

# Membrány a lipidy (modulace cytokinetiky)

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**Institute of Biophysics, Brno**  
**Academy of Sciences**  
**Czech Republic**

## The four families of small organic molecules in cells

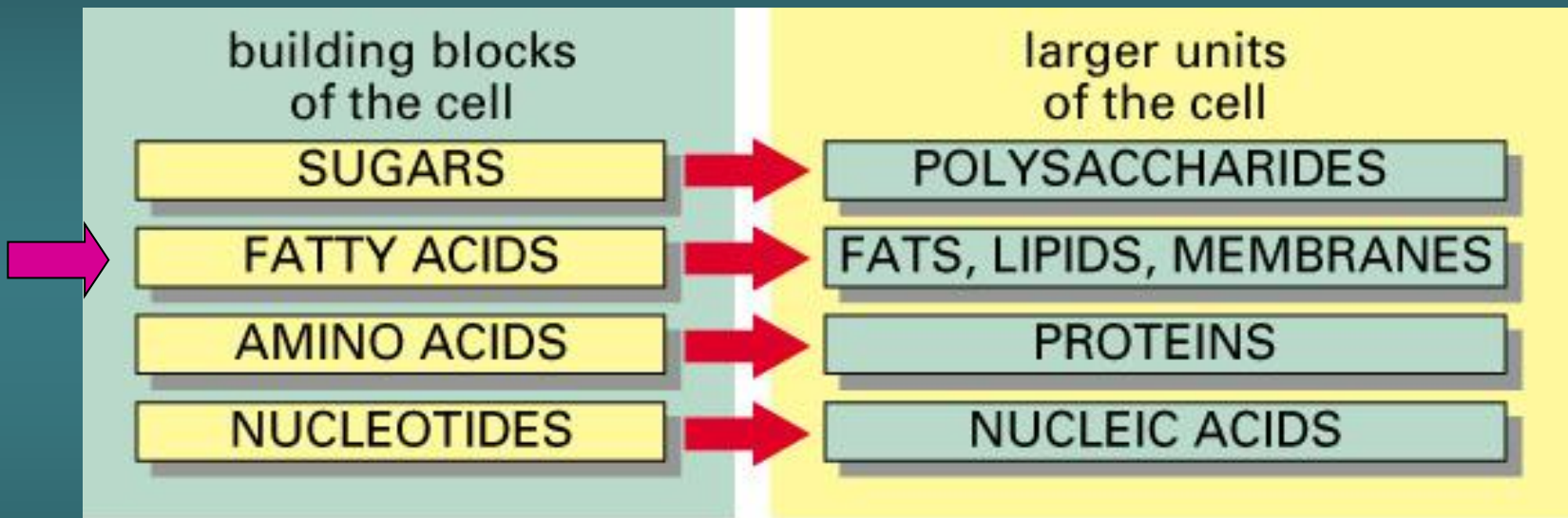
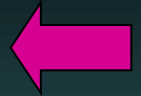


Figure 2-17. Molecular Biology of the Cell, 4th Edition.

**TABLE 2-3** The Approximate Chemical Composition of a Bacterial Cell

	PERCENT OF TOTAL CELL WEIGHT	NUMBER OF TYPES OF EACH MOLECULE
Water	70	1
Inorganic ions	1	20
Sugars and precursors	1	250
Amino acids and precursors	0.4	100
Nucleotides and precursors	0.4	100
Fatty acids and precursors	1	50
Other small molecules	0.2	~300
Macromolecules (proteins, nucleic acids, and polysaccharides)	26	~3000

# STRUCTURÁLNÍ ÚLOHA FOSFOPIDŮ v BUŇKÁCH



**MEMBRANOVÉ  
SYSTÉMY  
a buněčné  
kompartmenty**

**Protientropické  
důsledky**



**L**aboratoř  
**ytokinety**  
Biofyzikální ústav AVČR, BRNO

**NEODMYSLITELNÉ od BUNĚČNÝCH FUNKCÍ**

# A fatty acid

C-16

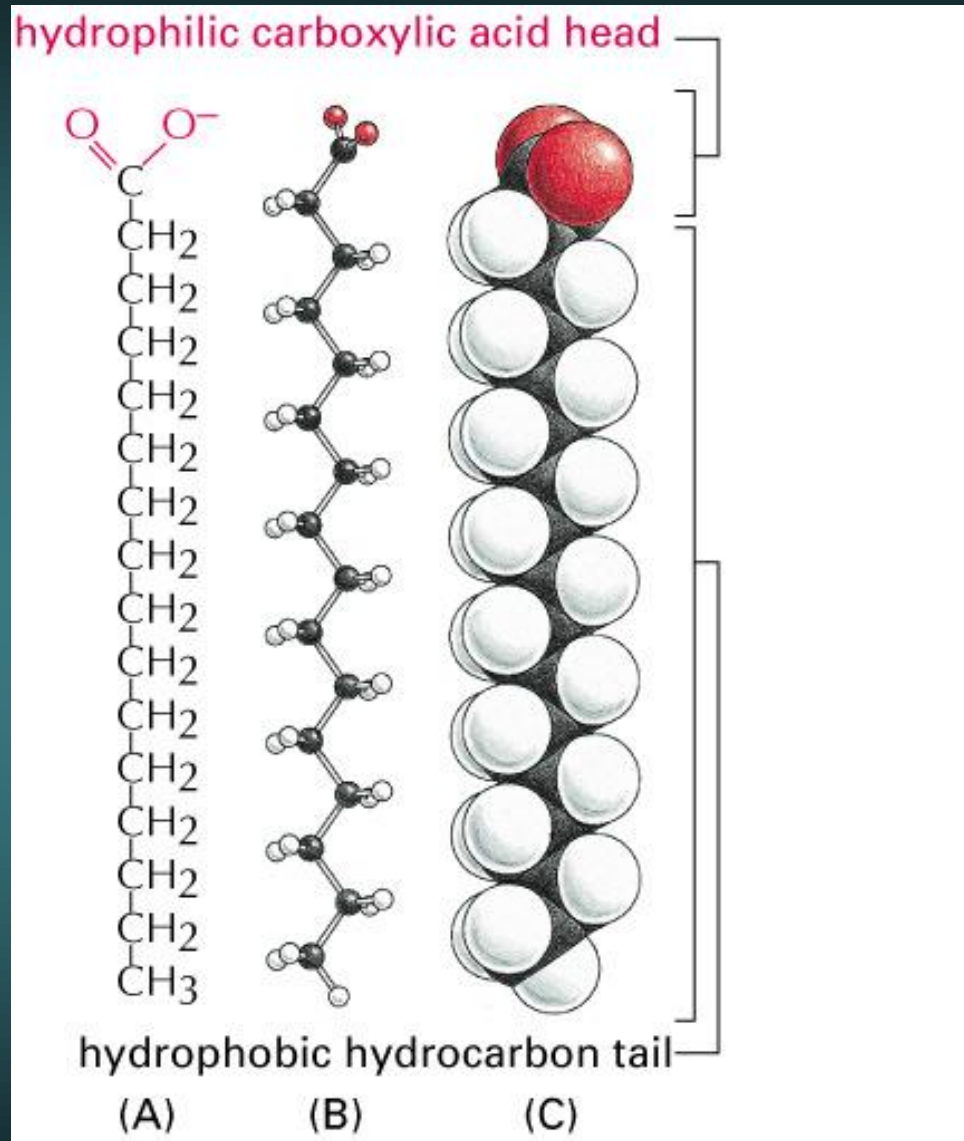


Figure 2-21. Molecular Biology of the Cell, 4th Edition.

