 type of a chimera does distinctly influence the specificity of the responding T-cell population (12, 13) and that it is the H-2 type of the thymus that is important (13). Most of this work has been done with semiallogeneic chimeras (e.g., "A" bone marrow into an irradiated [A × B]F_1, or [A × B]F_1 bone marrow into an "A" or [A × C]F_1) where the responses were very strongly restricted by the H-2 type of the host. A small number of completely allogeneic chimeras was tested (e.g., "A" bone marrow into "B") and appeared to be immunoincompetent. The virtually absolute restriction of the semiallogeneic chimeras as well as the immunoincompetence of the fully allogeneic chimeras has led to much speculation and has been quoted as suggestive evidence for the dual recognition model of T-cell receptors (13).

We report here that in contrast to the results with virus-infected mice, fully allogeneic chimeras made by repopulating irradiated BALB/c(H-2^d) mice with BALB.B(H-2^b) bone marrow are well able to respond to minor histocompatibility

* Supported by U. S. Public Health Service grants CA 09174 and AI 08795.

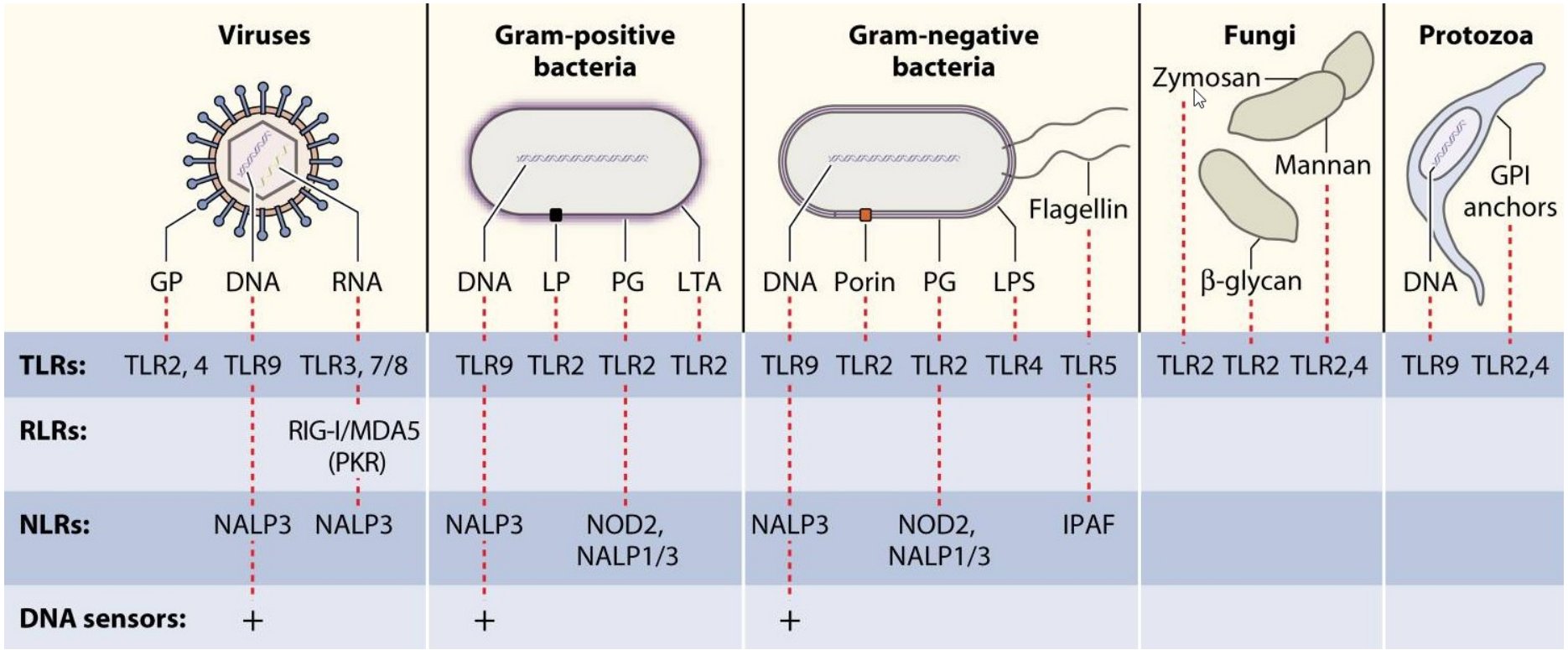
[1] *Abbreviations used in this paper*: B10, C57BL/10Sn; C, BALB/c; C.B, BALB.B; C.K., BALB.K; Con A, concanavalin A; CTL, cytotoxic T lymphocyte; H antigen, histocompatibility antigen.

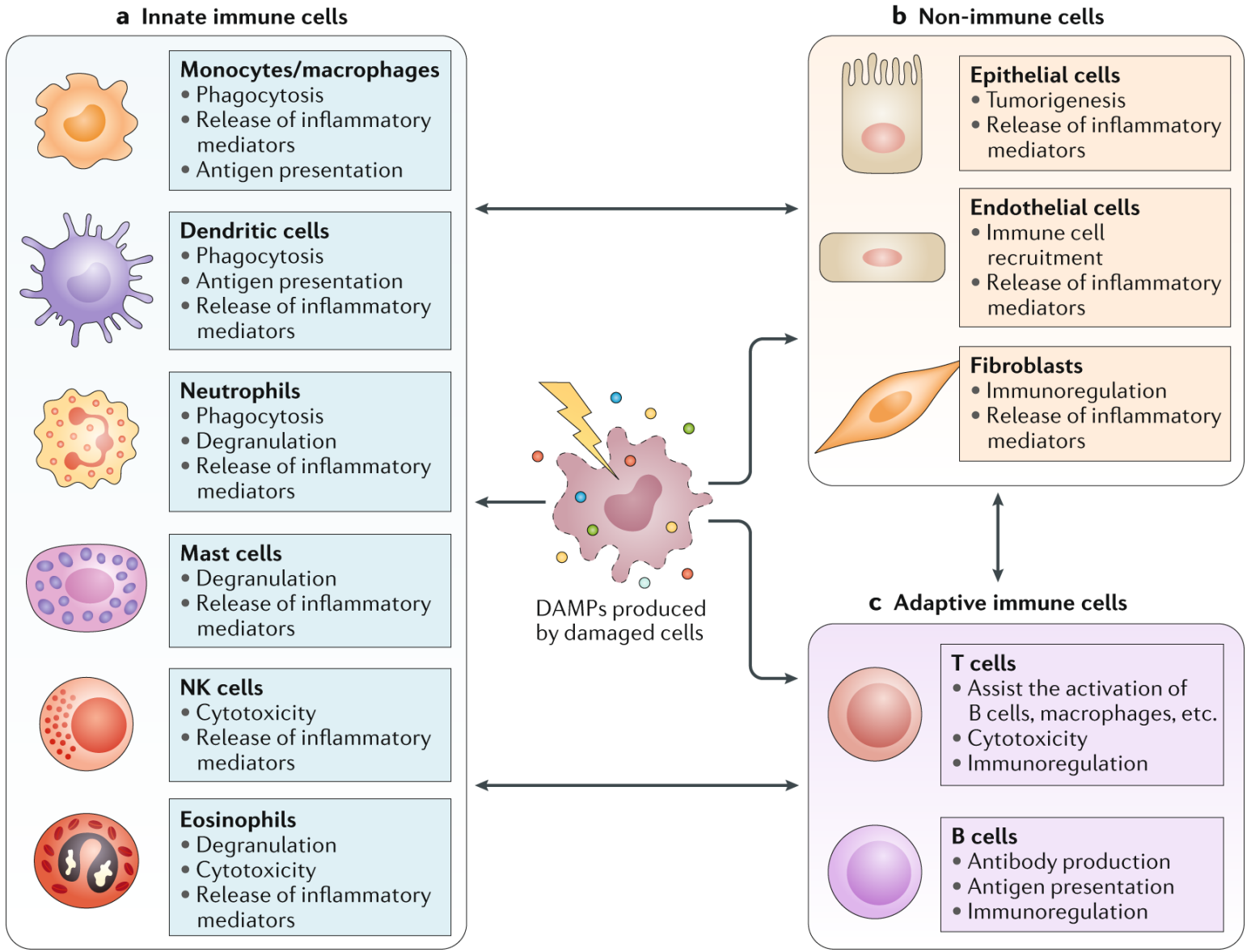
 J. EXP. MED. © The Rockefeller University Press · 0022-1007/78/0701-0084$1.00

PAMPs a DAMPs jsou rozpoznávány prostřednictvím:

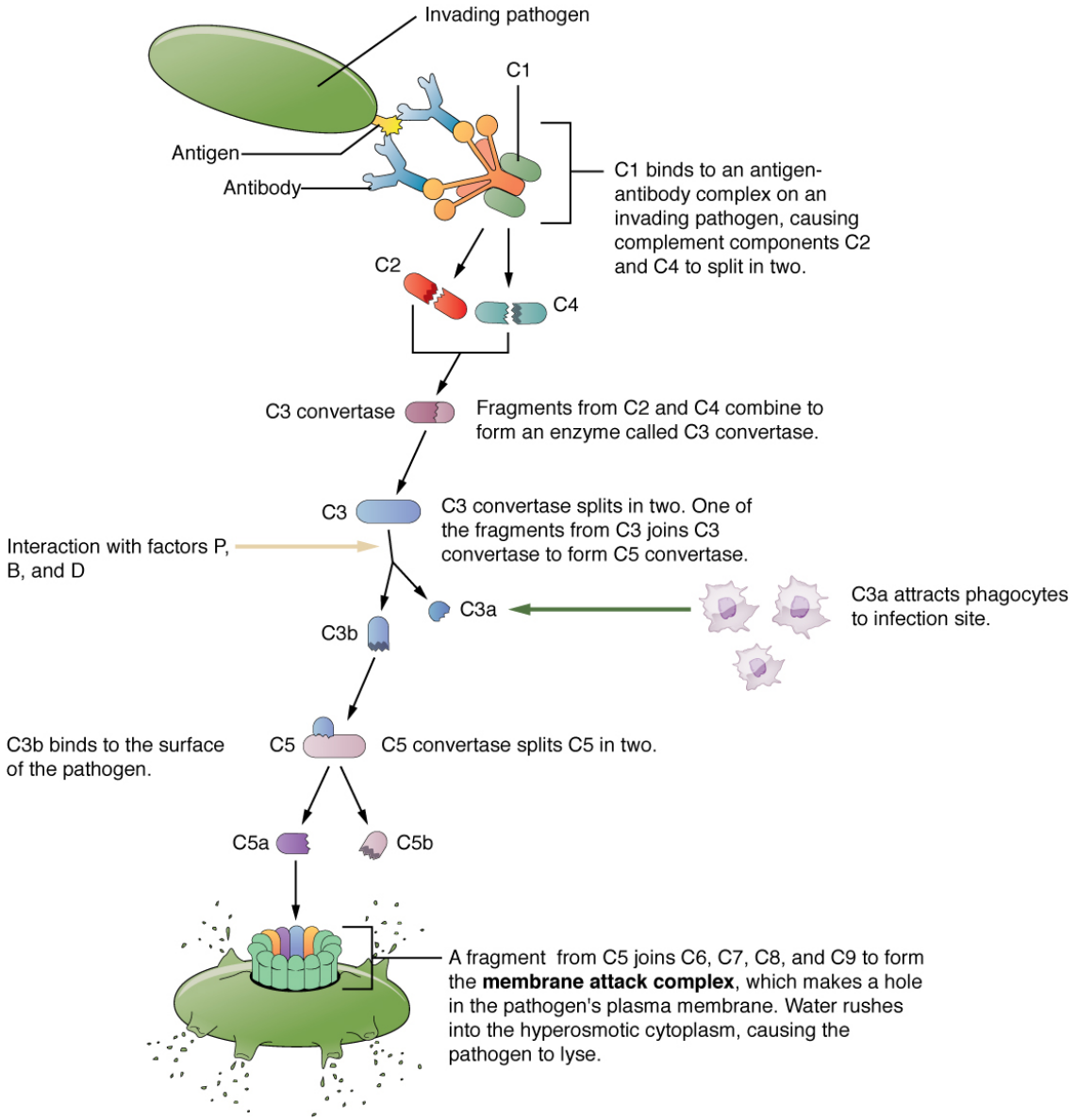
- **Pattern recognition receptory (PRRs)**
  - především na buňkách prezentujících antigen (ale i mimo buňky imunitního systému)
  - membránové Toll-like receptory (TLRs)
  - membránové C-type lectin receptory
  - cytoplazmatické retinoid acid-inducible gene I (RIG-I)-like receptory (RLRs)
  - cytoplazmatické nucleotide-binding oligomerization domain (NOD)-like receptory (NLRs)

- Po rozpoznání a navázání na receptor dochází k **aktivaci buněk** a **expresi molekul modulujících zánět** (cytokiny, chemokiny, adhezivní molekuly)
  - rychlá, relativně nespecifická reakce (minuty), bez imunologické paměti





