كلية الطب بصفاقس

FMSF- PCEM-UEF 109

# Métabolisme des

# EICOSAnoïdes

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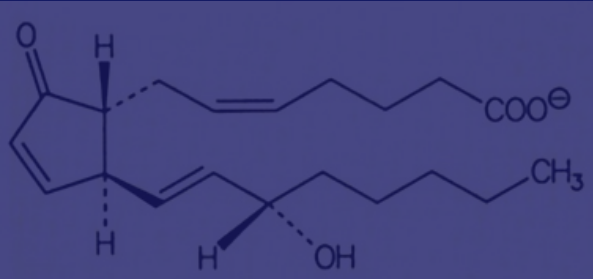
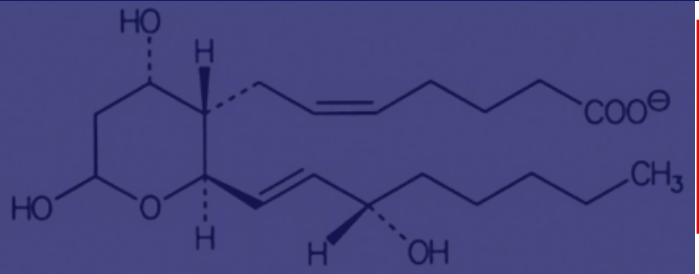
FMSF - Université de Sfax

University of Sfax
TUNISIA

# Eicosanoïdes




prostaglandine $A_2$