## Phospholipid structure and the orientation of phospholipids in membrane

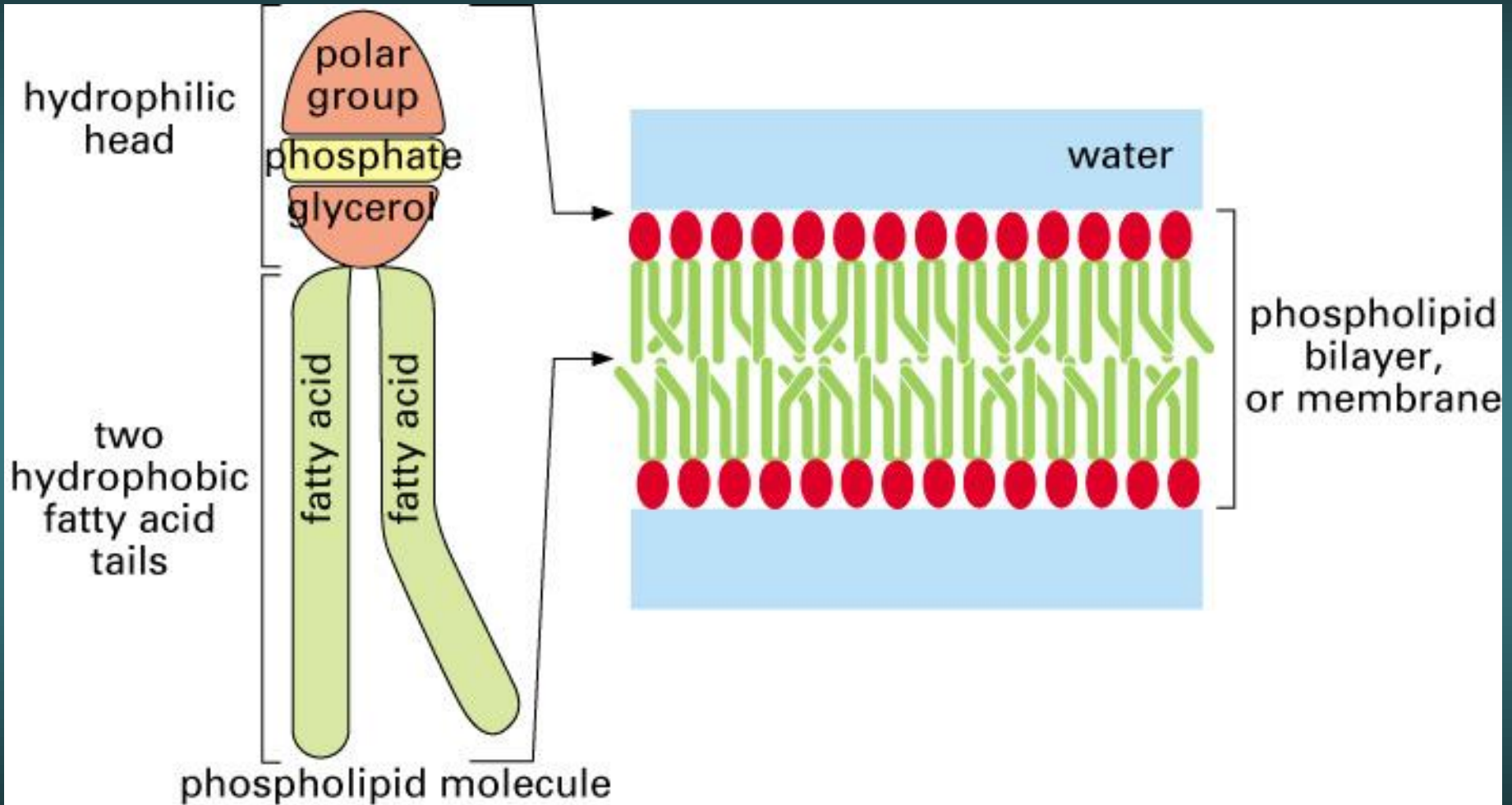
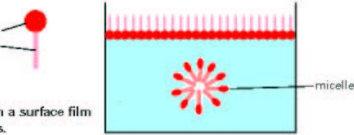


Figure 2-22. Molecular Biology of the Cell, 4th Edition.



### LIPID AGGREGATES

Fatty acids have a hydrophilic head and a hydrophobic tail.



In water they can form a surface film or form small micelles.

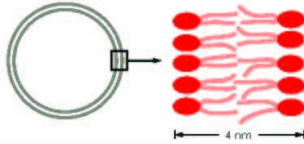
Their derivatives can form larger aggregates held together by hydrophobic forces:

**Triglycerides** can form large spherical fat droplets in the cell cytoplasm.



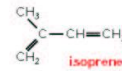
200 nm or more

**Phospholipids** and **glycolipids** form self-sealing lipid bilayers that are the basis for all cell membranes.



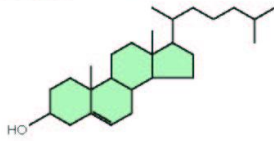
### OTHER LIPIDS

Lipids are defined as the water-insoluble molecules in cells that are soluble in organic solvents. Two other common types of lipids are steroids and polyisoprenoids. Both are made from isoprene units.

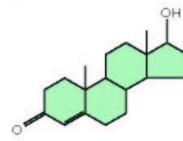


### STERIODS

Steroids have a common multiple-ring structure.



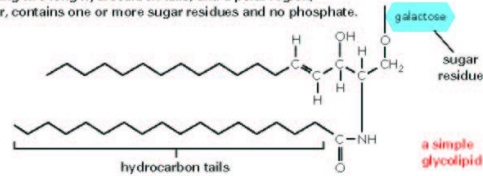
**cholesterol**—found in many membranes



**testosterone**—male steroid hormone

### GLYCOLIPIDS

Like phospholipids, these compounds are composed of a hydrophobic region, containing two long hydrocarbon tails, and a polar region, which, however, contains one or more sugar residues and no phosphate.



### POLYISOPRENOIDS

long-chain polymers of isoprene



**dolichol phosphate**—used to carry activated sugars in the membrane-associated synthesis of glycoproteins and some polysaccharides

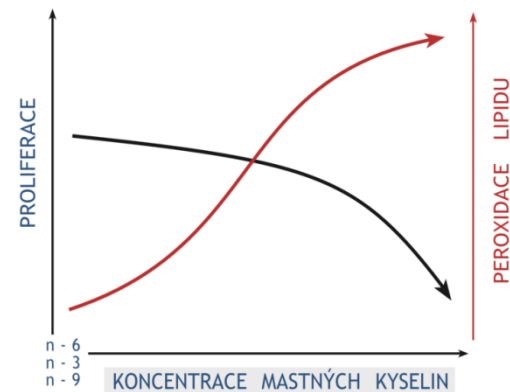
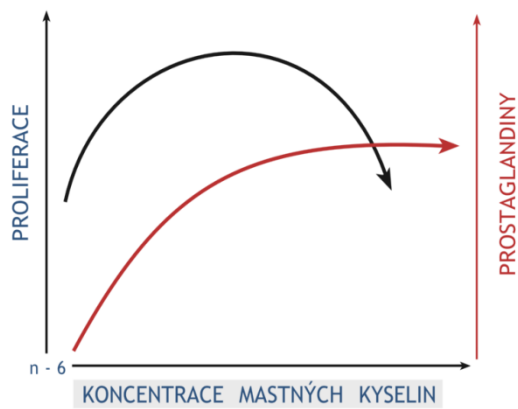
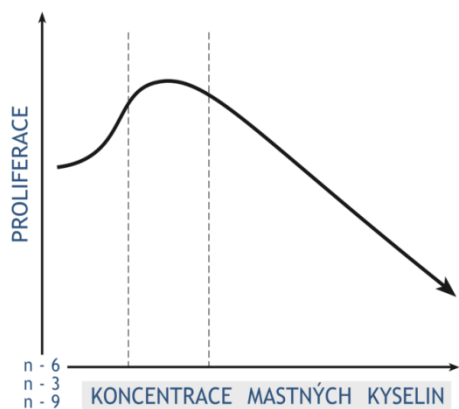


# Spektrum eikosanoisũ

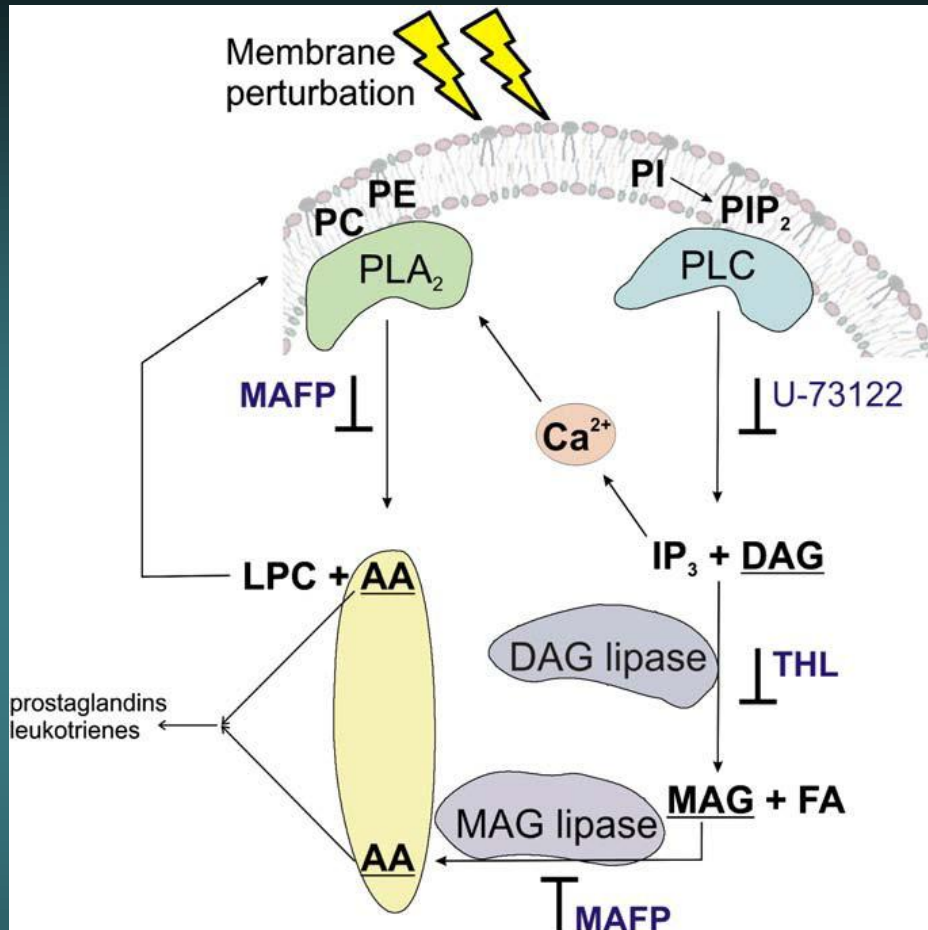
Efekty závisí na koncentraci – další důkazy z oblasti nádorové problematiky:

## VLIV KONCENTRACE NENASYCENÝCH MASTNÝCH KYSELIN NA PROLIFERACI NÁDOROVÝCH BUNĚK – shrnutí (do r. 1985)

(„FATTY ACID PARADOXES“ )



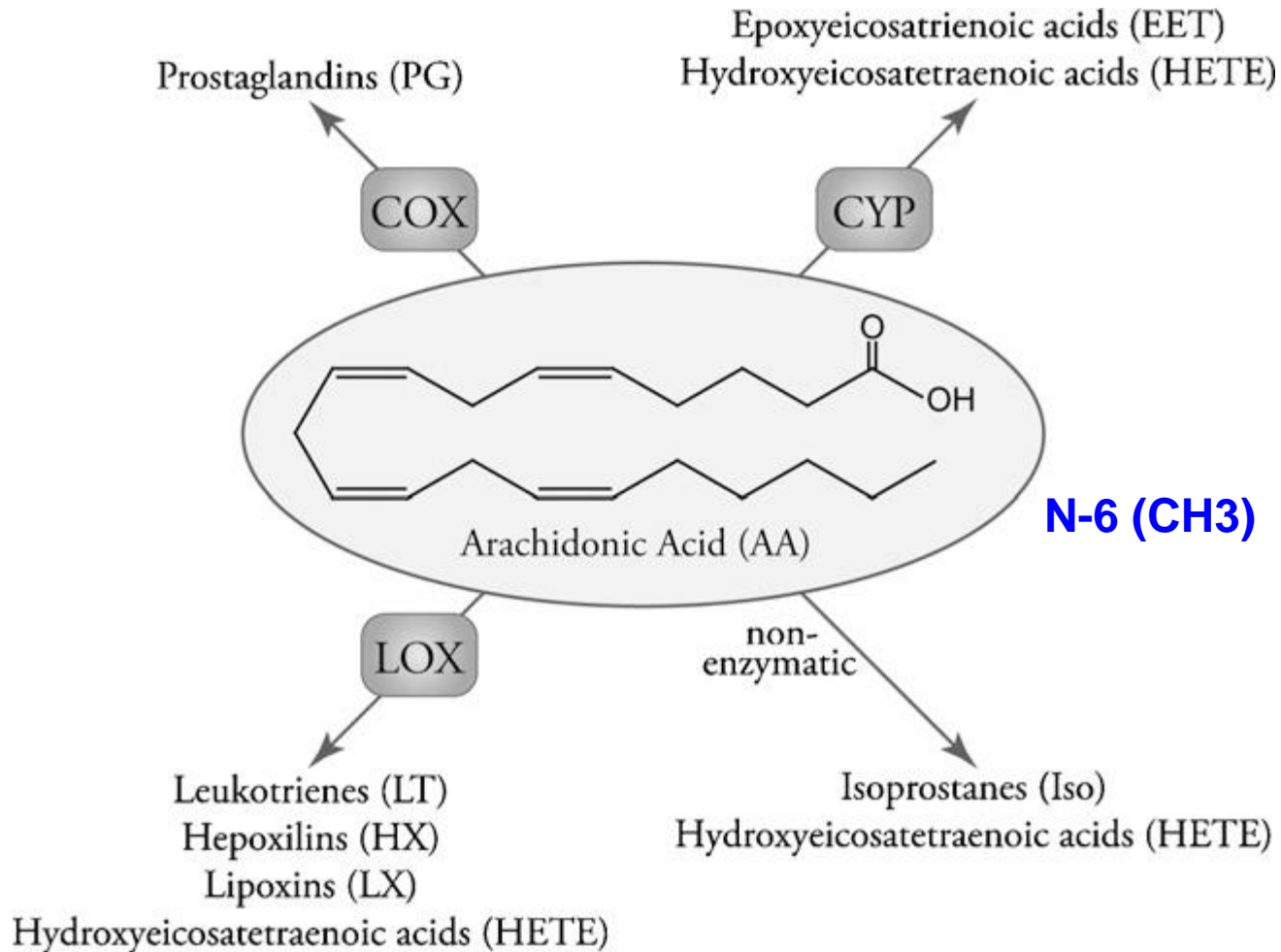
**(VNMK mohou generovat jak +, tak – signál na proliferaci)**



Overview of the potential arachidonic acid releasing pathways, applied inhibitors and detected lipid intermediates (underlined). Note that DAG, AA and Ca<sup>2+</sup> are known Hsp upregulators.

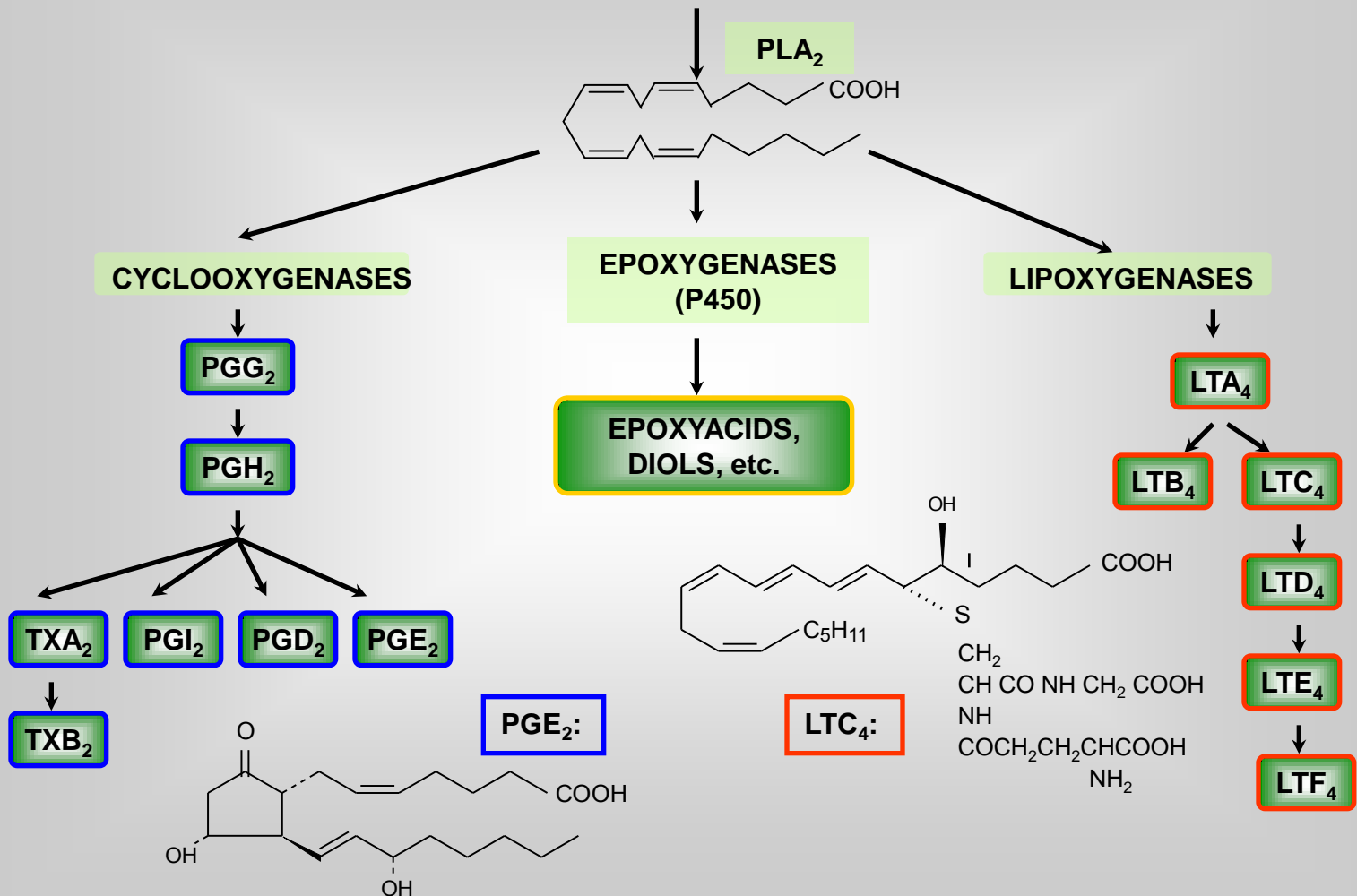
Lipidomics reveals membrane lipid remodelling and release of potential lipid mediators during early stress responses in a murine melanoma cell line