Komplementový systém



https://upload.wikimedia.org/wikipedia/commons/0/0b/2212_Complement_Cascade_and_Function.jpg

Endotel

Udržování cévního tonu, vazoaktivita, adheze

Exprese receptorů

P-Selectin, E-selectin

ICAM, intercellular adhesion molecule

JAM, junctional adhesion molecule

PECAM1, platelet/endothelial cell adhesion molecule 1

VE-cadherin, vascular endothelial cadherin

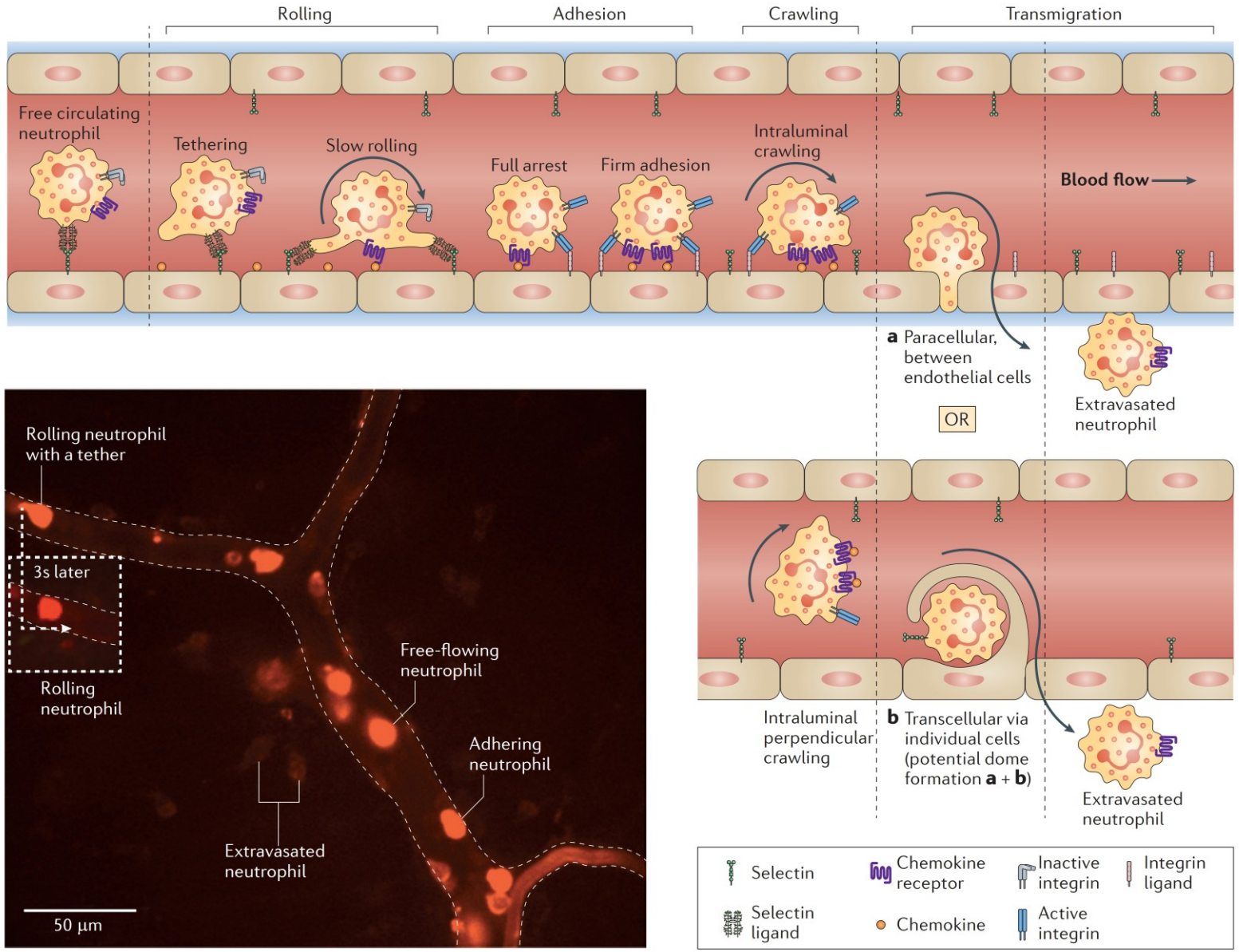
VCAM1, vascular cell adhesion protein 1

ligandy

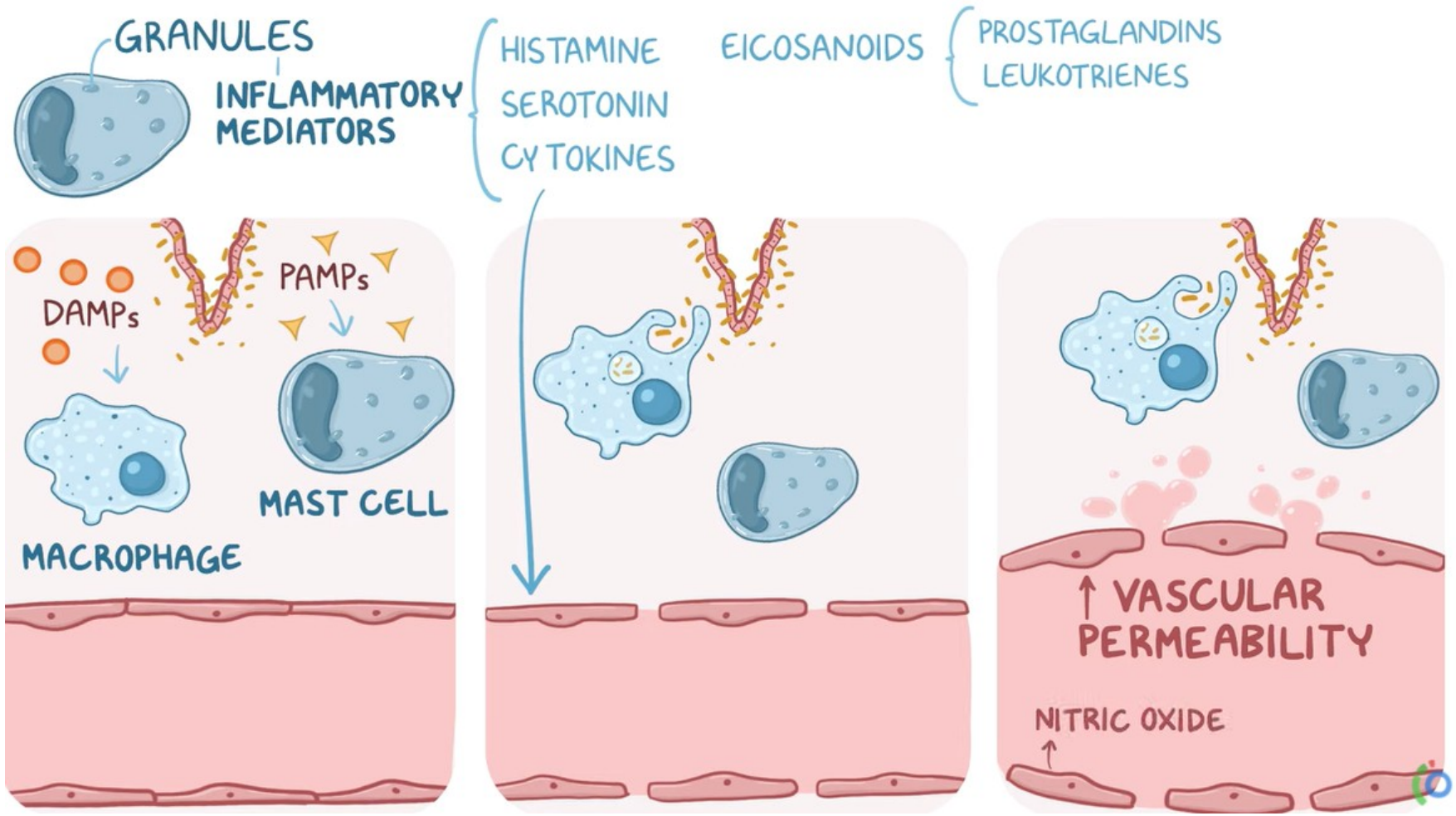
PSGL1, P-selectin glycoprotein ligand 1

LFA1, lymphocyte function-associated antigen 1

VLA4, very late antigen 4



https://www.nature.com/articles/nri3399



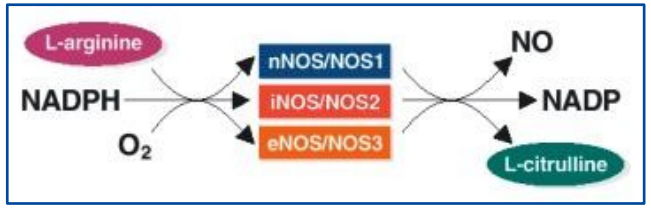
https://www.youtube.com/watch?v=LaG3nKGotZs&ab_channel=Osmosis

Regulace vazodilatace

Oxid dusnatý (NO)

klíčová role ve vazodilataci, antitrombická aktivita

Produkován **NO-syntázou**



- konstitutivní i inducibilní formy enzymu (nNOS, eNOS, iNOS)
- regulace průtoku krve cévami, difúze NO z endotelií do buněk hladké svaloviny, inhibice krevních destiček
- riziko vzniku peroxynitritu ($ONOO^-$) a oxidativního poškození okolí

Prostacyklin (PGI2)

- lipidový mediátor, syntetizován z kyseliny arachidonové (membránové fosfolipidy)
- enzym cykolooxygenáza

SCIENCE

EDITORIAL

The Molecule of the Year

The Molecule of the Year is nitric oxide, NO, a molecule of versatility and importance that has burst onto the scene in many guises. In the atmosphere it is a noxious chemical, but in the body in small controlled doses it is extraordinarily beneficial. It helps maintain blood pressure by dilating blood vessels, helps kill foreign invaders in the immune response, is a major biochemical mediator of penile erections, and is probably a major biochemical component of long-term memory. These are just a few of its many roles, which are just beginning to be discovered, and they are discussed in the accompanying Molecule of the Year story (p. 1862). That NO plays so many roles is not surprising because the same biological second messengers usually are used in many diverse systems, but a gas was indeed a surprise for an endogenous role, and a labile and toxic gas even more so. As the first surprise of such an unlikely agent was overcome, the gas as a messenger seemed logical because it could pass through biological membranes readily and oxidize foreign substances.

NO's role in sexual dysfunction, that of impotence, supports further a new liberation from old mental straitjackets. The future is sure to bring more insights into the effect on complex processes such as IQ, bad behavior, and alcoholism by single genes or chemical reactions. Many people will be happy to learn that some forms of sexual dysfunction may not be caused by psychiatric disorders or the failure of a marriage but may instead reflect a deficiency in a chemical reaction that can be compensated for by medical treatment. New research on the role of NO may also lead to new insights into the loss of memory, which is so debilitating to so many.

This year's Molecule of the Year once again shows that scientific rewards can come from pursuing unconventional thinking. The recent presidential election focused on the persistent question of providing jobs and correcting ailing economies. Hopefully, the political and social scientists advising our leaders will pursue these problems with the same creativity that characterized the research on NO. The new, the unexpected, and the incongruous will be needed to address these social problems. In addition, our elected officials as well as the general public must face unpleasant realities, including the need for the United States to work hard to maintain its standard of living in a competitive world and the need to be open-minded enough to welcome unexpected solutions such as gaseous messengers.

Every year *Science* picks a Molecule of the Year along the lines described in our editorial of 22 December 1989. Molecule is a term we use to emphasize that we are honoring the discovery rather than the people who made the discovery, not because people are unimportant but because many other awards honor the discoverers, and most discoveries involve the contributions of many people. As in the case of "people prizes," there are many "runner-up" discoveries that are extremely important to humanity but, in our opinion, are not yet quite as developed as our winner. For example, one of our runners-up, the discovery of the structure of nitrogenase, has no immediate industrial application, but the way enzymes fix nitrogen is bound to be of great importance to agriculture. As more intense farming and cheaper fuel become the necessities of the future, better mechanisms for nitrogen fixation become more important. Enzymes certainly appear to have solved the problem better than man-made solutions so far. The hope is that the enzyme mechanism and the chemical knowledge can be combined to make a new solution that will benefit millions. The widespread use of supercomputers is not a sudden event, but the increased utility of this powerful tool in industry and science for applications such as aircraft design and oil exploration will solve many problems that were previously beyond approach.

All of the runners-up are discussed in the accompanying story. This year they are an impressive group ranging from discoveries that are already being applied, such as fetal diagnosis and treatment (in utero treatment of a fetus to correct its deficiencies and transplanting fetal tissue to adults with Parkinson's disease), to those that are now far enough along so that application seems inevitable, for example, antisense RNA. In addition, there are landmarks such as the mapping of chromosomes Y and 21, which will certainly lead to medical discoveries, and the use of magnetic resonance imaging to diagnose medical problems and to locate areas of the brain identified with specific thought processes. Those who sometimes question the advances of science should think for a moment about the incredible developments that have slipped into everyday life without headlines. The Molecule of the Year and the runners-up are a good place to start for the discoveries that will inevitably make the future better than the past.