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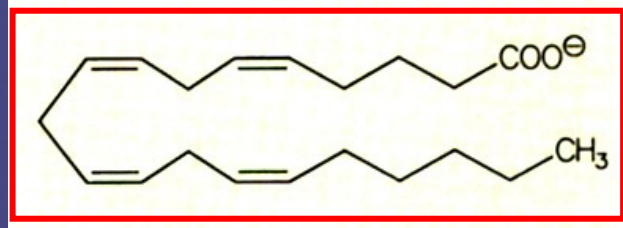
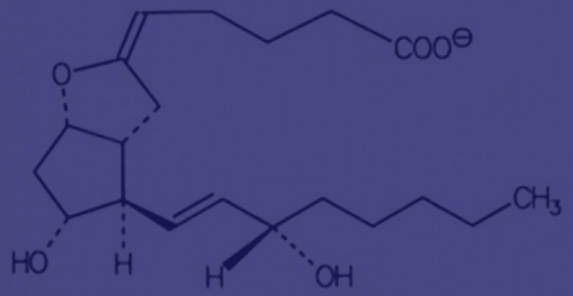
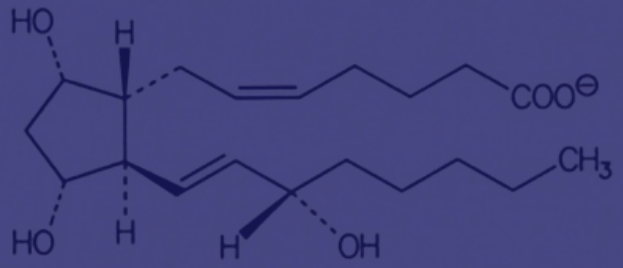



arachidonate




prostacycline $I_2$

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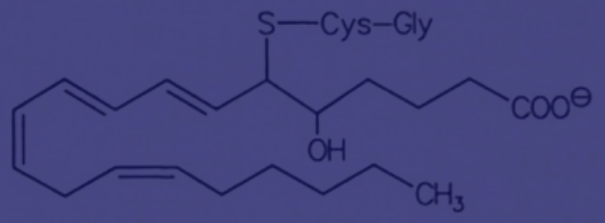
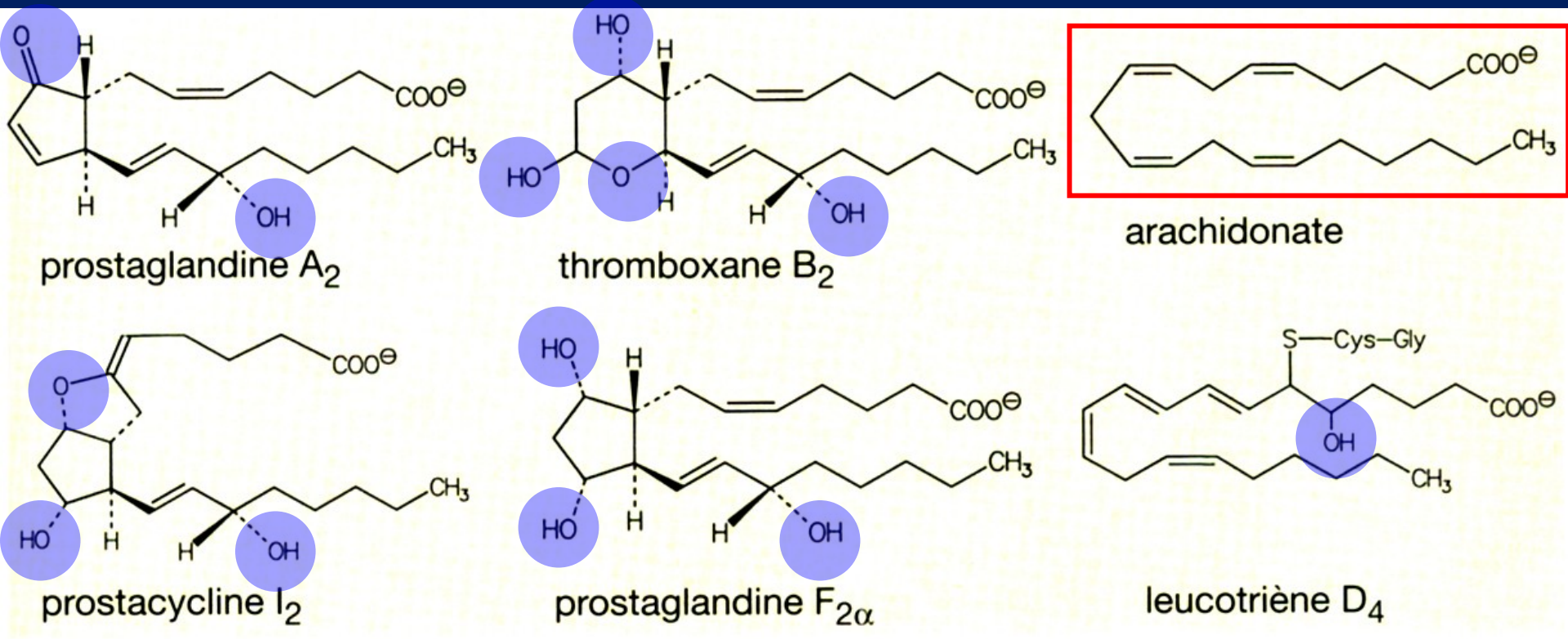
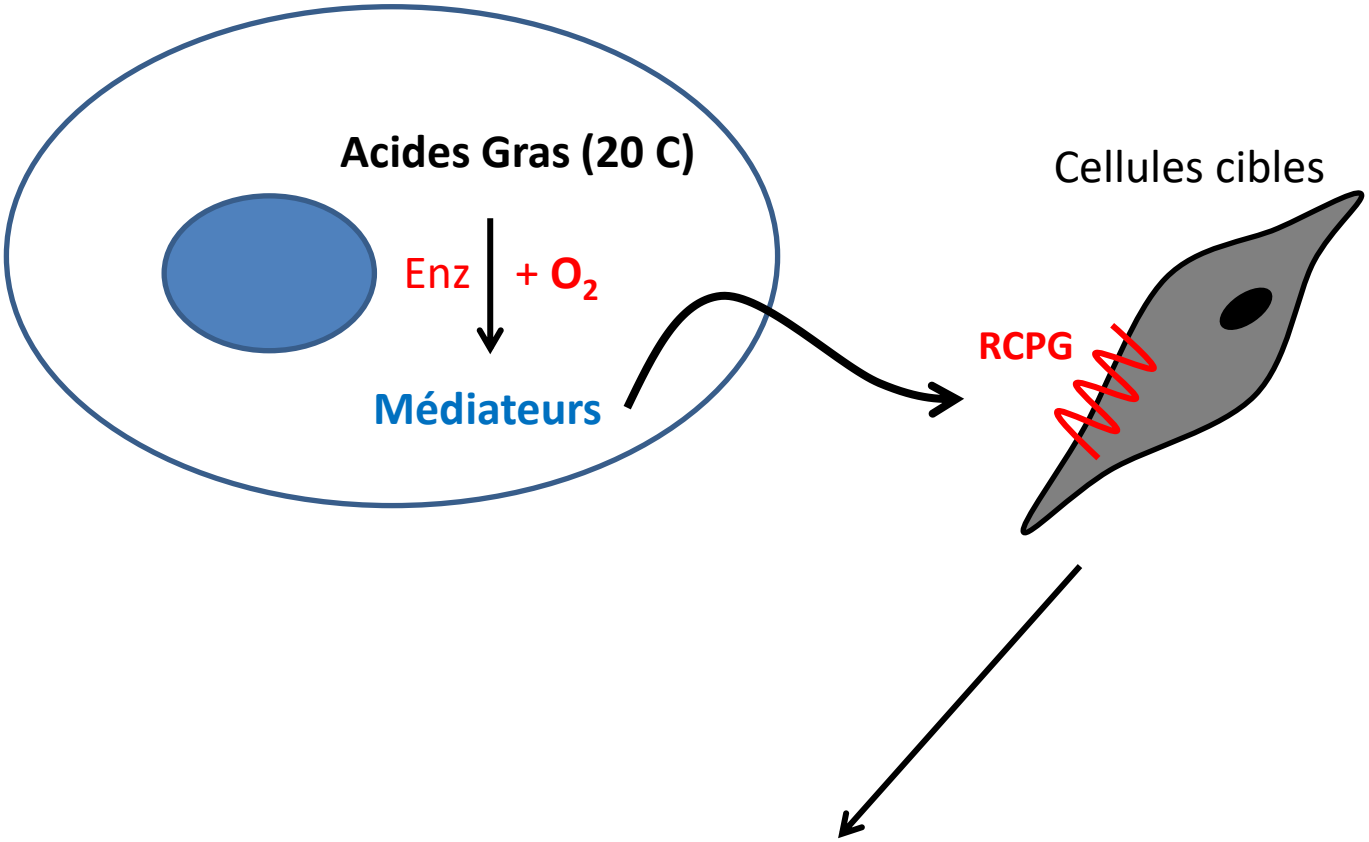