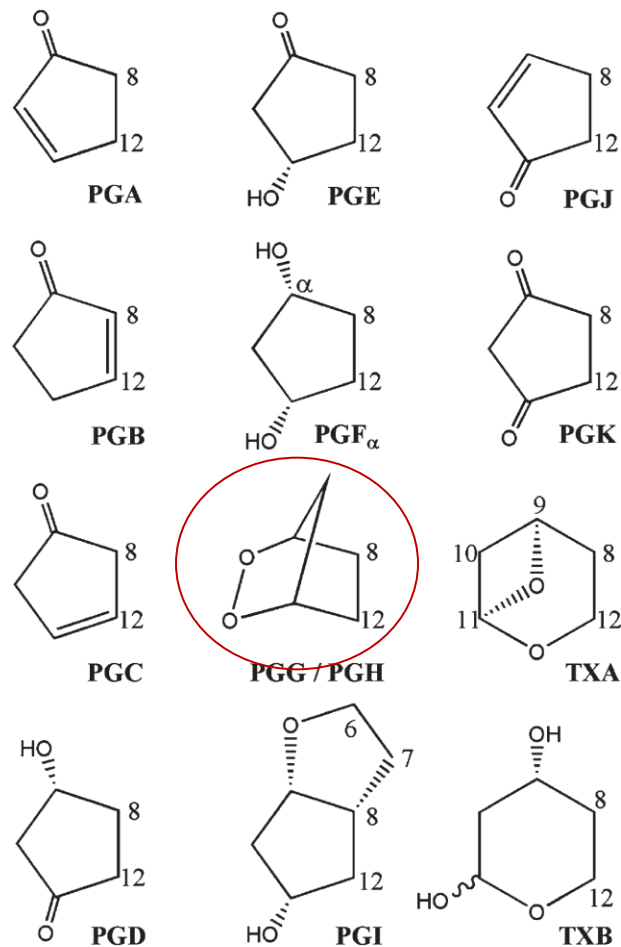
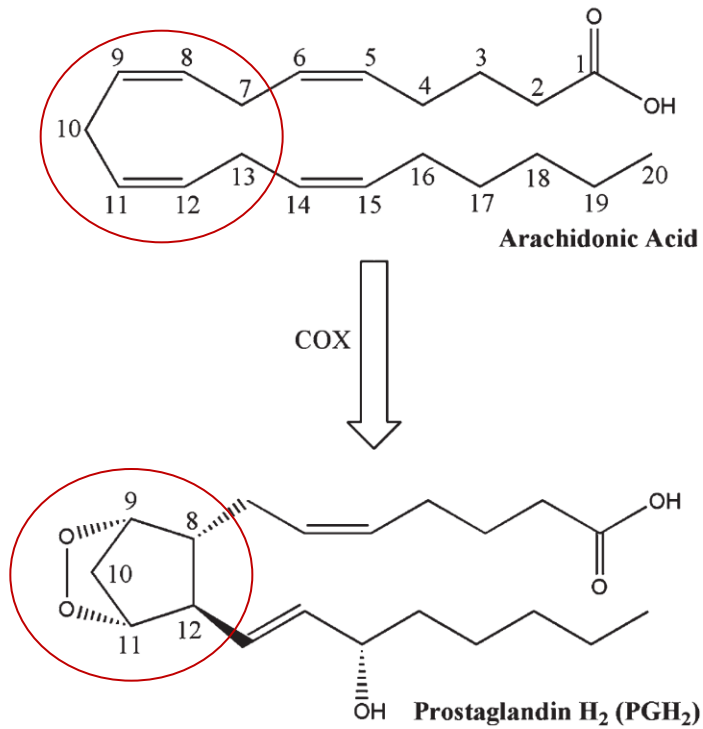
Gábor Balogh a, Mária Péter a, Gerhard Liebisch b, Ibolya Horváth a, Zsolt Török a, Enikő Nagy a, Andriy Maslyanko a, Sándor Benkő c, Gerd Schmitz b, John L. Harwood d, □, László Vigh a, □ Biochimica et Biophysica Acta xxx (2010) xxx–xxx

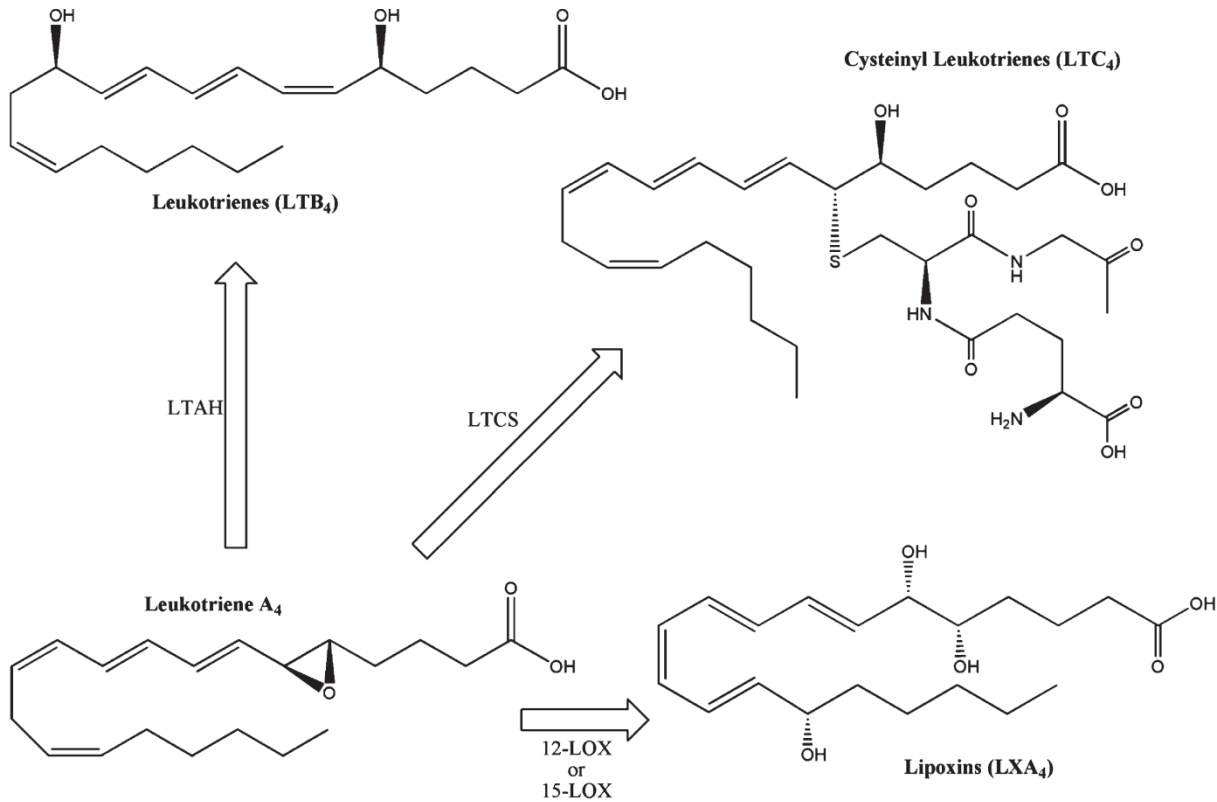




# MEMBRANE PHOSPHOLIPIDS







(cystein)

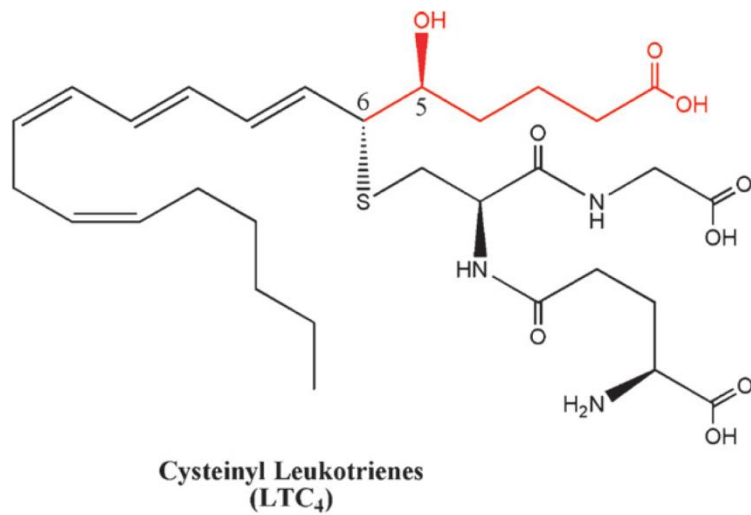
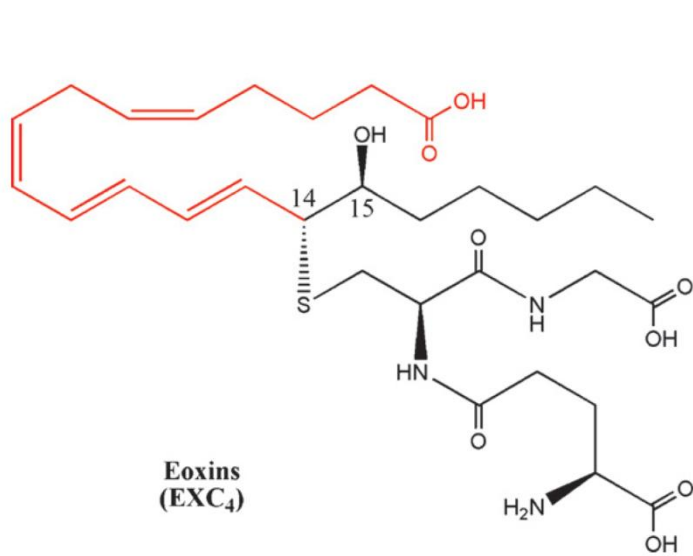
Structures of 5-lipoxygenase metabolites. 5-Lipoxygenase creates the labile epoxide LTA<sub>4</sub>, which can be enzymatically converted into LTB<sub>4</sub>, LTC<sub>4</sub>, and LXA<sub>4</sub>.