Daniel E. Koshland, Jr.

https://science.sciencemag.org/content/258/5090/1861

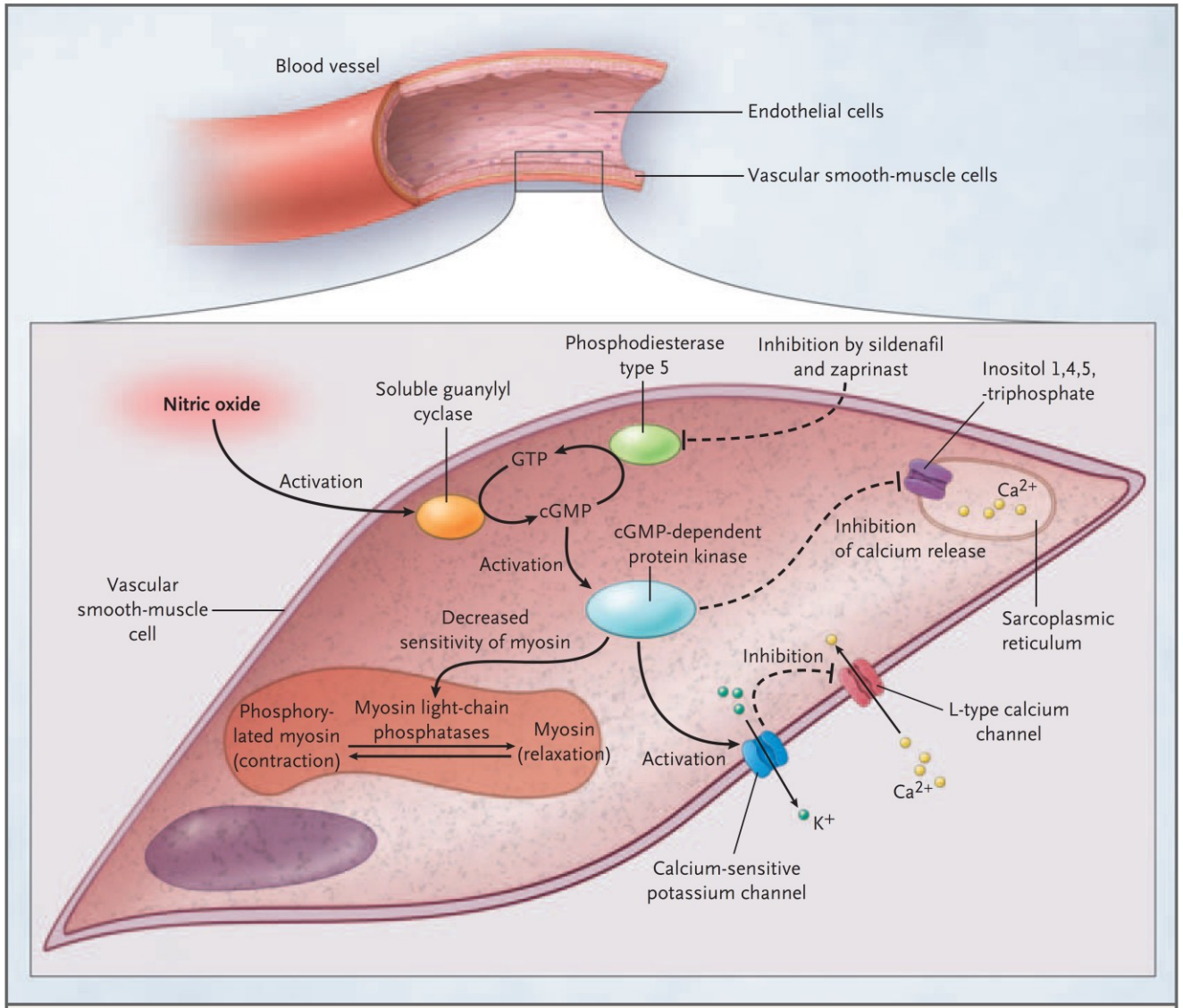


Figure 1. Regulation of the Relaxation of Vascular Smooth Muscle by Nitric Oxide.

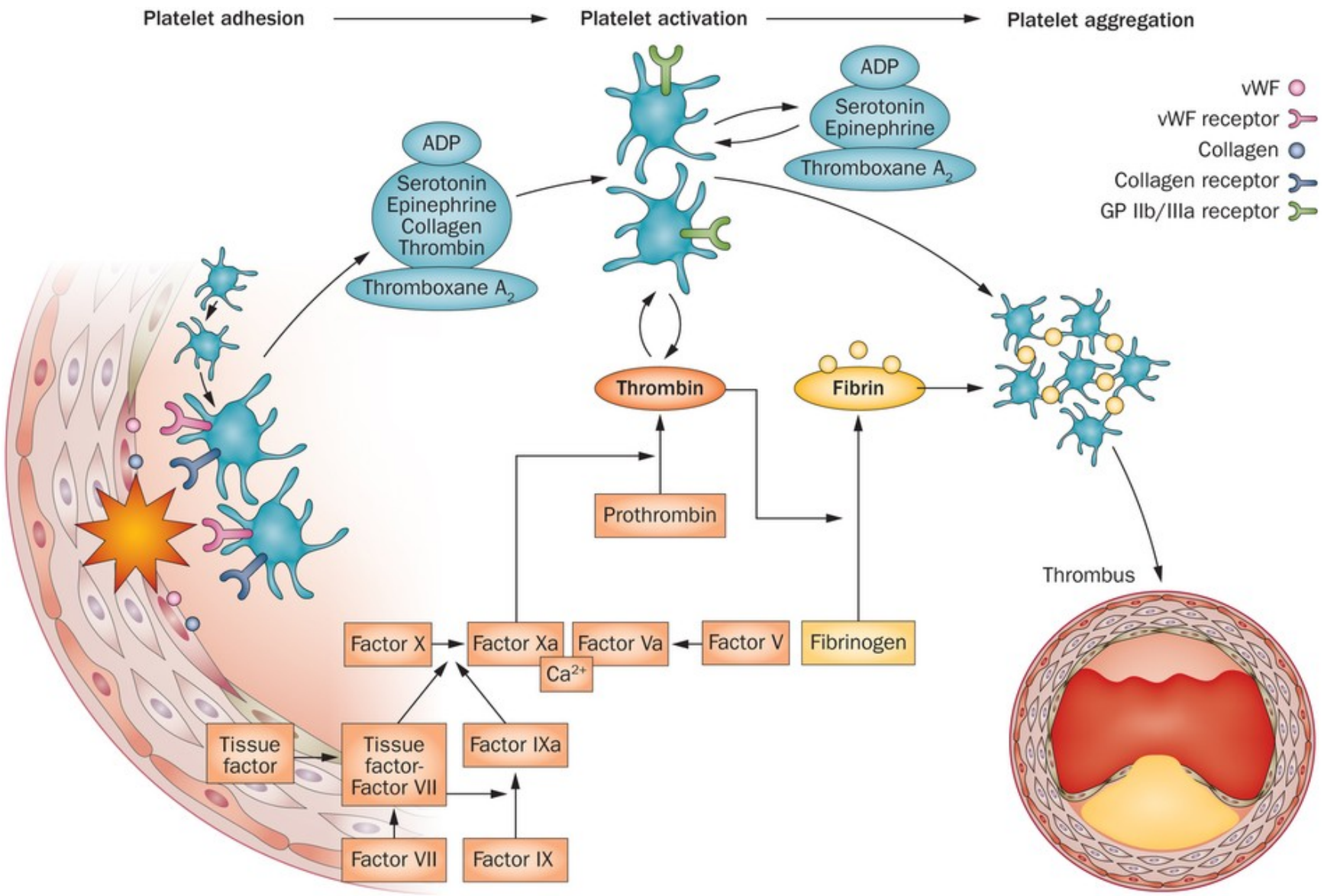
Nitric oxide activates soluble guanylyl cyclase, leading to the activation of cyclic guanosine 3′, 5′-monophosphate (cGMP)–dependent protein kinase (cGKI). In turn, cGKI decreases the sensitivity of myosin to calcium-induced contraction and lowers the intracellular calcium concentration by activating calcium-sensitive potassium channels and inhibiting the release of calcium from the sarcoplasmic reticulum. cGMP is degraded by phosphodiesterase type 5, which is inhibited by sildenafil and zaprinast. GTP denotes guanosine triphosphate.

Prozánětová a hemostatická role endotelu

vazokonstrikce, aktivace krevních destiček a plazmatického koagulačního systému

- endotelin 1
- tromboxan A2
- noradrenalin
- enzym konvertující angiotenzin (ACE), angiotenzin II
- von Willebrandův faktor (vWf)
- tkáňový faktor
- exprese membránových fosfolipidů => vhodná matrix pro aktivaci destiček a plazmatického koagulačního systému

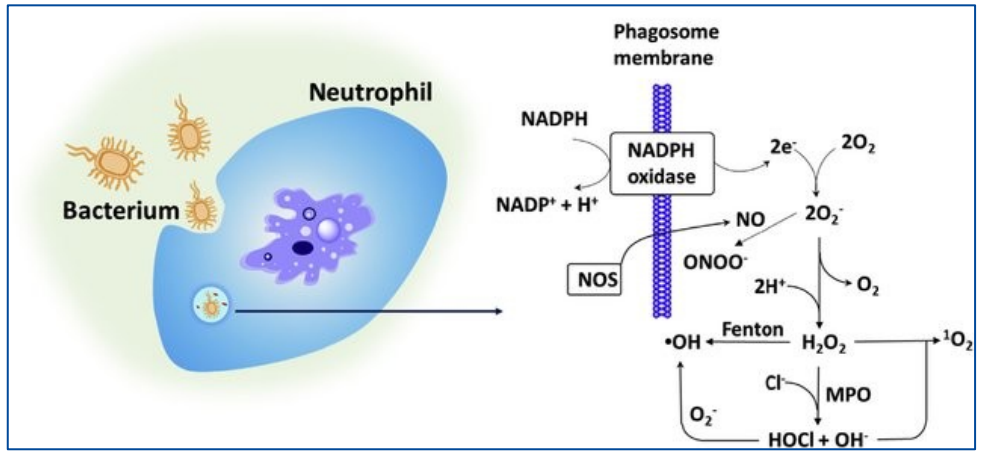
Plazmatický koagulační systém a destičky

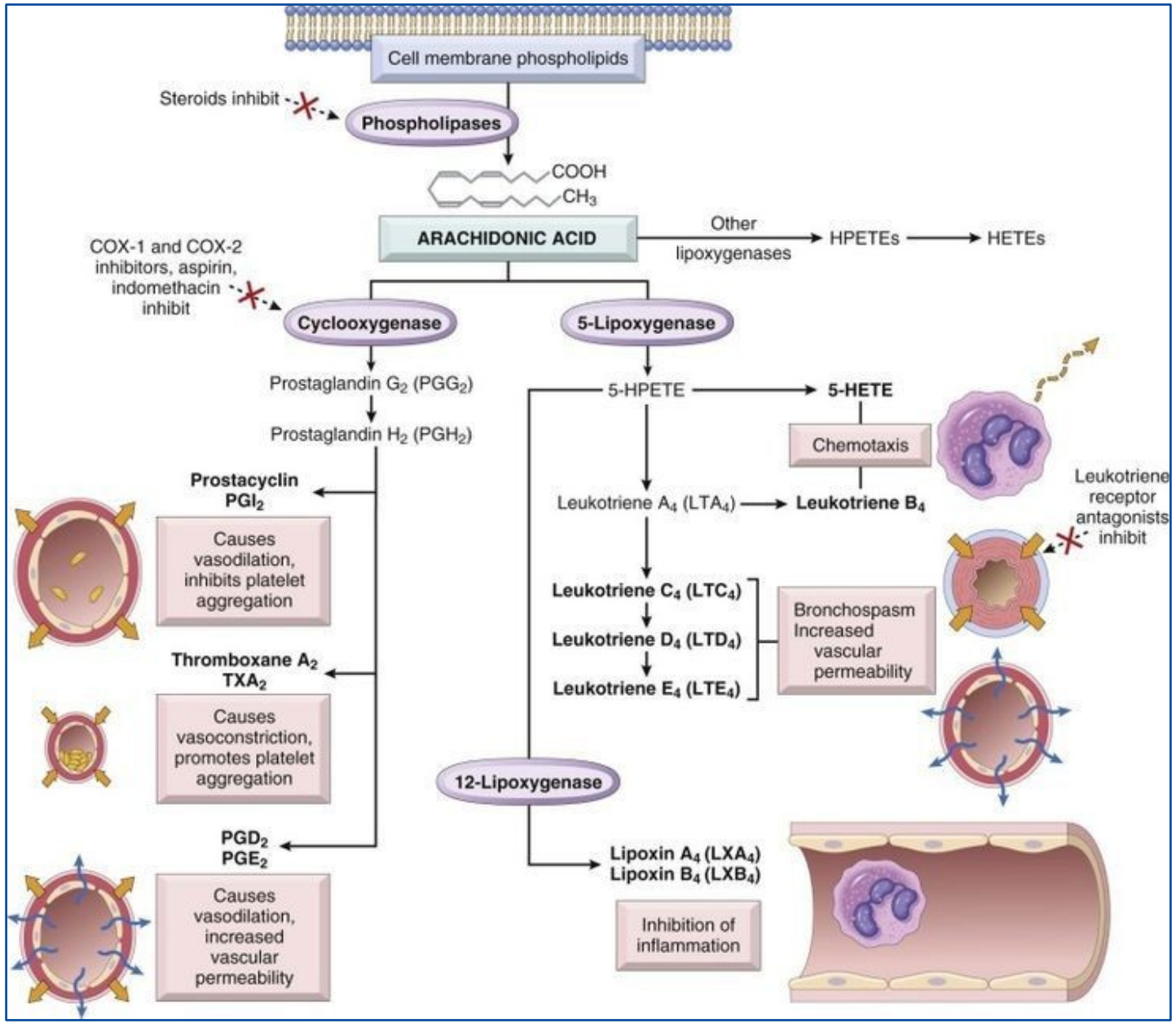


https://blog.antiaging.com/wp-content/uploads/2016/07/thrombus-evolution.jpg

Mediátory zánětu

- lipidové mediátory
- volné radikály (ROS)