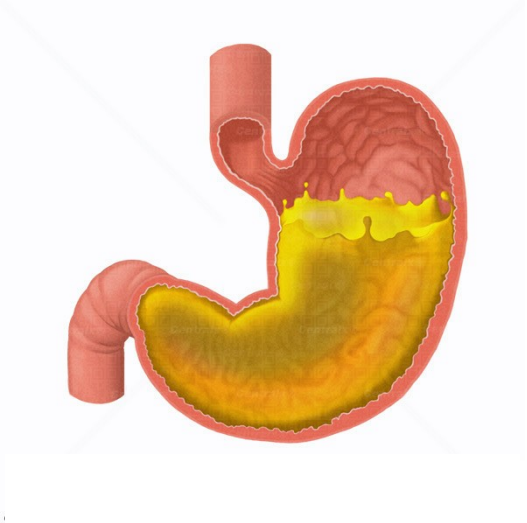

leucotriène $D_4$

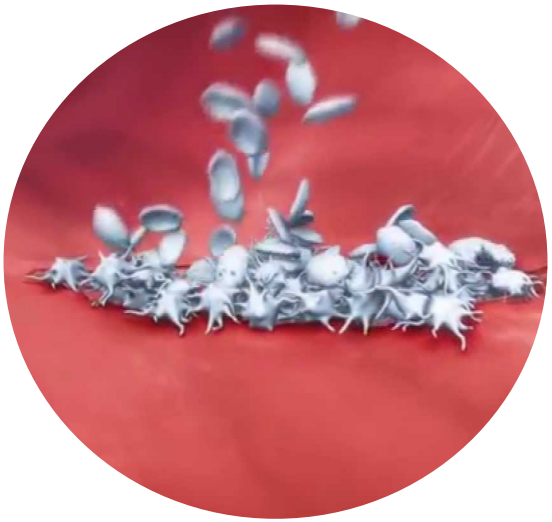
# Eicosanoïdes

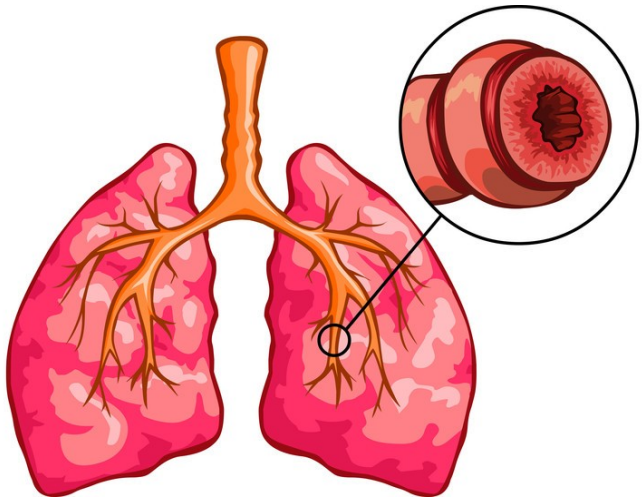


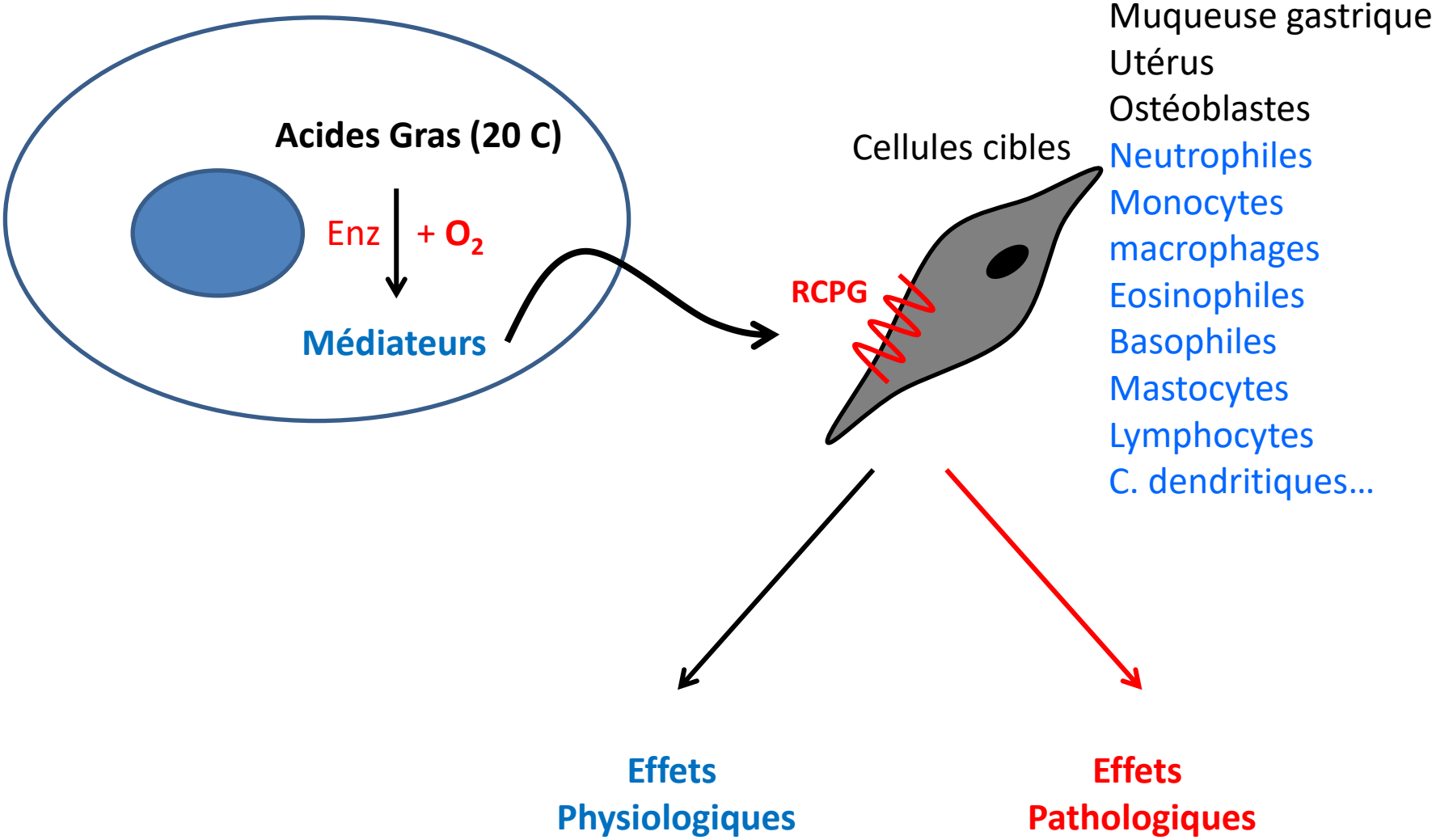


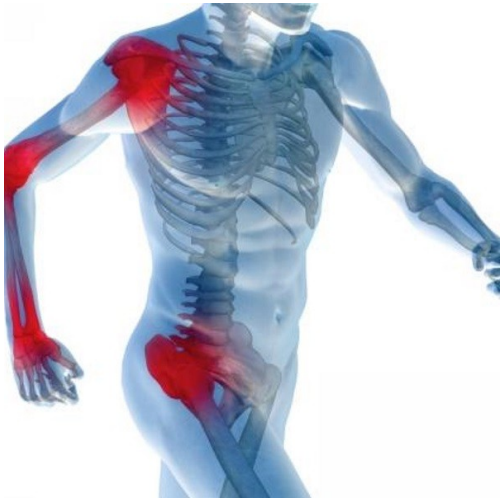

C. Endothéliales
Plaquettes
C. Rénales corticales
C. Rénale médullaires
Muqueuse gastrique
Utérus
Ostéoblastes
Neutrophiles
Monocytes
macrophages
Eosinophiles
Basophiles
Mastocytes
Lymphocytes
C. dendritiques…