From:

[J Lipid Res. 2009 June; 50\(6\): 1015-1038.](#)

doi: 10.1194/jlr.R900004-JLR200.





Structure of eoxin C<sub>4</sub>. Eoxins are the 15-LOX analogs of the cysteinyl leukotrienes, where the thiol attachment occurs at C-14.

From:

[J Lipid Res. 2009 June; 50\(6\): 1015–1038.](#)

doi: 10.1194/jlr.R900004-JLR200.

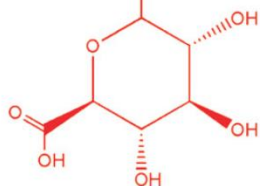
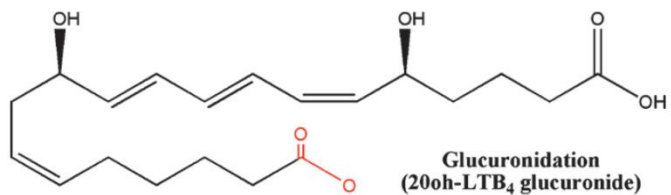
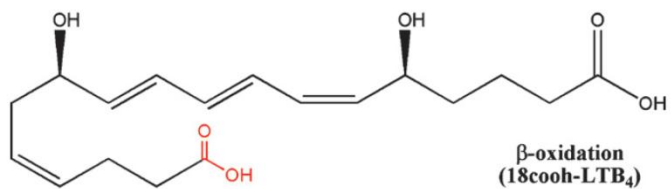
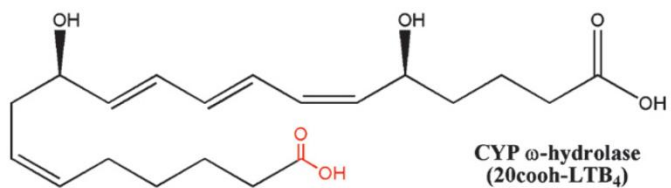
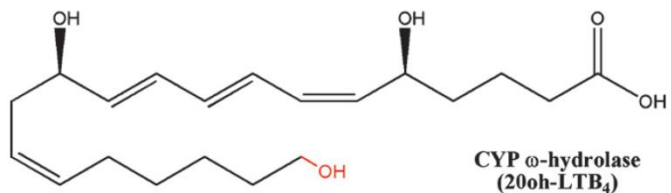
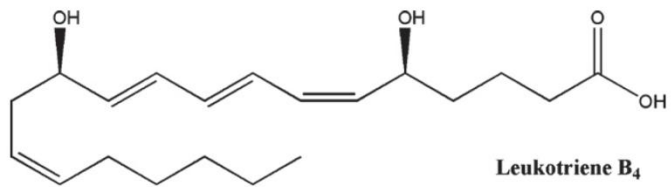
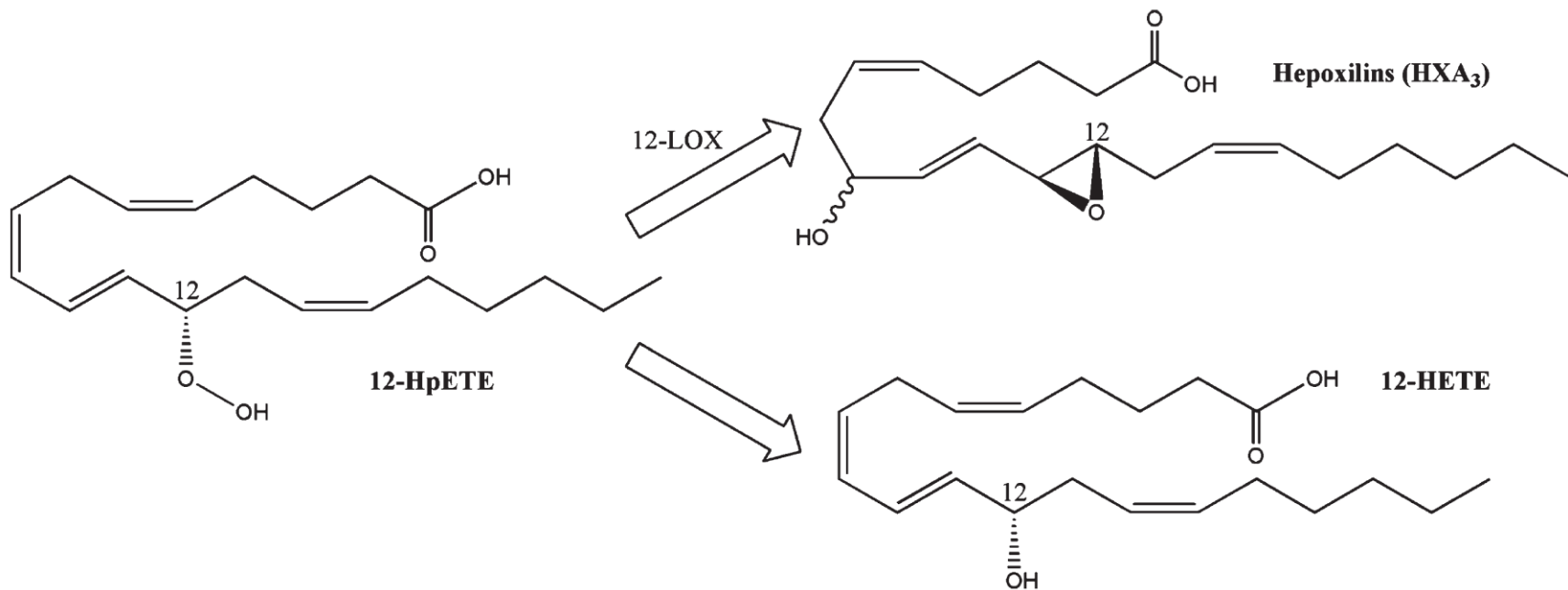
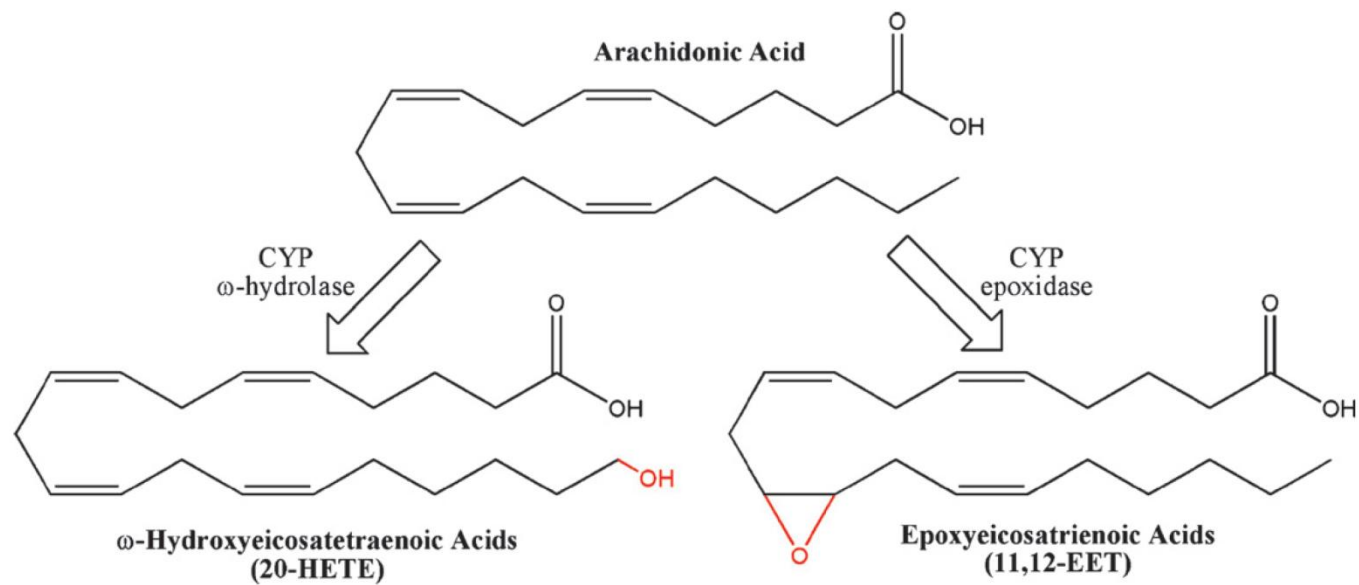


Fig. 8. Examples of LTB<sub>4</sub> metabolism by  $\beta$ -oxidation, CYP  $\omega$ -hydrolases, and glucuronidation.