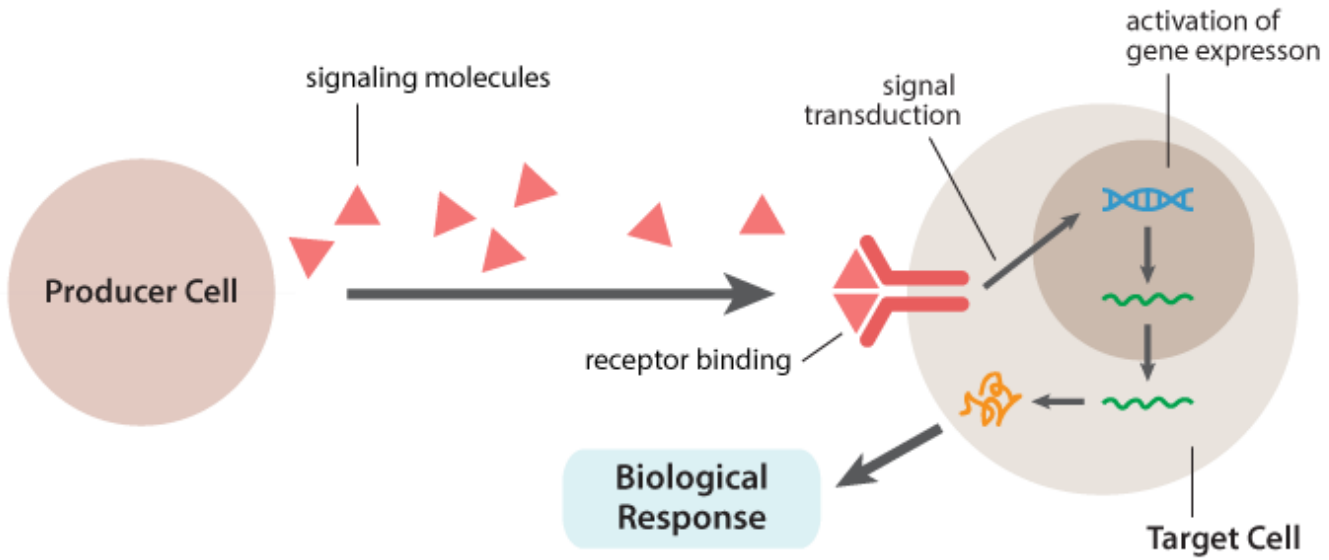
https://www.researchgate.net/publication/321466965_Bioanalytical_Methods_for_Hypochlorous_Acid_Detection_Recent_Advances_and_Challenges/figures?lo=1

Mediátory zánětu

Cytokiny

Různorodá skupina malých proteinů secernovaných za účelem komunikace mezi buňkami

- Autokrinní, parakrinní a endokrinní účinky
- Působení v překrývajících se sítích, redundance, často pleiotropní efekty, závislé na buněčném kontextu



https://old.abmgood.com/marketing/knowledge_base/growth_factors_cytokines_introduction.php

- **Interferony**

  Regulace nespecifické imunity, antivirové a antiproliferativní účinky (IFNα, IFNβ, IFNγ, IFNλ)

- **Interleukiny**

  Růst a diferenciace leukocytů (IL-1, IL-6, IL-12, IL-17, IL-18, IL-4, IL-10, IL-11, IL-13)

- **Chemokiny**

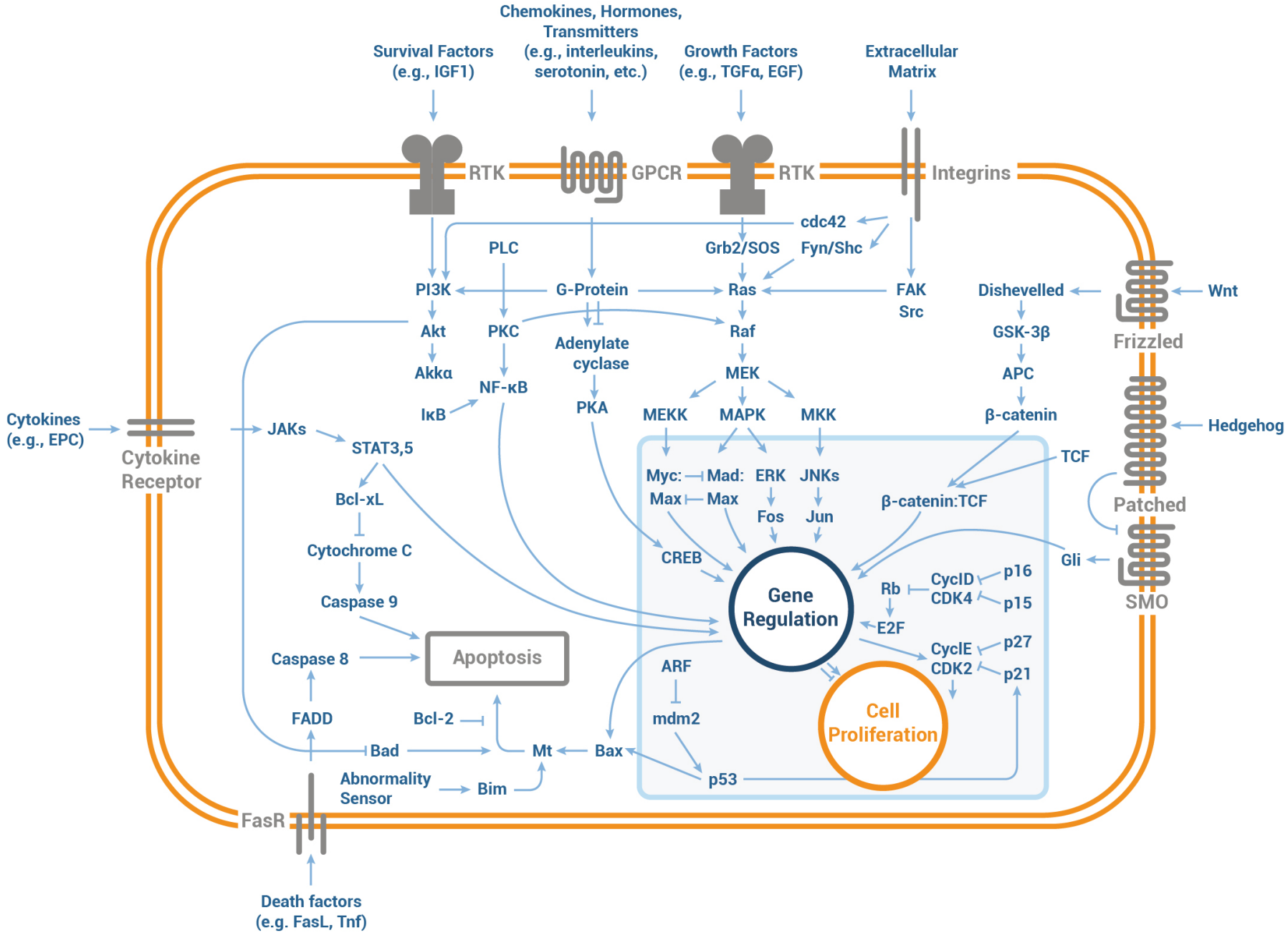
  Chemotaxe (IL-8, MCP1, RANTES)

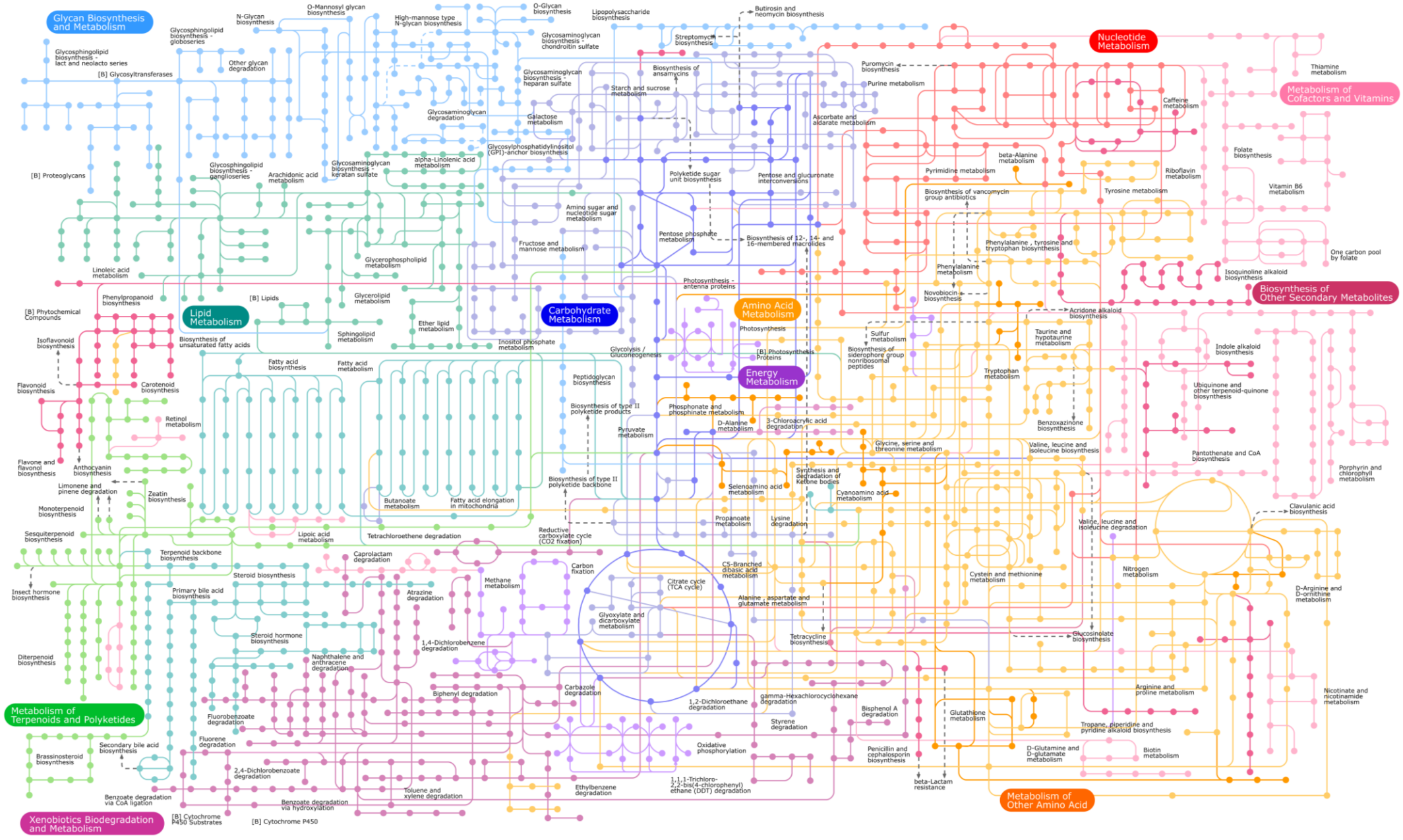
- **Kolonie stimulující faktory**

  Stimulace progenitorů, podpora růstu a diferenciace (M-CSF, GM-CSF, G-CSF)

- **Tumor nekrotizující faktory**

  Prozánětlivé působení, aktivace cytotoxických T lymfocytů (TNFα, TNFβ)





Systémový zánět, souhra působení inzultu a cytokinů

SIRS (syndrom systémové zánětové odpovědi, systemic inflammatory response syndrome)