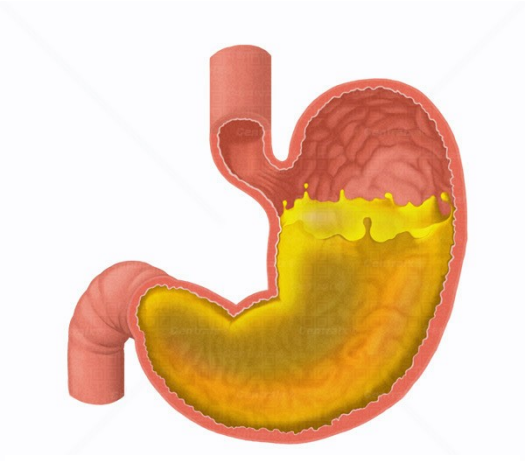


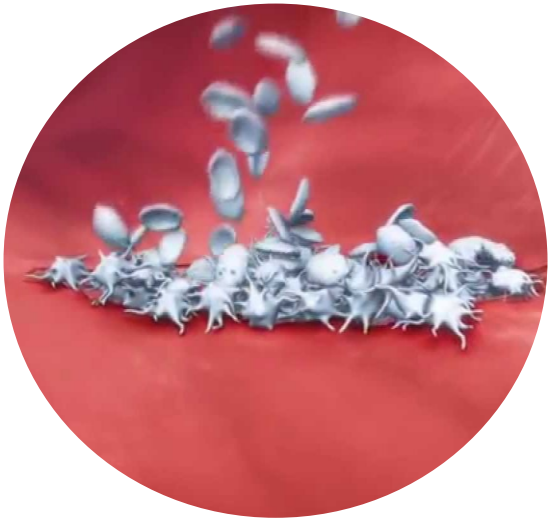


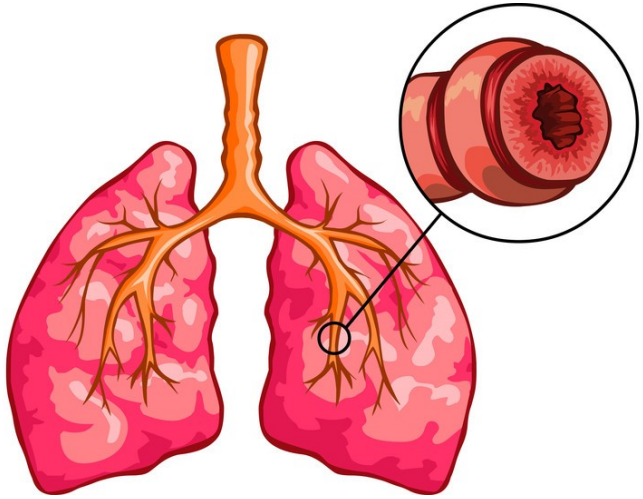


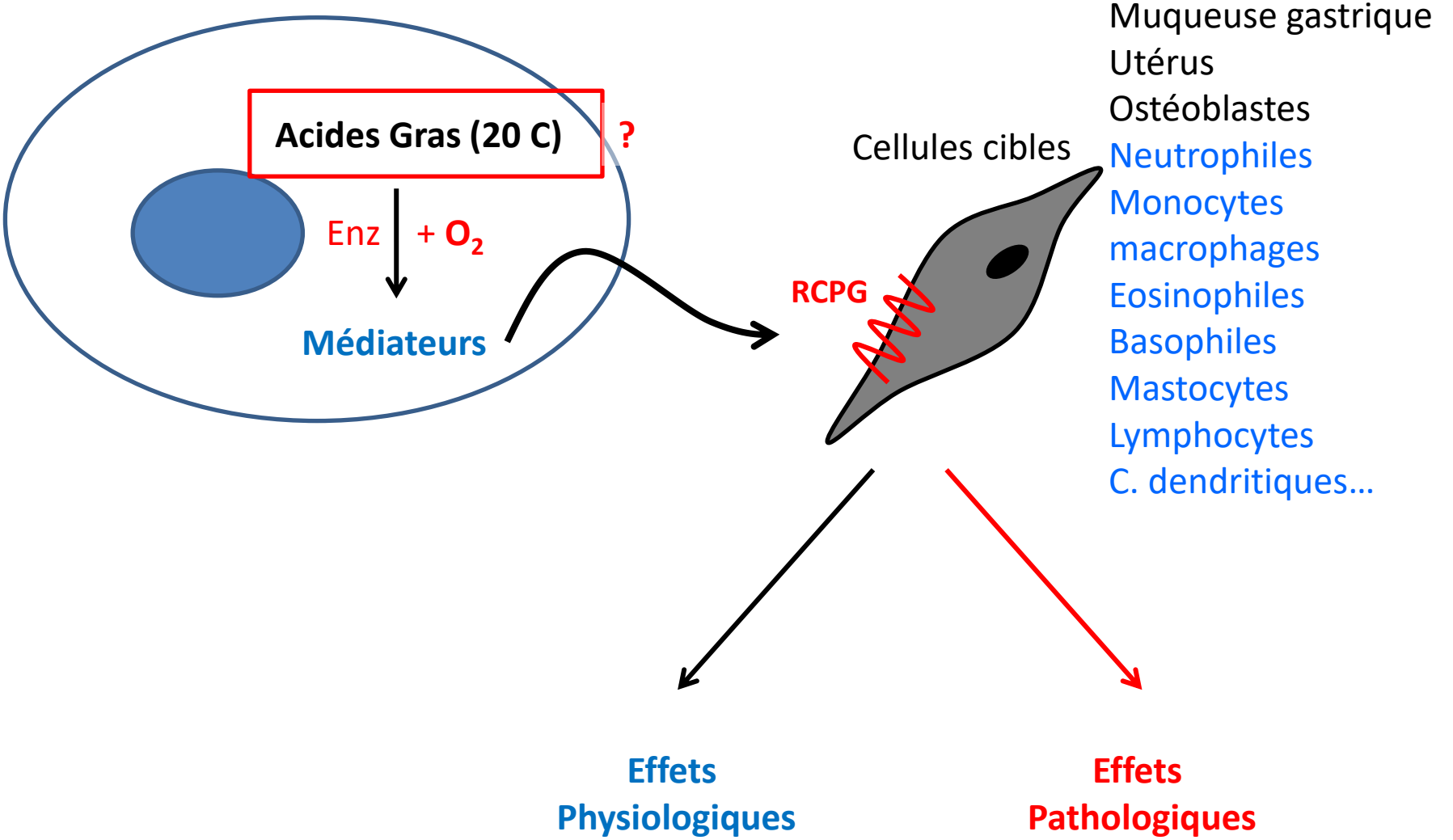

Acides Gras (20 C)
Enz
+ $O_2$
Médiateurs
Cellules cibles
RCPG
C. Endothéliales
Plaquettes
C. Rénales corticales
C. Rénale médullaires
Muqueuse gastrique
Utérus
Ostéoblastes
Neutrophiles
Monocytes
macrophages
Eosinophiles
Basophiles
Mastocytes
Lymphocytes
C. dendritiques…
Effets
Physiologiques
Effets
Pathologiques