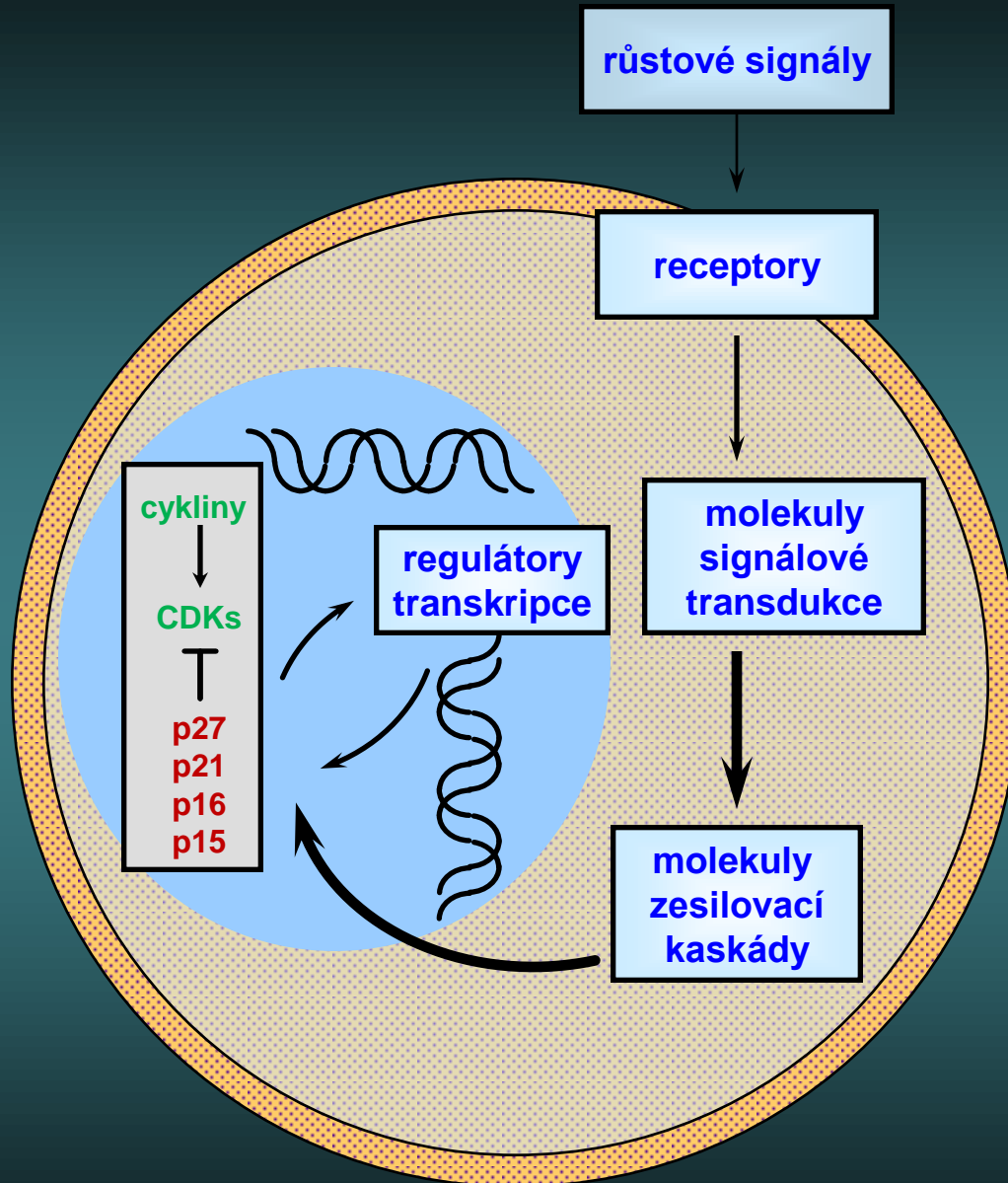
Structures of 12-lipoxygenase metabolites. 12-Lipoxygenase creates 12-HpETE, which can further isomerize to form HXA<sub>3</sub>.

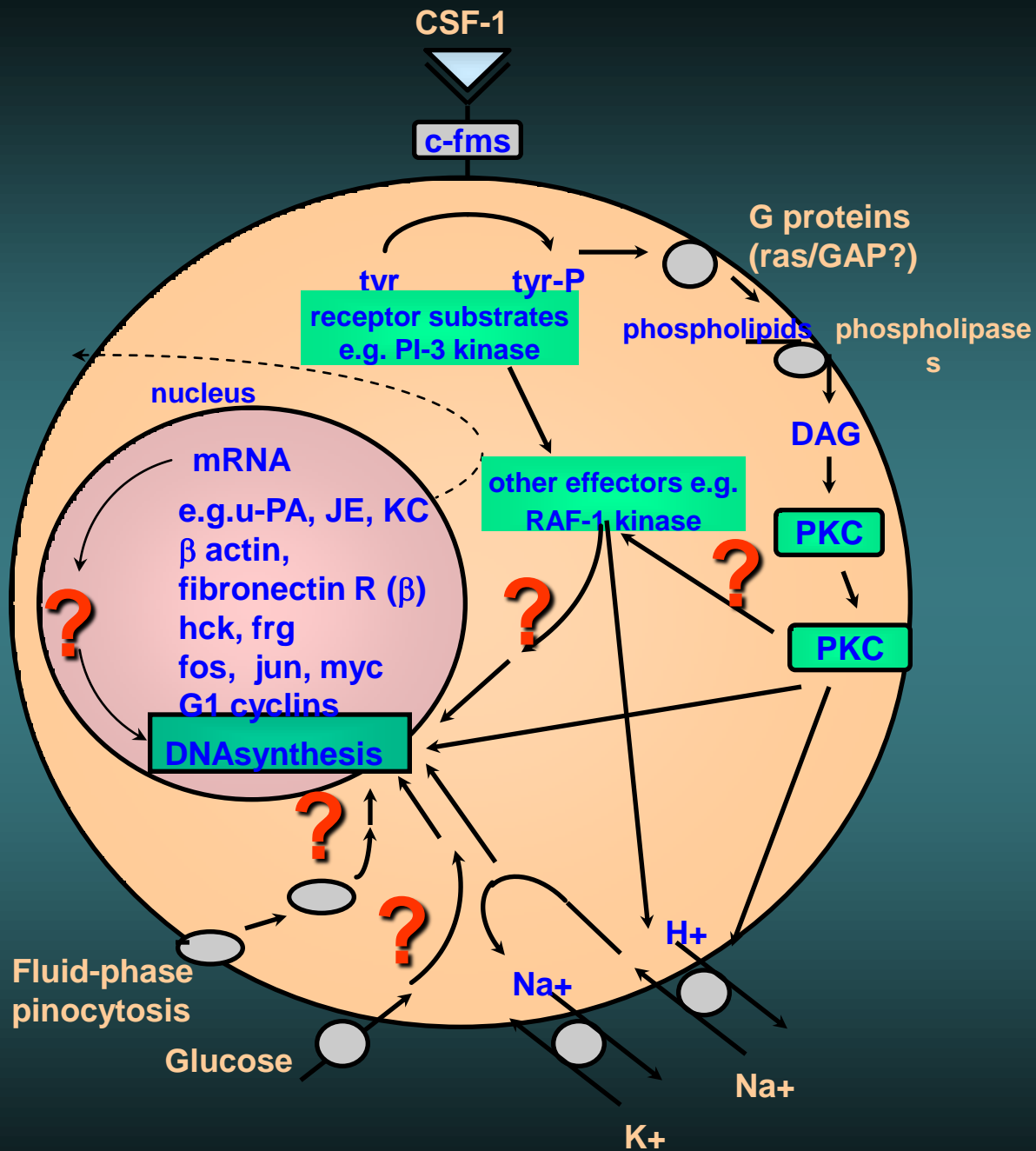


**Fig. 7.** Structures of cytochrome P450 metabolites. Cytochrome P450 enzymes can catalyze  $\omega$ -oxidation (example: 20-HETE) and epoxidation (11,12-EET) reactions.

From:

[J Lipid Res. 2009 June; 50\(6\): 1015–1038.](#)





# Faktory, které mohou modulovat rychlost dělení, diferenciaci anebo zánik buněk

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## Faktory, které mohou ovlivnit cytokinetiku změnami

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1) exprese anebo funkce molekul zapojených v přenosu signálů přímo regulujících proliferaci, diferenciaci a buněčnou smrt (apoptózou), včetně exprese protoonkogenů a nádorově-supresorových genů

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2) signálů, které tyto funkce ovlivňují do určité míry nepřímo, jako jsou inhibice mezibuněčných spojení, ovlivnění funkce enzymů reparujících DNA, metylace DNA apod.

# Modulace cytokinetiky látkami tukové povahy

Lipidy a zejména jejich složky *vysoce nenasycené kyseliny (PUFA)*, včetně jejich metabolitů *eikosanoidů*,

patří mezi významné epigeneticky působící faktory schopné ovlivnit jak dělení a zánik normálních,

ale i transformovaných buněčných populací, tak proces maligní transformace.



# Hlavní mechanismy působení PUFAs

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- 1) přímé ovlivnění aktivity transkripčních faktorů regulujících expresi genů významných z hlediska cytokinetiky
- 2) produkce eikosanoidů působících na přenos signálů cytokinů a imunitní systém
- 3) produkce reaktivních kyslíkových metabolitů vznikajících peroxidací lipidů.