- teplota nad 38 °C nebo pod 36 °C
- tep nad 90/min
- dechová frekvence nad 20/min nebo CO2 pod 32 mmHg
- leukocyty nad 12 tis./µl nebo pod 4 tis./µl nebo víc jak 10 % nezralých forem

Sepse

SIRS z infekčních příčin

(i původně neinfekční rozvinutý SIRS zpravidla přechází v sepsi – selhání mikrocirkulace střevní stěny, proniknutí bakterií do cirkulace)

MODS (syndrom multiorgánového selhání, Multiple organ dysfunction syndrome)

přítomnost takových změn orgánových funkcí že homeostáza nemůže být udržena bez intervence

- primární MODS – přímé působení inzultu (těžké trauma, cirkulační selhání)
- sekundární MODS – autoagresivní působení zánětu

Syndrom akutní dechové tísně (ARDS, acute respiratory distress syndrome, adult respiratory distress syndrome)

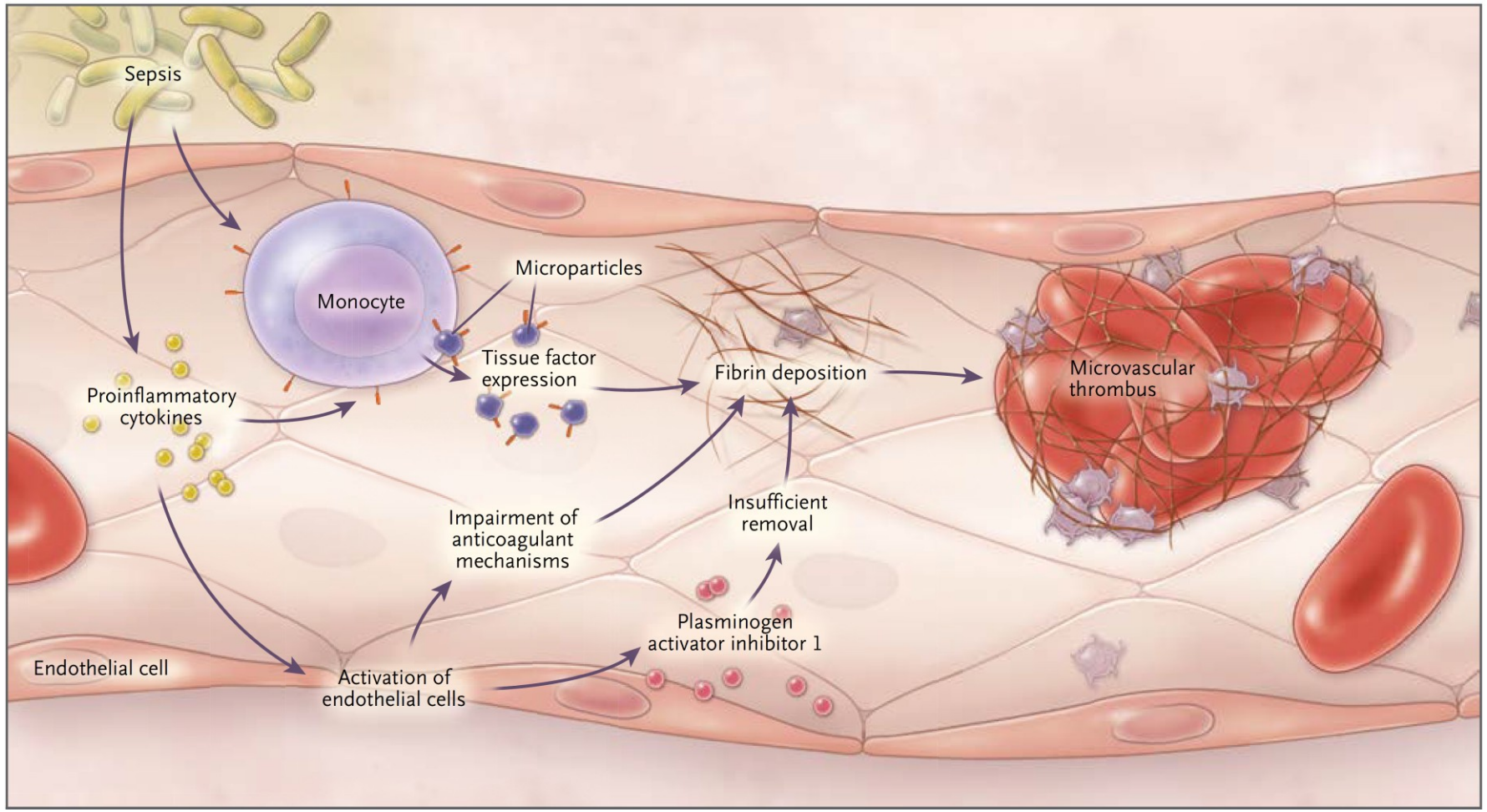
- zvýšená propustnost plicních kapilár
- akumulace tekutiny v parenchymu a alveolech
- poškození epitelu alveolů

https://www.ncbi.nlm.nih.gov/books/NBK547669/

Diseminovaná intravaskulární koagulace (DIC)

systémová aktivace koagulace (infekce, trauma, nádory, porodní komplikace, postransfusní reakce)

- intravaskulární depozice fibrinu => trombózy, ischemie a orgánová selhání
- vyčerpání destiček a koagulačních faktorů => krvácení



https://www.nejm.org/doi/10.1056/NEJMra1208626

Cytokiny se bouří…

„…while the general concept of an excessive or uncontrolled release of proinflammatory cytokines is well known, an actual definition of what constitutes a cytokine storm is lacking…“

cytokinová bouře (hypercytokinemie)

- deregulace působení prozánětlivých cytokinů
- systémové působení vedoucí k MODS

ORIGINAL ARTICLE BRIEF REPORT

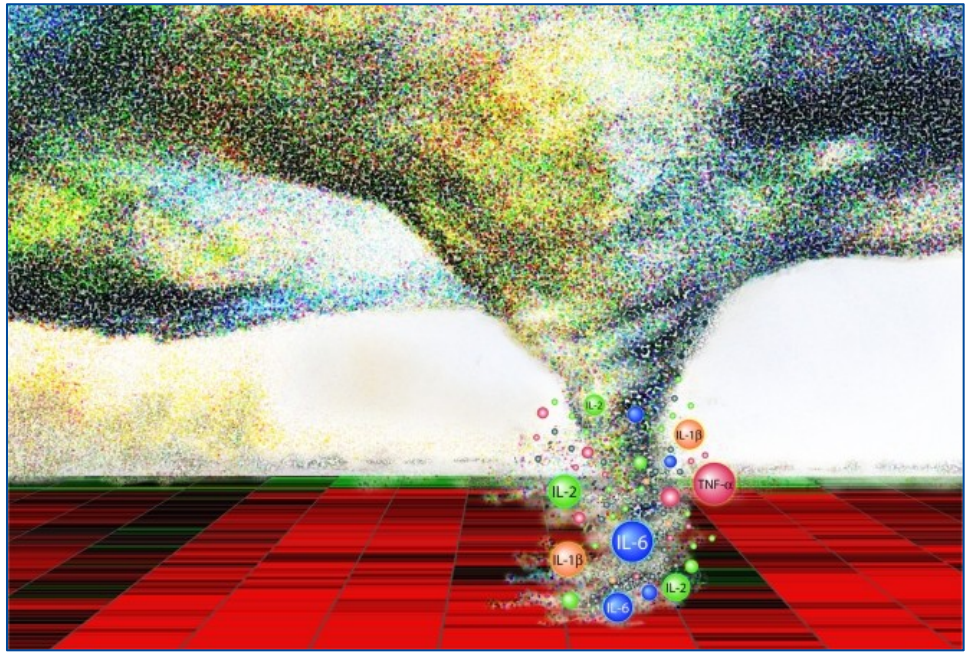
Shock and Multiple-Organ Dysfunction after Self-Administration of Salmonella Endotoxin

Angelo M. Taveira da Silva, Helen C. Kaulbach, Francis S. Chuidian, David R. Lambert, Anthony F. Suffredini, and Robert L. Danner

ORIGINAL ARTICLE BRIEF REPORT

Cytokine Storm in a Phase 1 Trial of the Anti-CD28 Monoclonal Antibody TGN1412

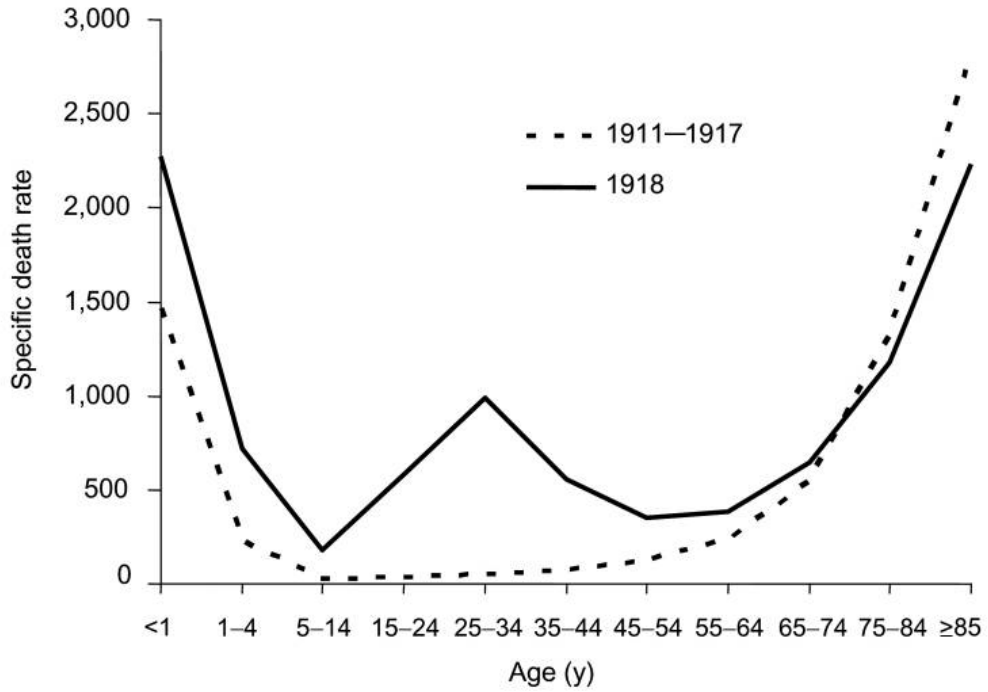
1 hour – simultaneously, the six men begin suffering excruciating headaches, shivering, back pain, gut pain, diarrhoea, swelling and nausea
4 hrs – all have fevers, are flushed, their blood pressure drops dangerously low and their hearts start to race. Blood tests show their lymphocytes and monocytes are fast vanishing.
5 hrs – one patient begins fighting for his breath. All suffer lung pain. They are all given steroids and other medications to ease inflammation.
12 hrs – the patient fighting for his breath is so bad that he has to be taken into intensive care and put on a ventilator to keep him alive. Suntharalingam decides to take all the volunteers into intensive care as a precaution.
24 hrs – two people are on ventilators, and the four others need support with breathing.
48 hrs – the four least affected men start to recover, but all six begin to suffer multi-organ failure, and have to be attached to kidney machines…



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3294426/

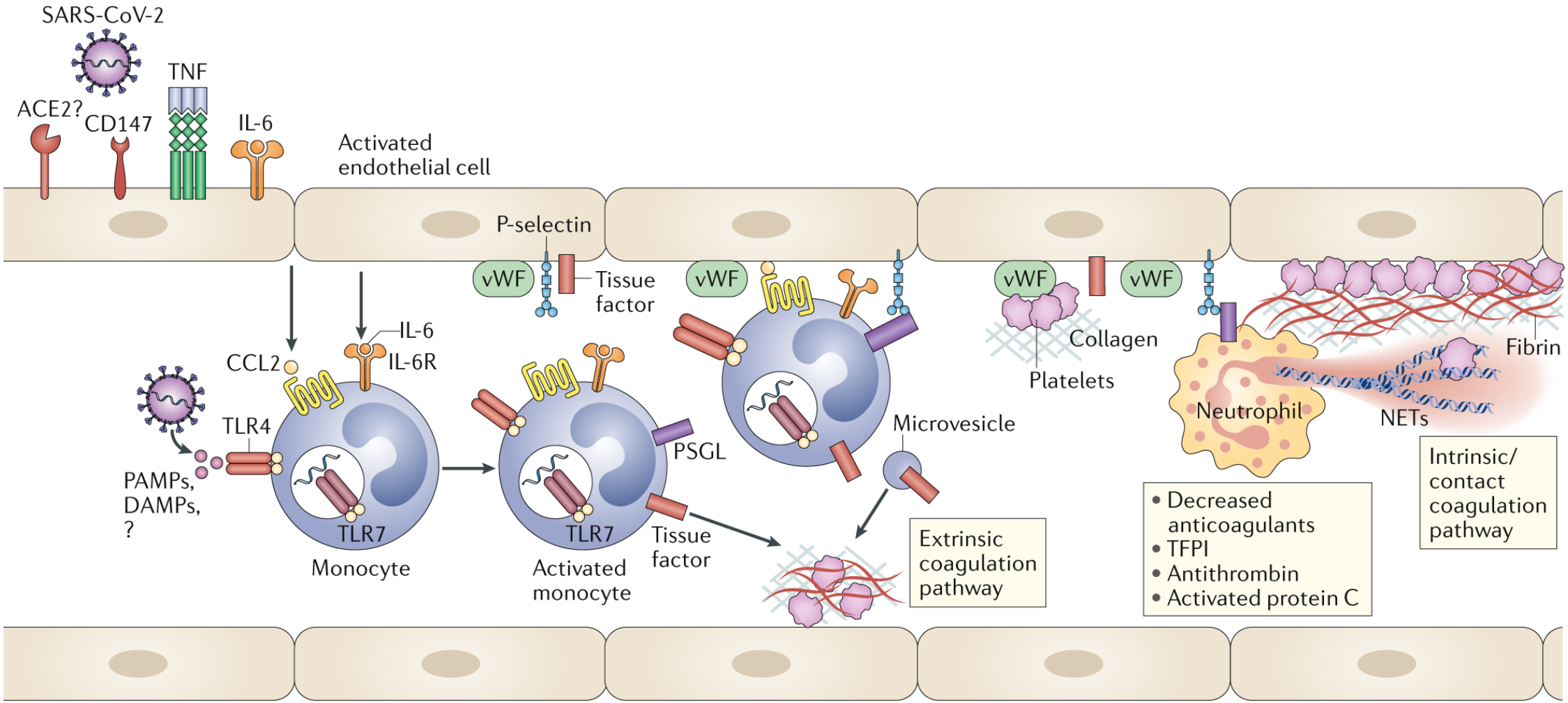
Co stojí za náchylností k cytokinové bouři?