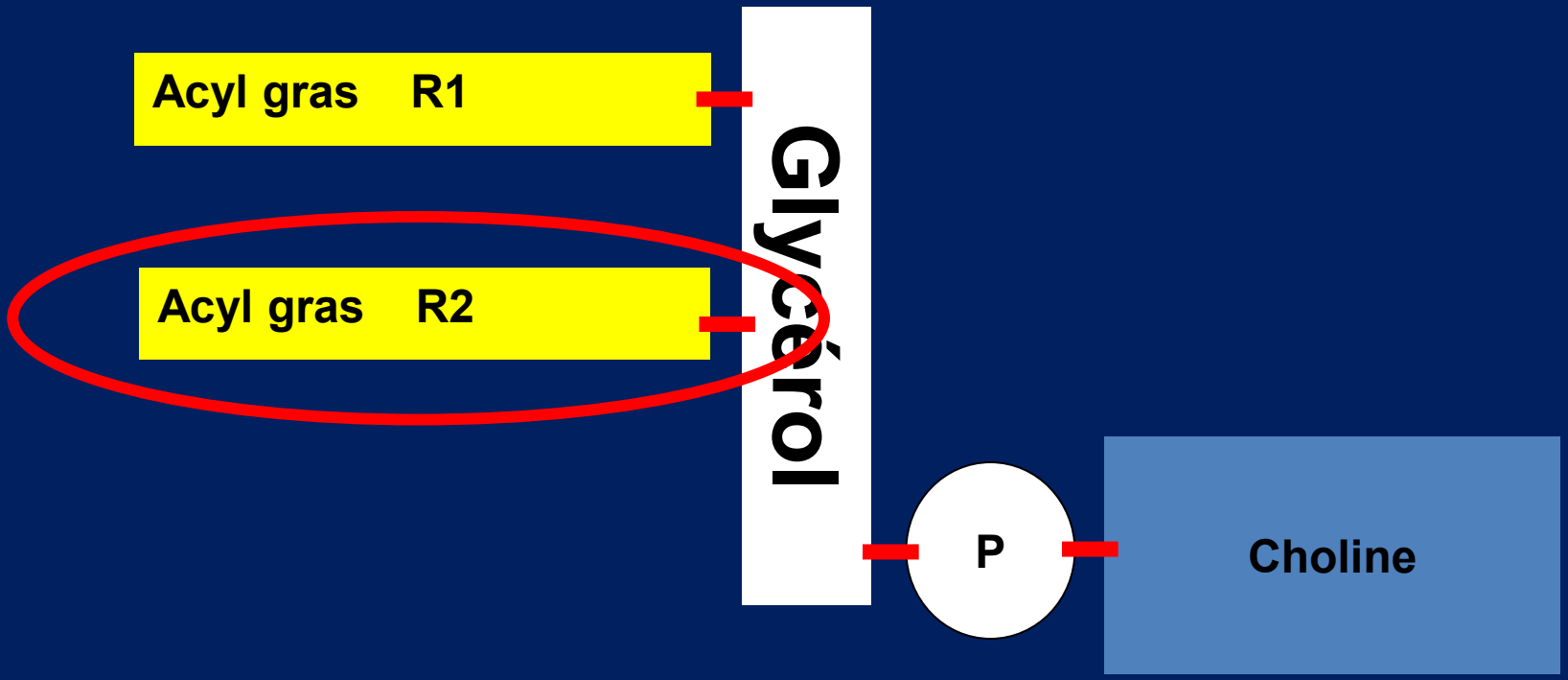






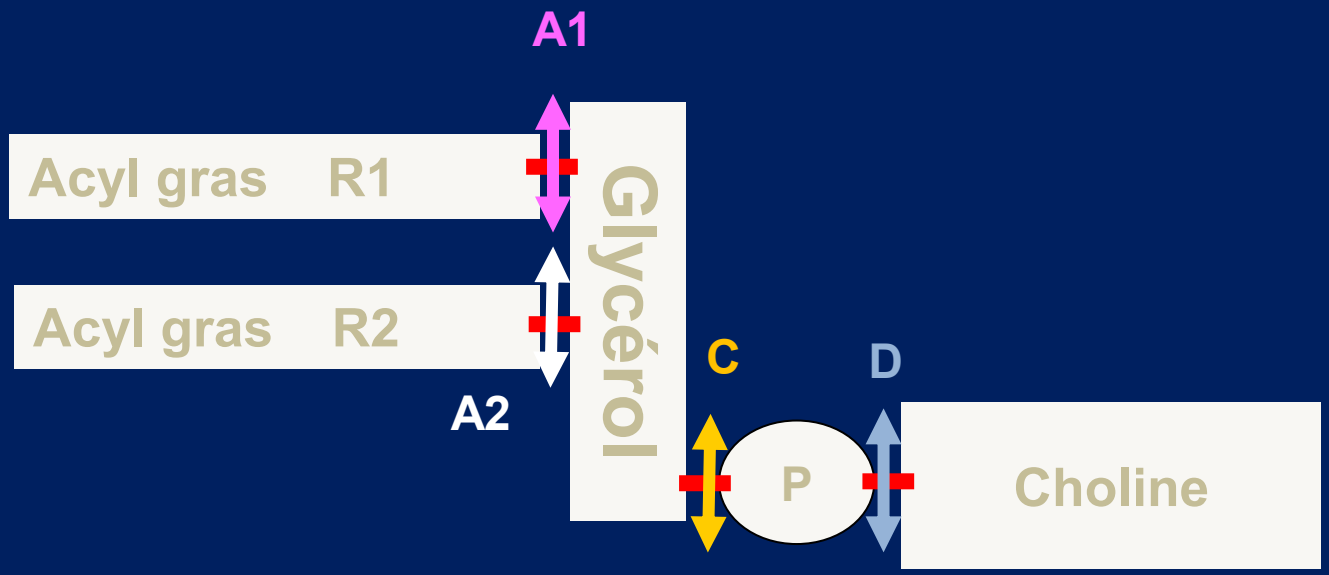


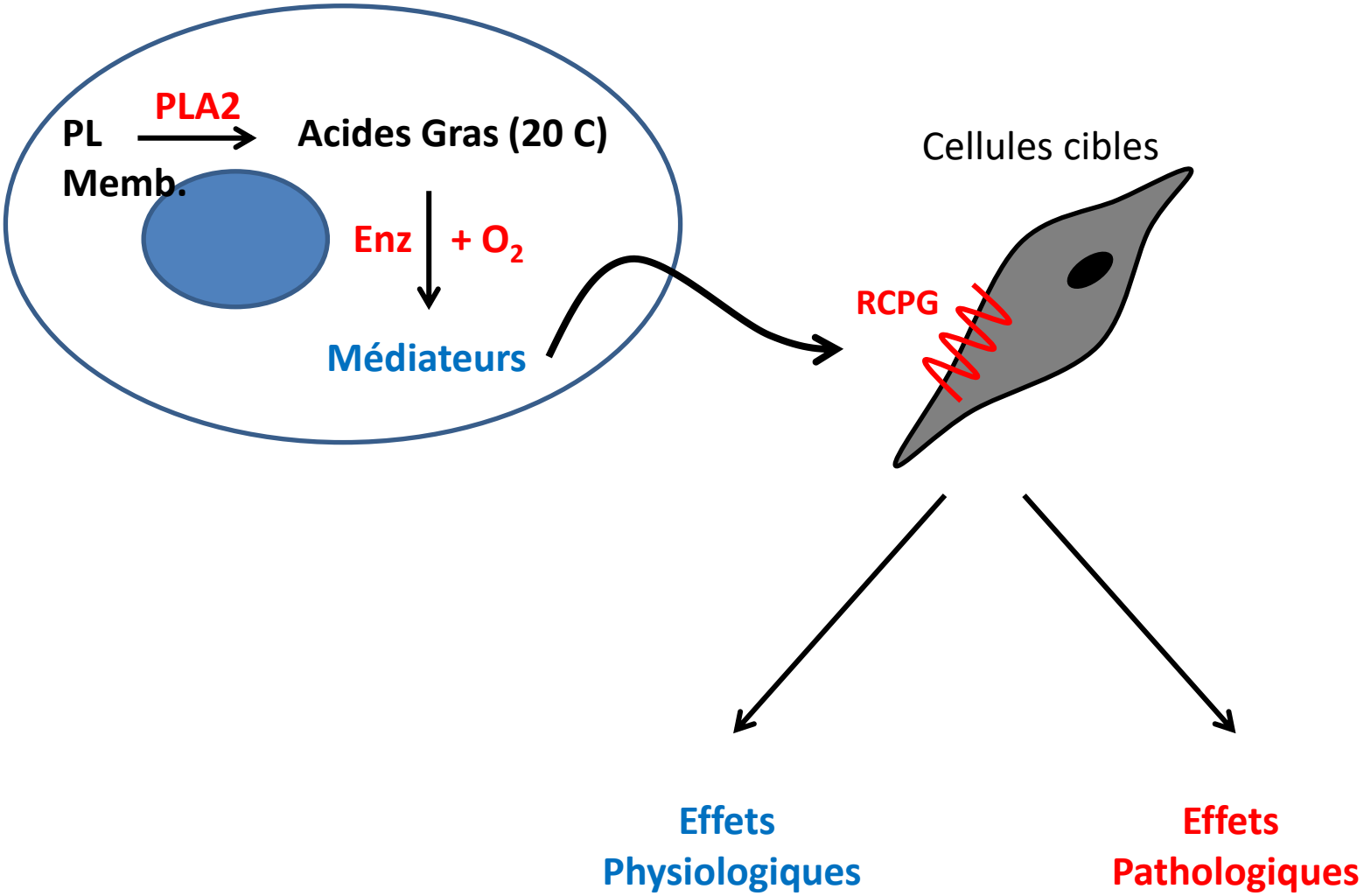

Acides Gras (20 C)
?
Enz
+ $O_2$
Médiateurs
Cellules cibles
RCPG
C. Endothéliales
Plaquettes
C. Rénales corticales
C. Rénale médullaires
Muqueuse gastrique
Utérus
Ostéoblastes
Neutrophiles
Monocytes
macrophages
Eosinophiles
Basophiles
Mastocytes
Lymphocytes
C. dendritiques…
Effets
Physiologiques
Effets
Pathologiques