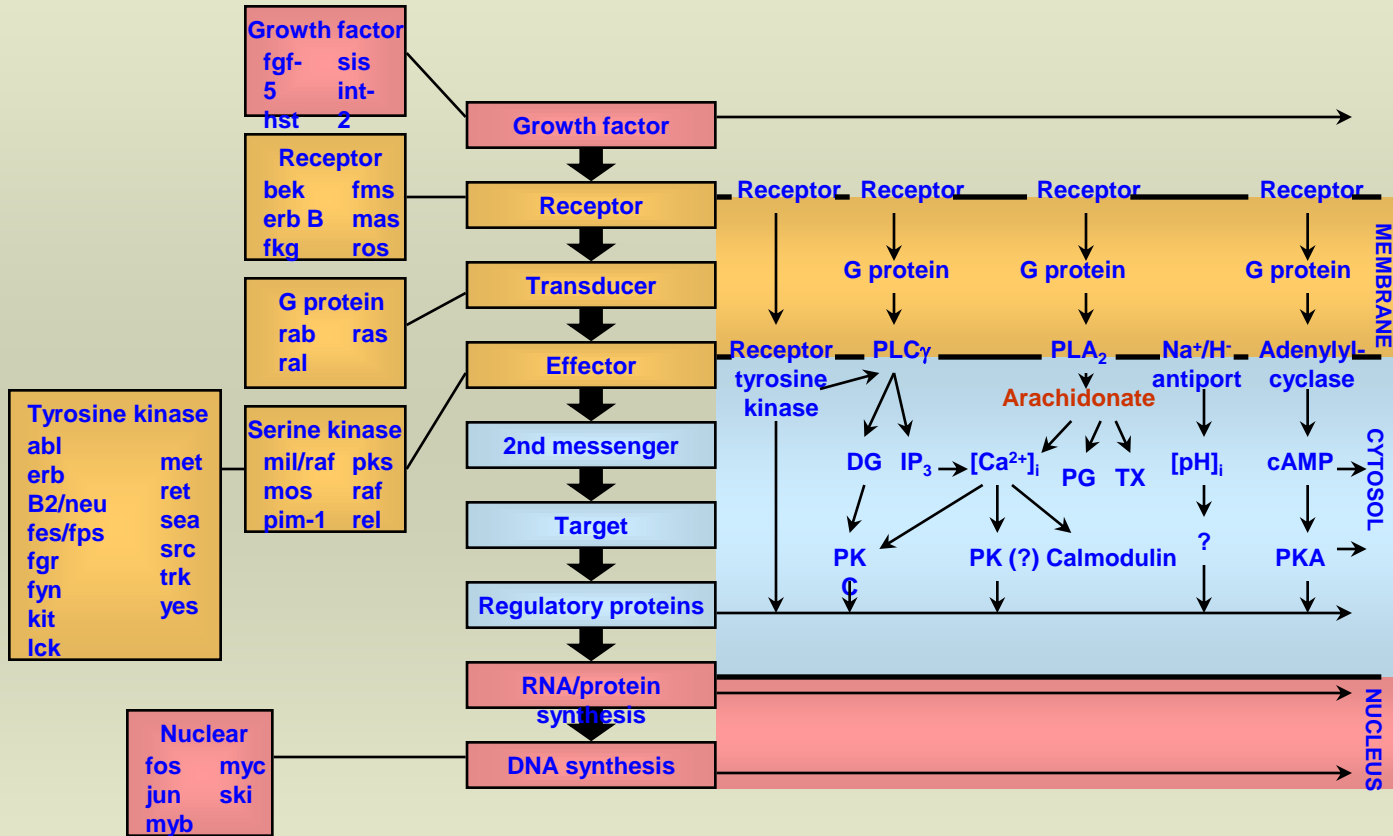
**Význam rovnováhy v přísunu prekursorových  
PUFAs**

**a**

**v produkci jednotlivých jejich metabolitů**

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# Oncogenes



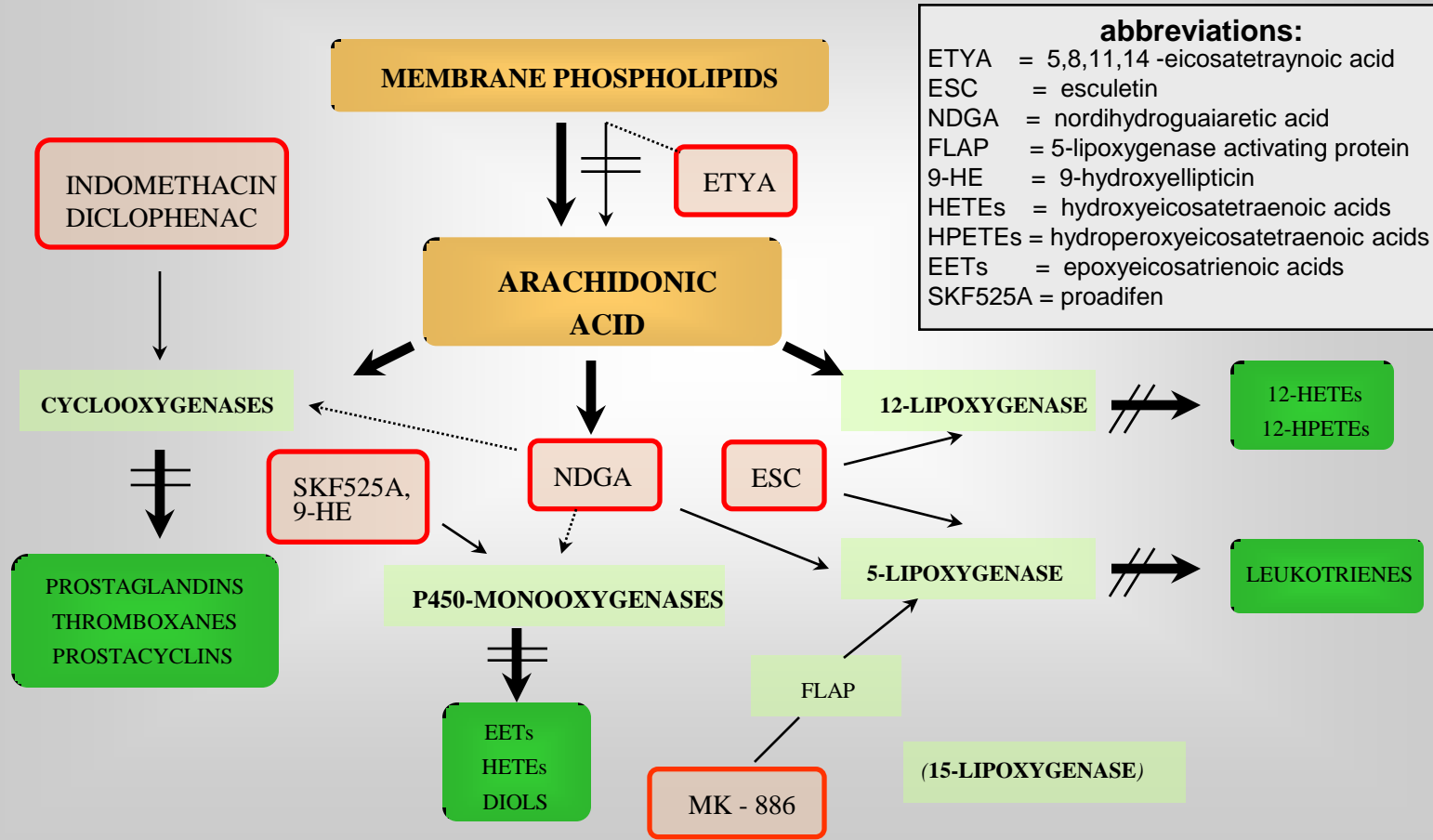
According to: G.Powis: TIPS; 12: 188 -194, 1991

# Efekty inhibitorů metabolismu AA

význam rovnováhy  
v přísunu prekursorových PUFAs  
a  
v produkci jednotlivých jejich metabolitů