- hyperfunkční varianty Toll-like receptorů (TLR1, TLR4)?
- polymorfismy v SOCS (supresory cytokinové signalizace)?
- original antigenic sin?
- imunosenescence, Inflamm-aging
- environmentální faktory?
- vitamin D status?
- Something Completely Different?

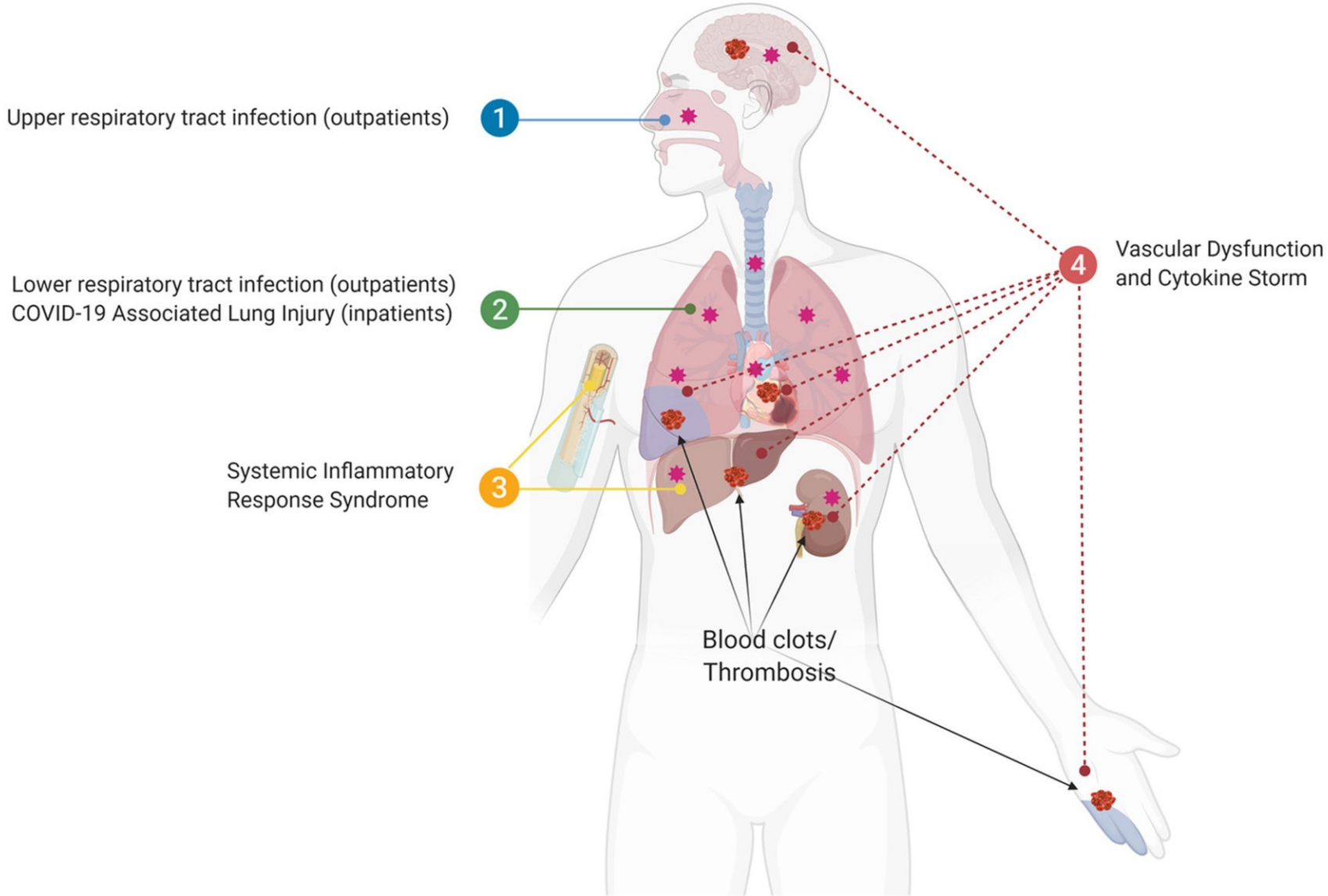


https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3291398/

SARS-CoV-2 koagulopatie

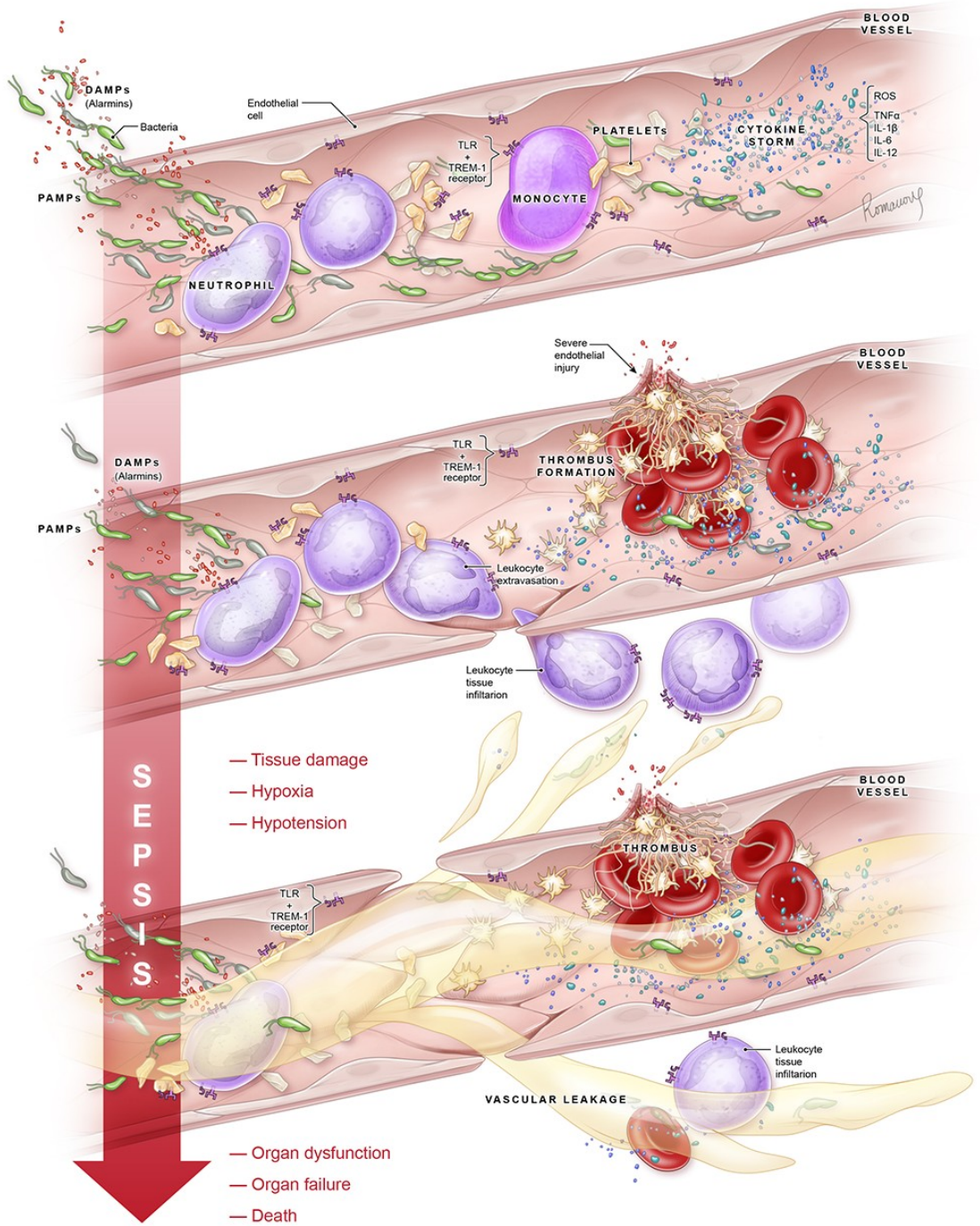


https://www.nature.com/articles/s41577-020-0331-4/figures/2



https://www.frontiersin.org/files/Articles/564628/fimmu-11-01626-HTML/image_m/fimmu-11-01626-g001.jpg

Sepse



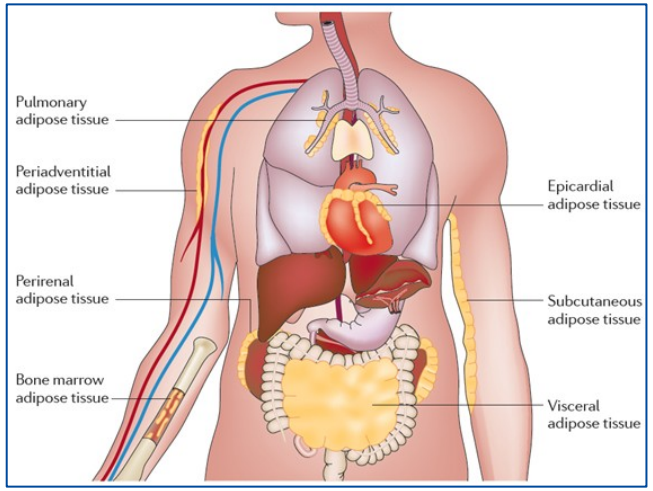
https://mariaromanova.org/illustration.html#gallery-3