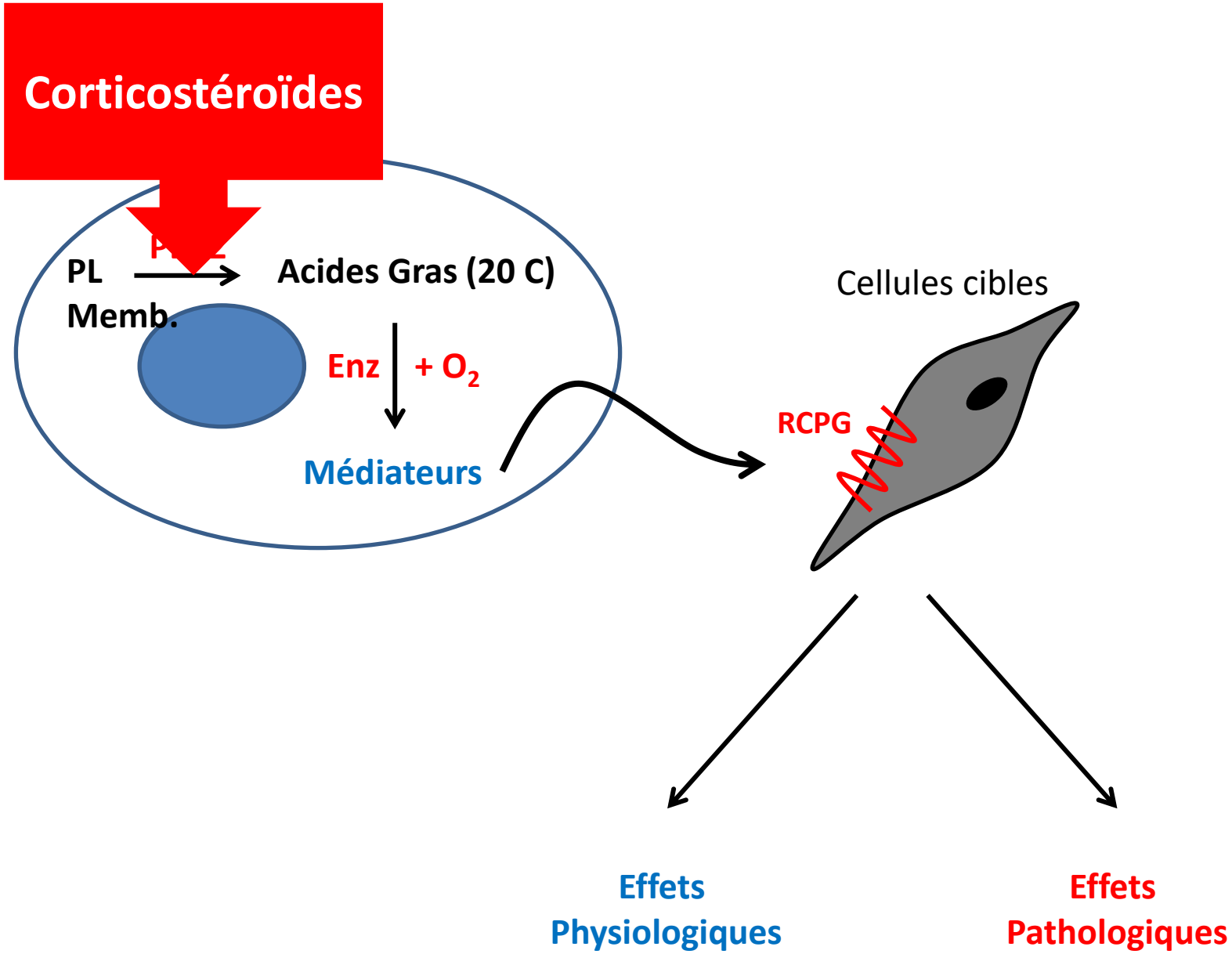

Acyl gras R1
Acyl gras R2
Glycérol
P
Choline

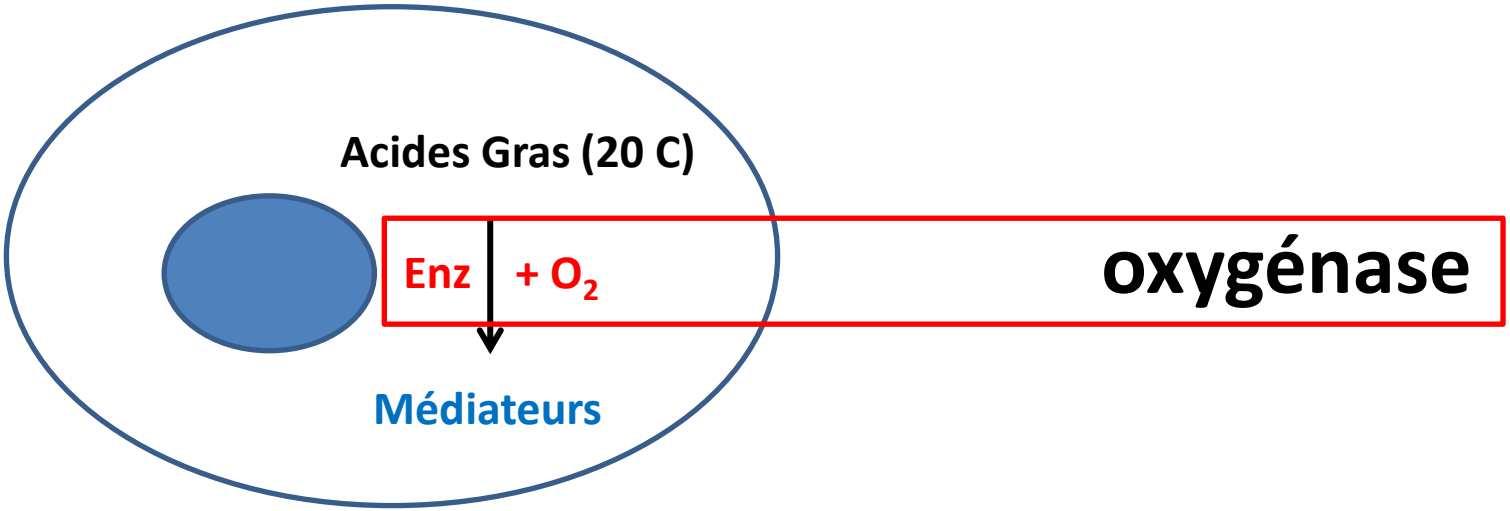
# Phospholipases

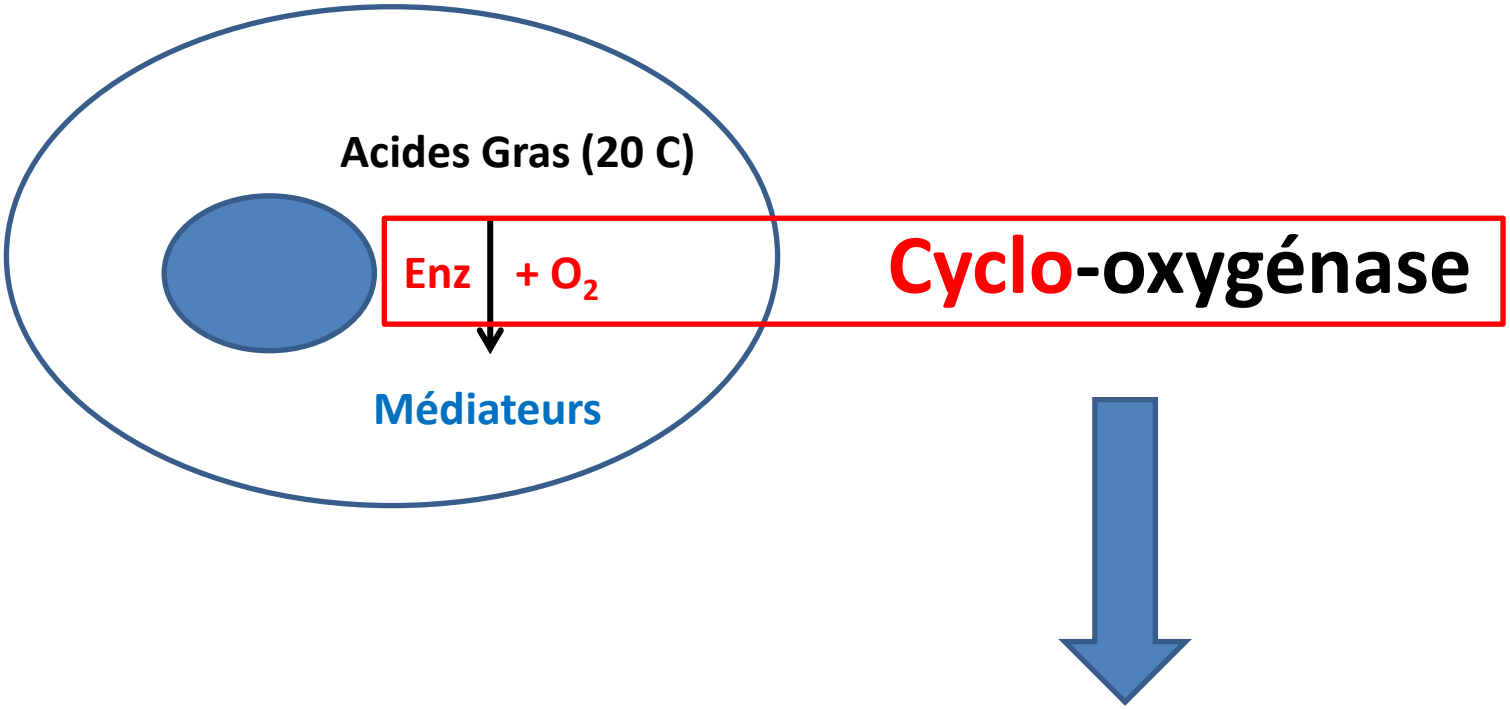
- A1
- A2
- C
- D




PLA2
PL
Acides Gras (20 C)
Memb.
Enz
+ $O_2$
Médiateurs
Cellules cibles
RCPG
Effets
Physiologiques
Effets
Pathologiques

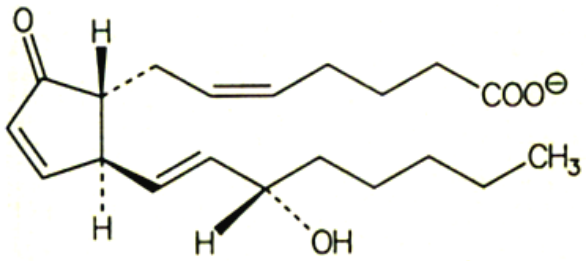