# Arachidonic acid: metabolic pathways and its possible modulations

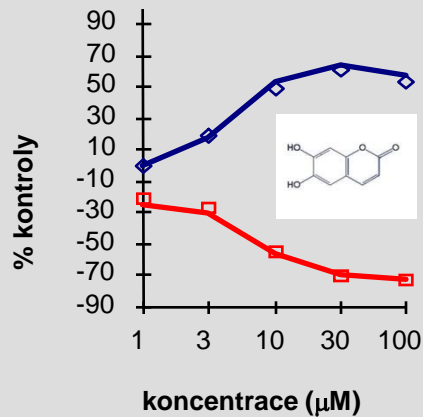


# PRODUKTY

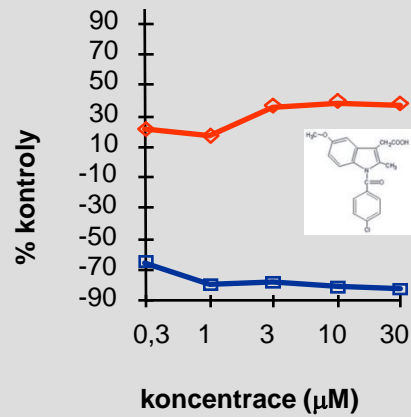
## LIPOXYGENÁZ A CYKLOOXYGENÁZ

VORE et al., J. Immunol. :  
11, 435 - 442, 1989

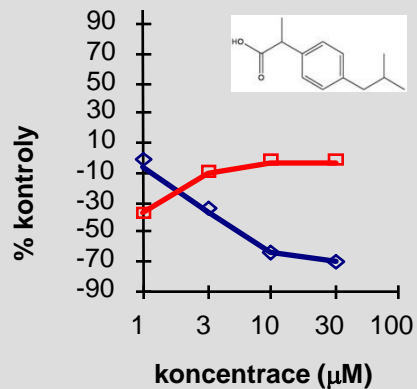
### Esculetin



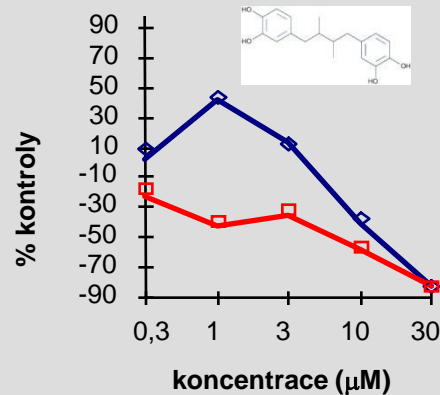
### Indomethacin

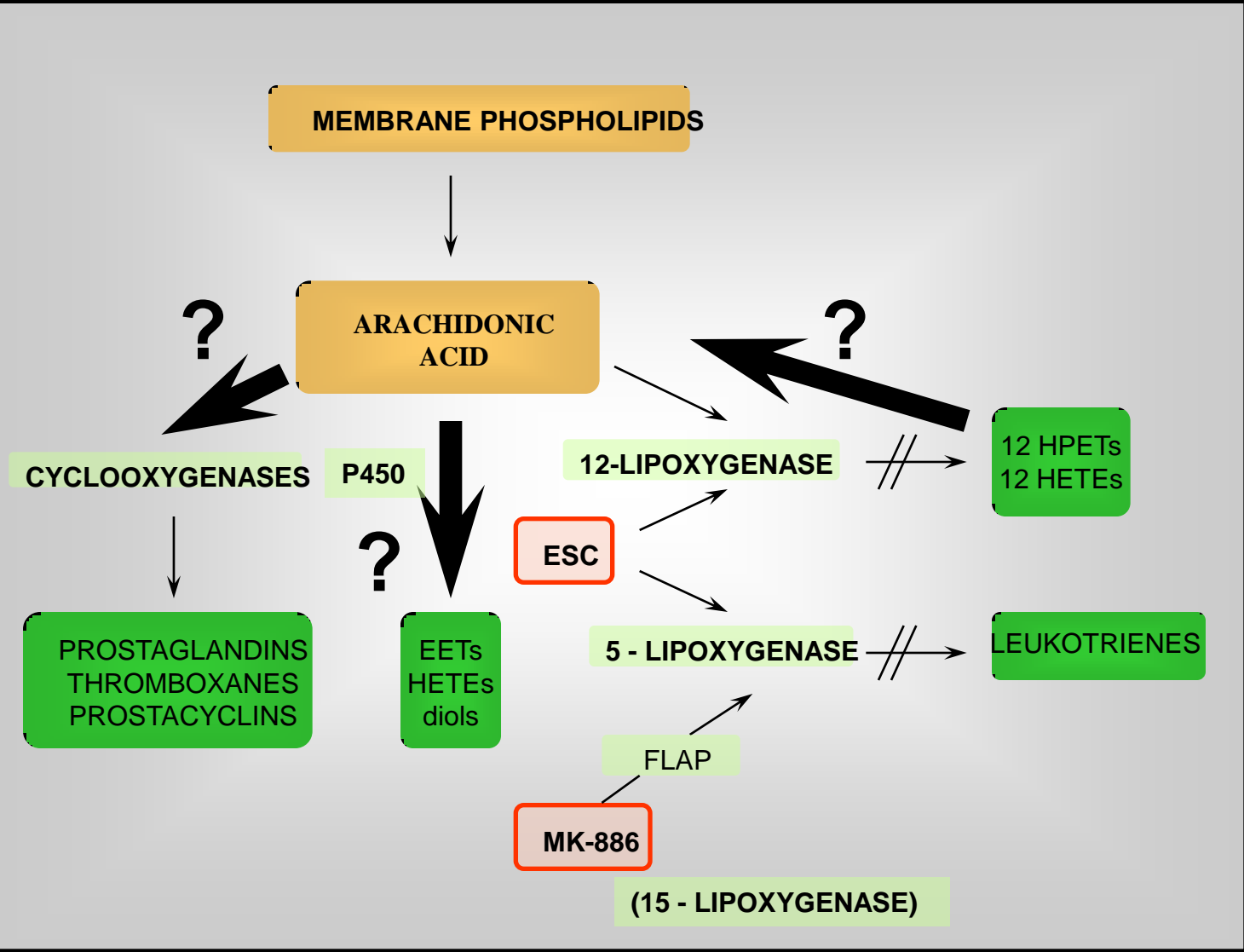


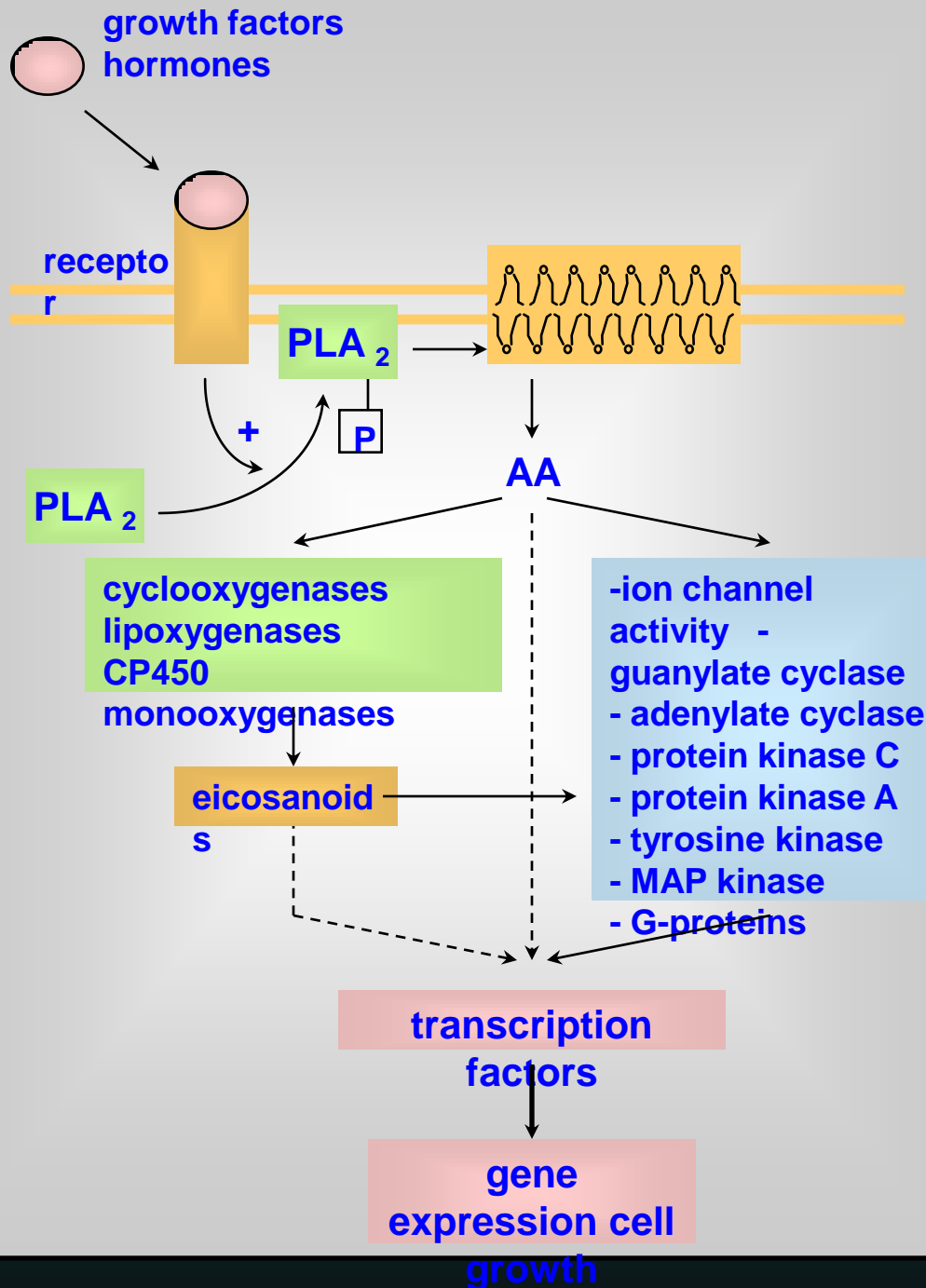
### Ibuprofen



### NDGA







According to: A. Sellmayer et al.:  
Prostaglandins, Leukotrienes  
and Essential Fatty Acids ;  
57: 353 - 357, 1997.





**Děkujeme za pozornost**

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**cytokinety**  
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