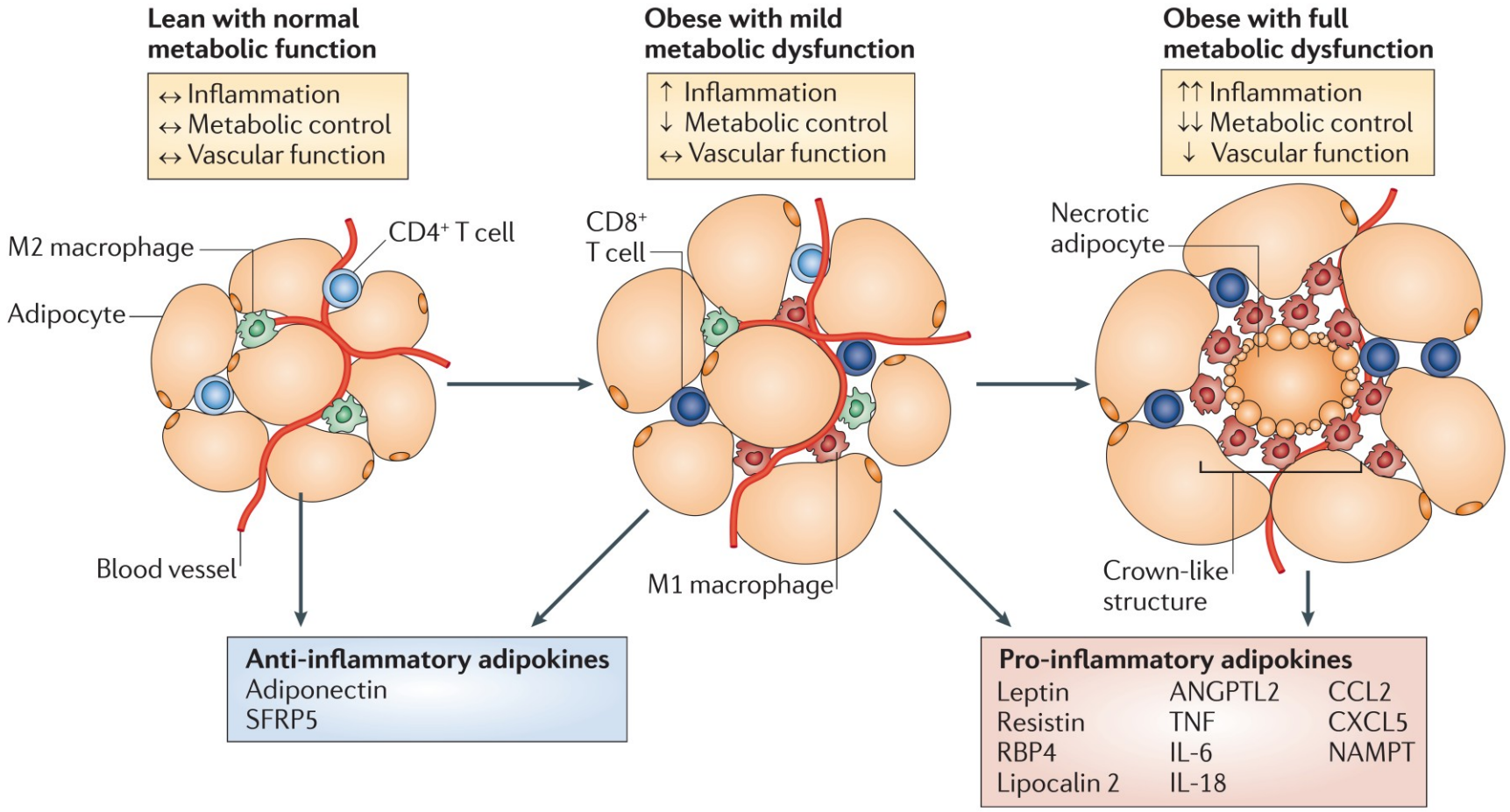
Chronický zánět

- perzistující infekce (TBC, Syfilis, Lepra)
- prolongovaná expozice iritantům
- opakované akutní záněty
- primárně chronický zánět – nízce virulentní agens, sterilní zánět (silikóza)
- autoimunitní záněty (trvalé ukládání imunokomplexů)
- neznámé příčiny

Chronický zánět

obezita jako chronický zánětlivý stav





https://www.semanticscholar.org/paper/Adipokines-in-inflammation-and-metabolic-disease-Ouchi-Parker/b409ed2312330ef9a123f5eb700e93537ee9c21c/figure/3

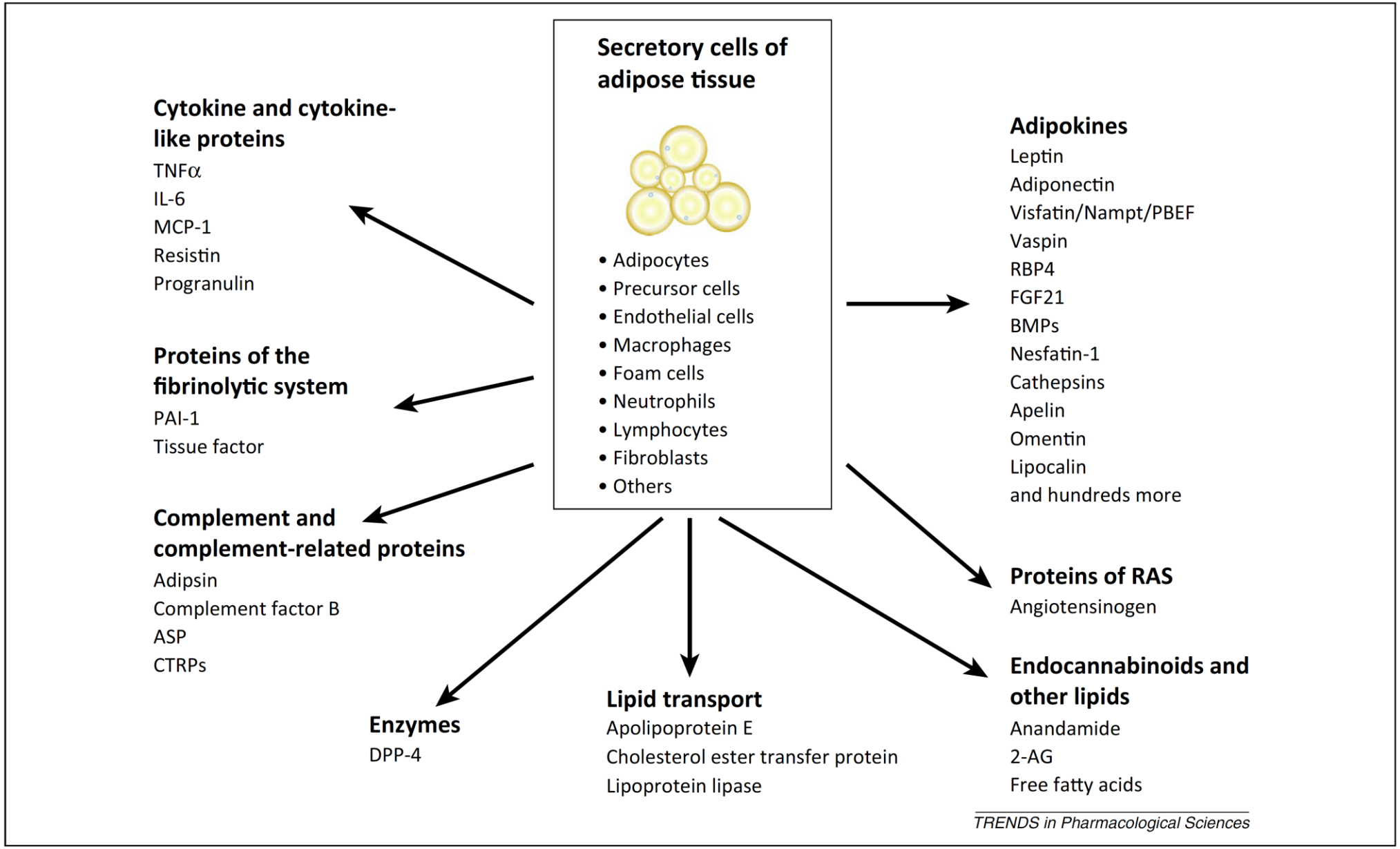


Figure 1. Factors released or secreted by adipose tissue. Adipocytes, immune cells, fibroblasts, endothelial cells, and others contribute to the release of metabolites, lipids, and adipokines. Examples of adipose tissue-derived molecules are provided here. Abbreviations: 2-AG, 2-Arachidonoylglycerol; ASP, acylating simulation protein; BMPs, bone morphogenetic proteins; CTRPs, C1q/TNF-related proteins; FGF21, fibroblast growth factor 21; MCP-1, monocyte chemotactic protein-1; PAI-1, plasminogen activator inhibitor-1; RAS, renin angiotensin system; RBP4, retinol binding protein 4. Modified from [3,5,6].

Chronický zánět asociovaný s rakovinou

více než 20% malignit je asociováno s chronickým zánětem a infekcemi

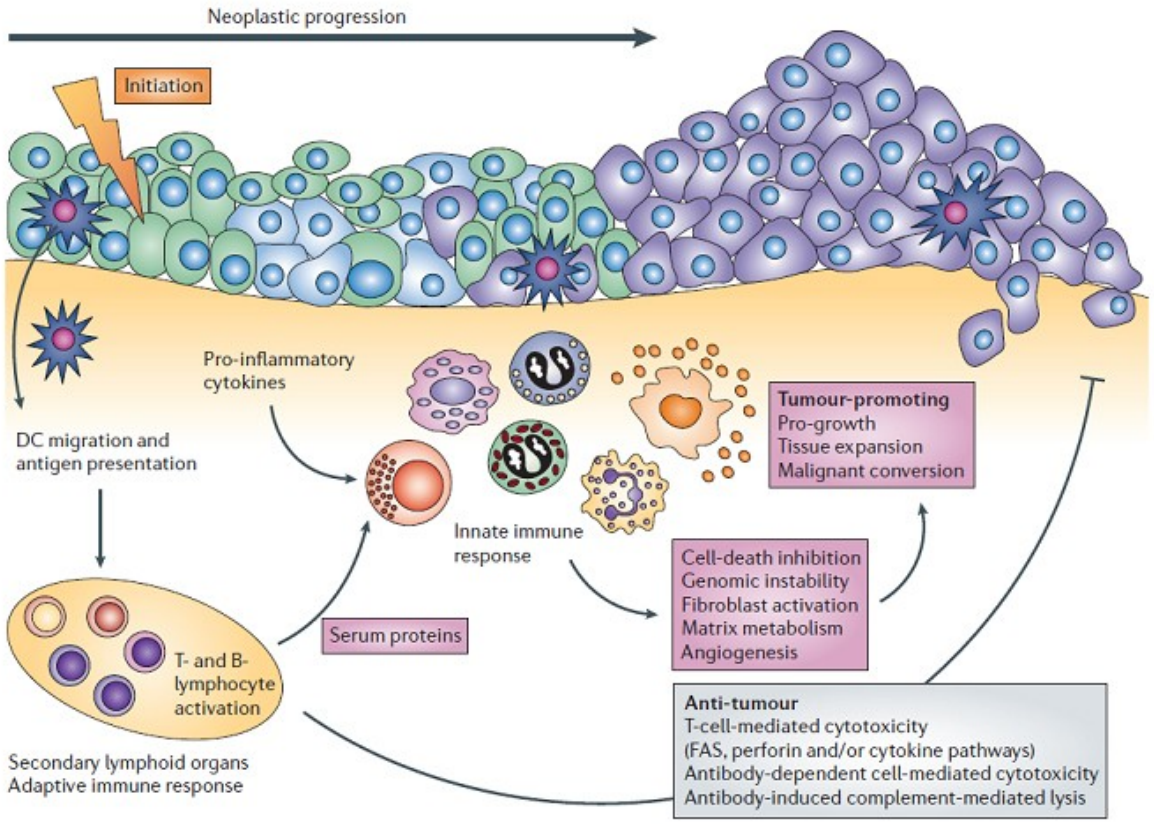
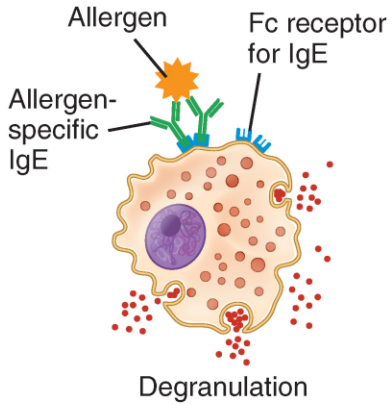


Table 1 **Chronic inflammatory conditions associated with neoplasms**

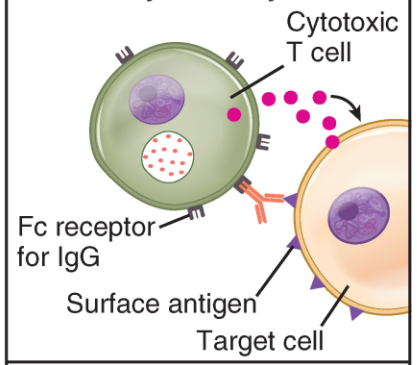
Pathologic condition	Associated neoplasm(s)	Aetiologic agent
Asbestosis, silicosis	Mesothelioma, lung carcinoma	Asbestos fibres, silica particles
Bronchitis	Lung carcinoma	Silica, asbestos, smoking (nitrosamines, peroxides)
Cystitis, bladder inflammation	Bladder carcinoma	Chronic indwelling, urinary catheters
Gingivitis, lichen planus	Oral squamous cell carcinoma	
Inflammatory bowel disease, Crohn's disease, chronic ulcerative colitis	Colorectal carcinoma	
Lichen sclerosus	Vulvar squamous cell carcinoma	
Chronic pancreatitis, hereditary pancreatitis	Pancreatic carcinoma	Alcholism, mutation in trypsinogen gene on Ch. 7
Reflux oesophagitis, Barrett's oesophagus	Oesophageal carcinoma	Gastric acids
Sialadenitis	Salivary gland carcinoma	
Sjögren syndrome, Hashimoto's thyroiditis	MALT lymphoma	
Skin inflammation	Melanoma	Ultraviolet light
Cancers associated with infectious agents		
Opisthorchis, Cholangitis	Cholangiosarcoma, colon carcnoma	Liver flukes (*Opisthorchis viverrini*), bile acids
Chronic cholecystitis	Gall bladder cancer	Bacteria, gall bladder stones
Gastritis/ulcers	Gastric adenocarcinoma, MALT	*Helicobacter pylori*
Hepatitis	Hepatocellular carcinoma	Hepatitis B and/or C virus
Mononucleosis	B-cell non-Hodgkin's lymphoma, Burkitts lymphoma,	Epstein-Barr Virus
AIDS	Non-Hodgkin's lymphoma, squamous cell carcinomas, Kaposi's sarcoma	Human immunodeficiency virus, human herpesvirus type 8
Osteomyelitis	Skin carcinoma in draining sinuses	Bacterial infection
Pelvic inflammatory disease, chronic cervicitis	Ovarian carcinoma, cervical/anal carcinoma	Gonnorrhoea, chlamydia, human papillomavirus
Chronic cystitis	Bladder, liver, rectal carcinoma, follicular lymphoma of the spleen	Schistosomiasis