Corticostéroïdes
PL
Memb.
Acides Gras (20 C)
Enz
+ $O_2$
Médiateurs
Cellules cibles
RCPG
Effets
Physiologiques
Effets
Pathologiques


Acides Gras (20 C)
Enz
+ $O_2$
oxygénase
Médiateurs

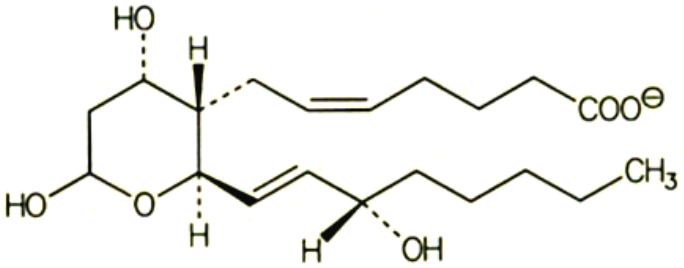



Dérivés Cycliques

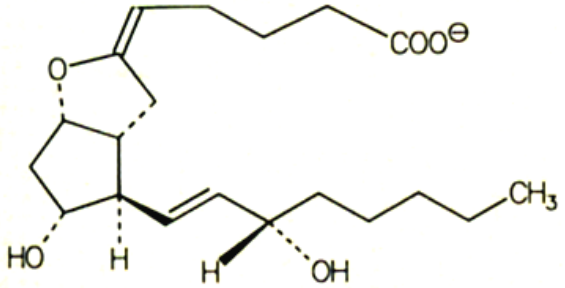
# Exemples de Médiateurs dérivés de l'AA