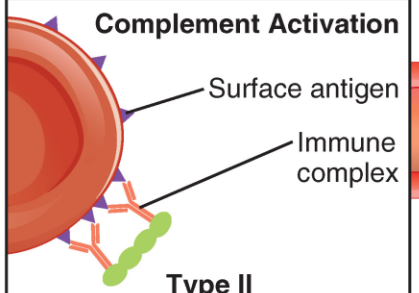
https://www.nature.com/articles/nature01322
https://www.astro.org/Patient-Care-and-Research/Research/Professional-Development/Research-Primers/Tumor-Immune-Interactions

Hypersenzitivita

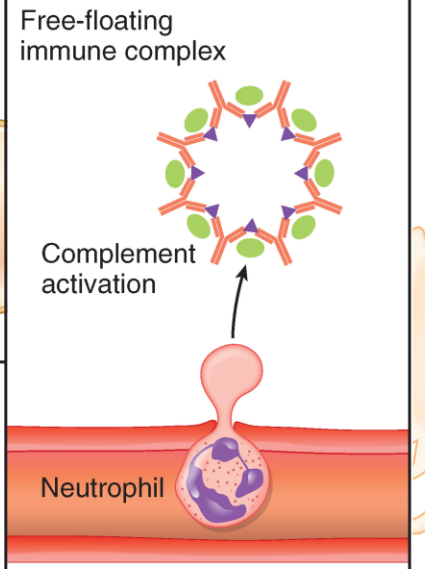


Type I

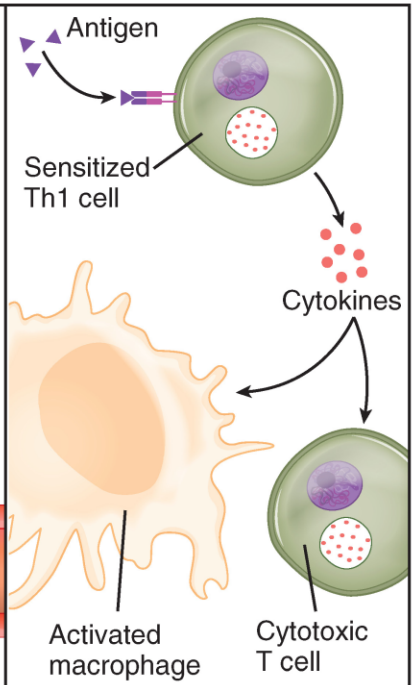




Type II



Type III



Type IV

IgE-Mediated Hypersensitivity	IgG-Mediated Cytotoxic Hypersensitivity	Immune Complex-Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
IgE is bound to mast cells via its Fc portion. When an allergen binds to these antibodies, crosslinking of IgE induces degranulation.	Cells are destroyed by bound antibody, either by activation of complement or by a cytotoxic T cell with an Fc receptor for the antibody (ADCC)	Antigen–antibody complexes are deposited in tissues, causing activation of complement, which attracts neutrophils to the site	Th1 cells secrete cytokines, which activate macrophages and cytotoxic T cells and can cause macrophage accumulation at the site
Causes localized and systemic anaphylaxis, seasonal allergies including hay fever, food allergies such as those to shellfish and peanuts, hives, and eczema	Red blood cells destroyed by complement and antibody during a transfusion of mismatched blood type or during erythroblastosis fetalis	Most common forms of immune complex disease are seen in glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus	Most common forms are contact dermatitis, tuberculin reaction, autoimmune diseases such as diabetes mellitus type I, multiple sclerosis, and rheumatoid arthritis

https://upload.wikimedia.org/wikipedia/commons/f/fe/2228_Immune_Hypersensitivity_new.jpg

Hypersenzitivita - souhrn

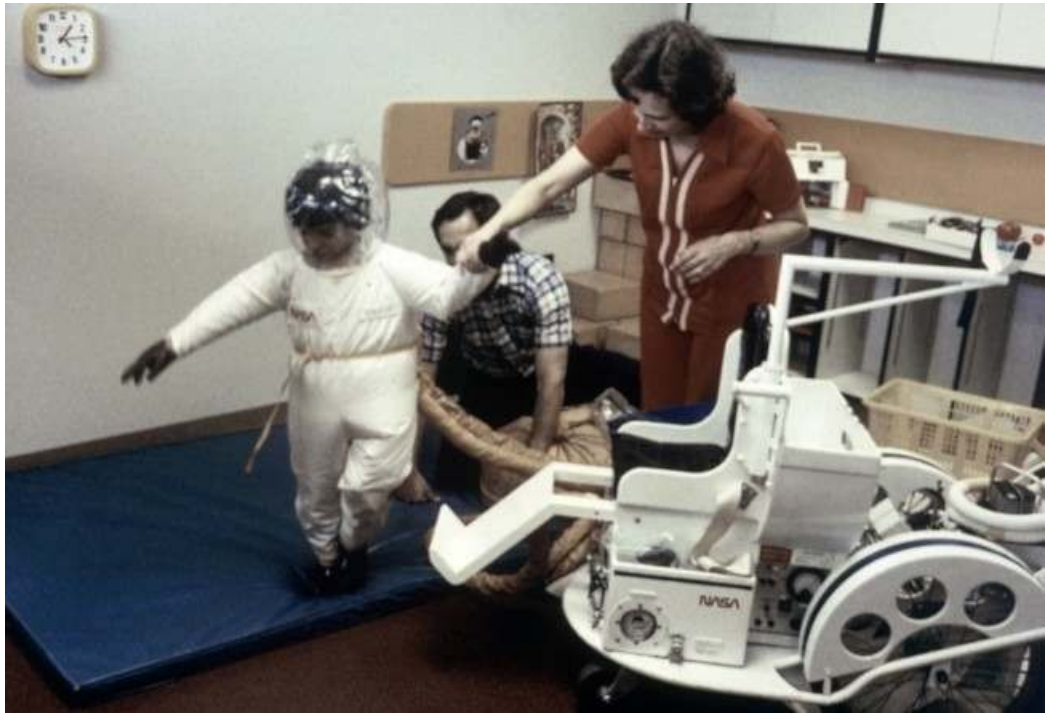
	Type I	Type II	Type III	Type IV
Mediators	IgE	IgG/ IgM	Antigen-antibody complex	T cells
Antigen form	Soluble antigen	Cell-bound antigen	Soluble antigen	Soluble/cell bound antigen
Mechanism of action	Allergen-specific IgE causes mast-cell degranulation releasing histamine and other inflammatory mediators	IgG/IgM antibodies bind to cell antigens, leading to complement activation and destruction of the cell	Antigen-antibody complexes are deposited in tissues where they activate complement chain causing local inflammation and recruitment of leucocytes	Antigen-presenting cells activate Th1/cytotoxic T cells. T-cells recruit macrophages and release inflammatory cytokines
Time course	Immediate-phase: minutes Late-phase: 8-12 hours	Hours to days	Hours to days	Days (delayed)
Examples	• Anaphylaxis • Hay fever • Food allergies • Drug allergies • Eczema • Asthma	• Acute transfusion reaction • Haemolytic disease of the newborn	• Rheumatoid arthritis • Post-streptococcal glomerulonephritis • Systemic lupus erythematosus	• Contact dermatitis • Tuberculin test • Graft rejection

https://www.grepmed.com/images/10267/physiology-overview

Imunodeficience

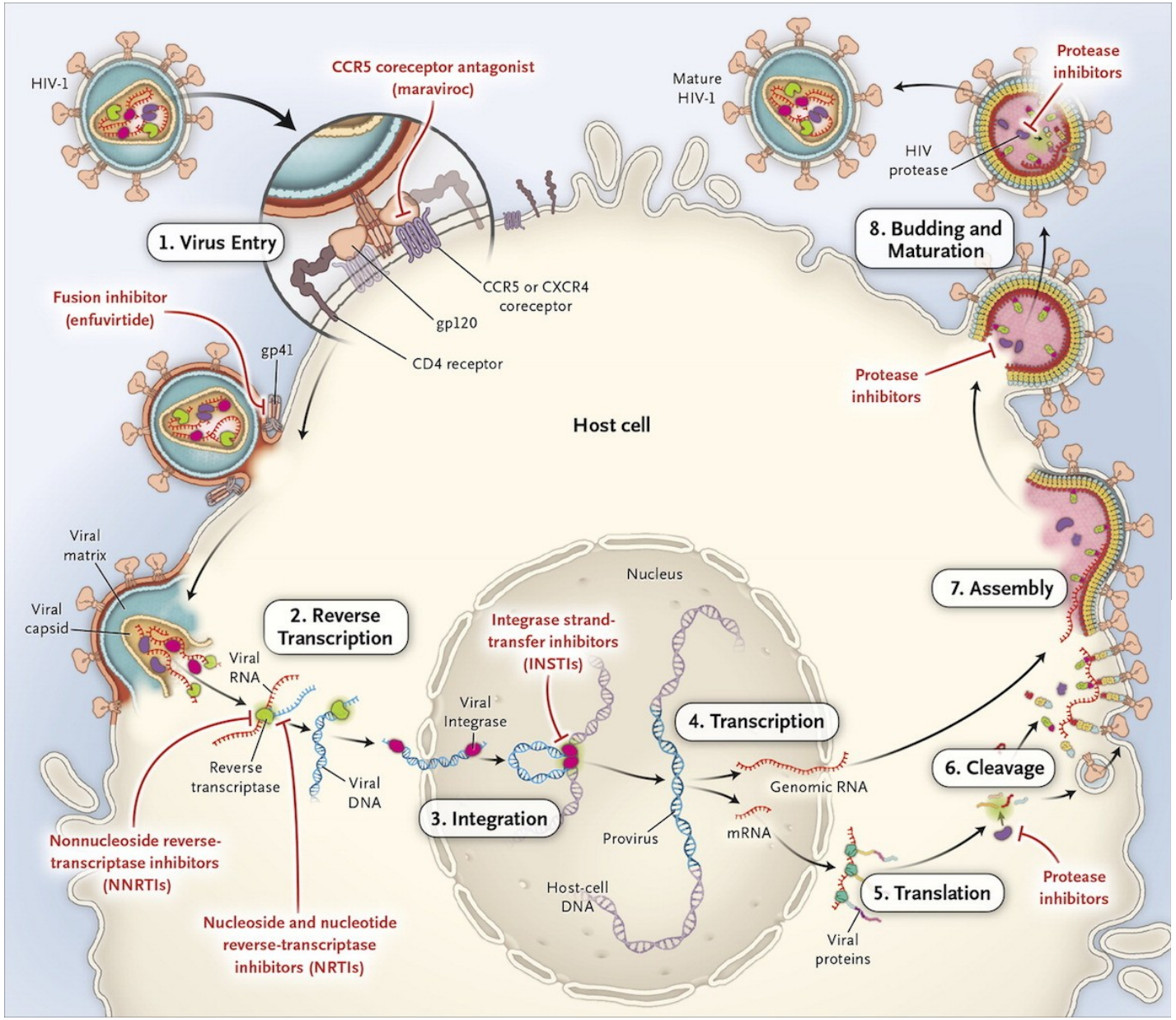
1. Primární (vrozené)
    - Geneticky podmíněné vznikající jako následek mutací
2. Sekundární (získané)

- Defekty specifické imunity – poruchy T-lymfocytů a B-lymfocytů (porucha tvorby protilátek) (případně obojího => **SCID**)
- Defekty nespecifické imunity – poruchy fagocytózy, komplementu, NK buněk.
- Imunodeficity sdružené s jinými vrozenými syndromy

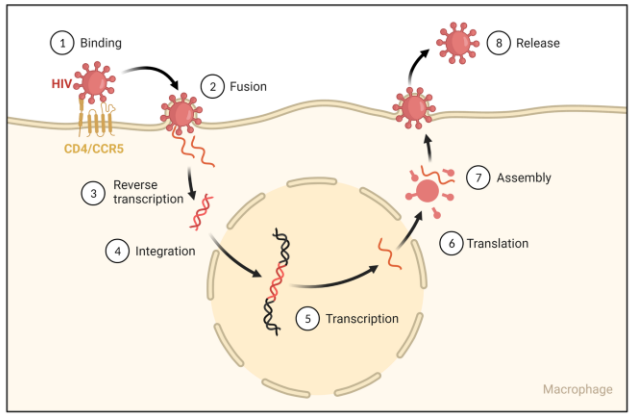


https://flashbak.com/david-vetter-was-the-boy-in-the-bubble-1971-1984-4175/

HIV/AIDS



HIV Mechanism of Infection



https://www.hiv.uw.edu/go/antiretroviral-therapy/general-information/core-concept/all