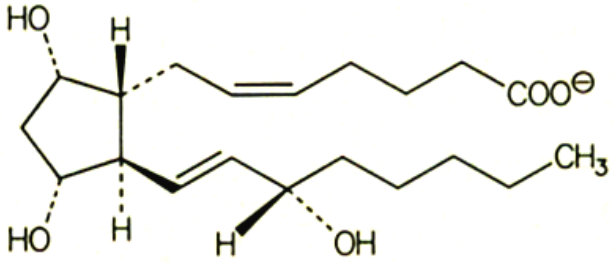

prostaglandine $A_2$




thromboxane $B_2$

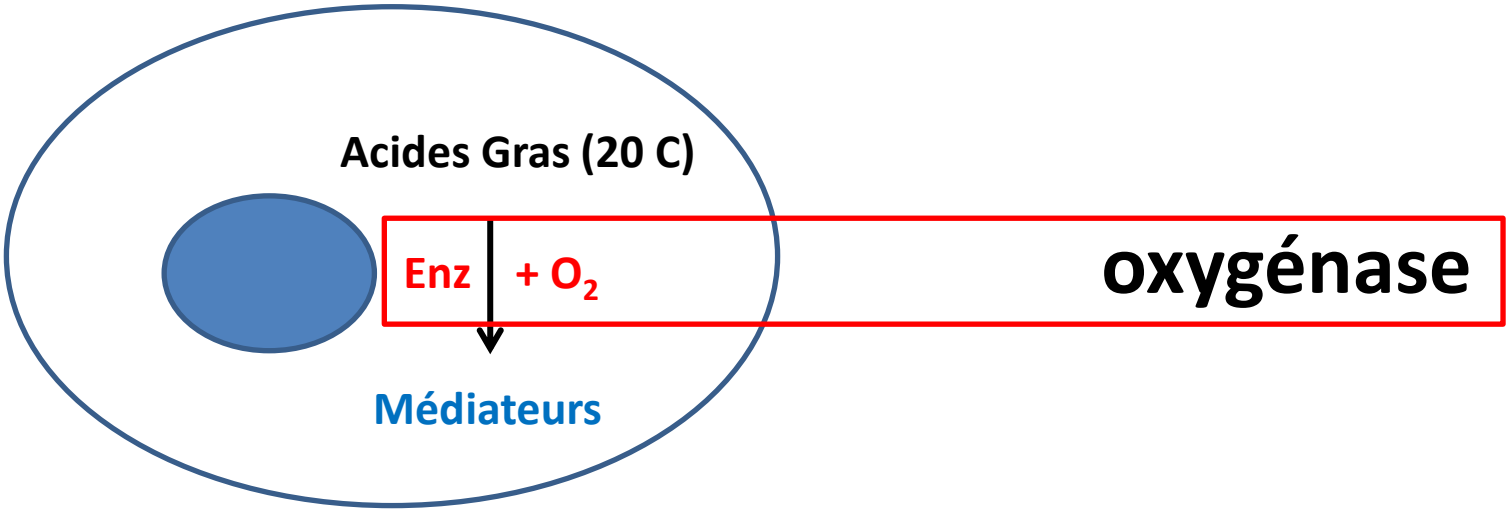


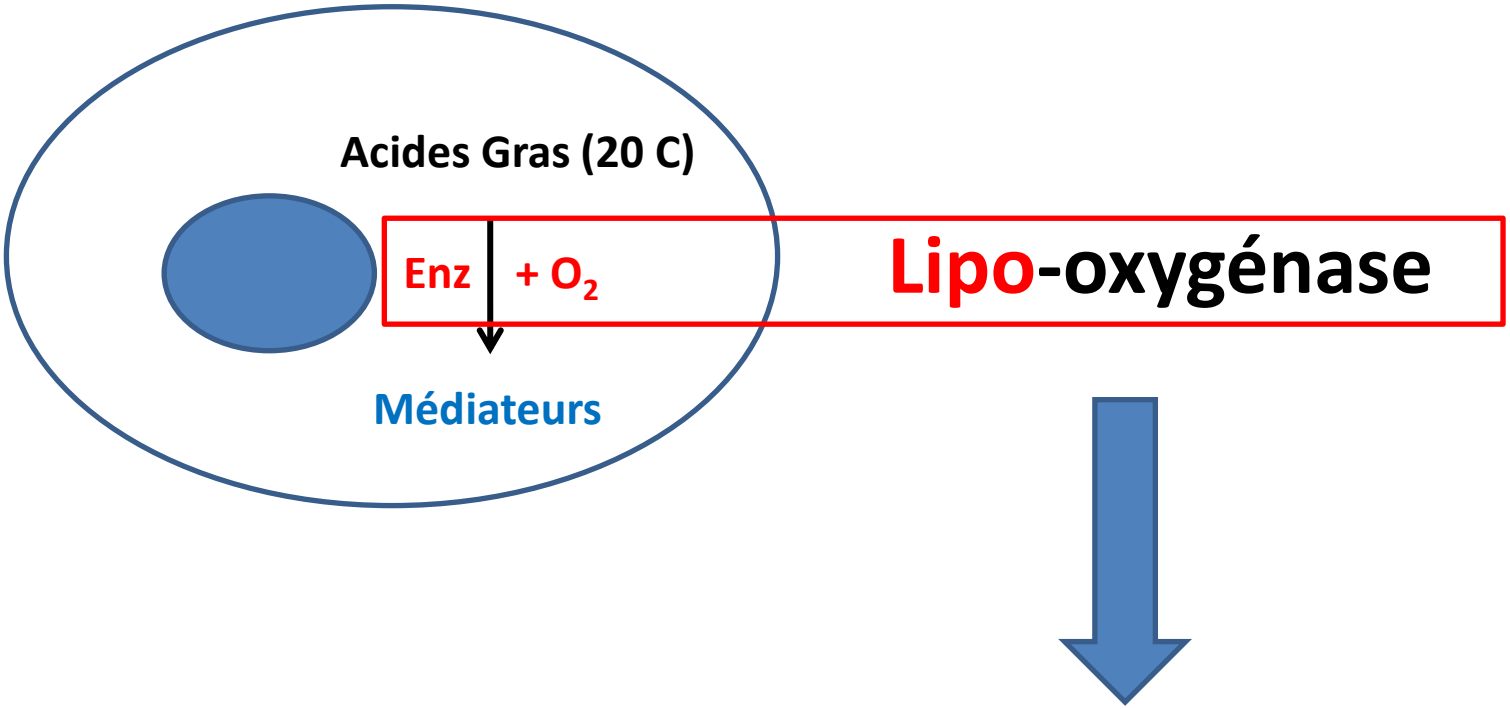

prostacycline $I_2$



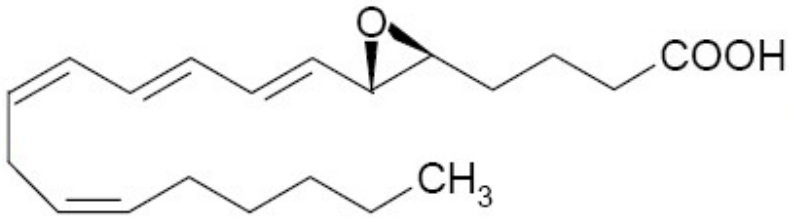

prostaglandine $F_{2\alpha}$

Structures
Cycliques

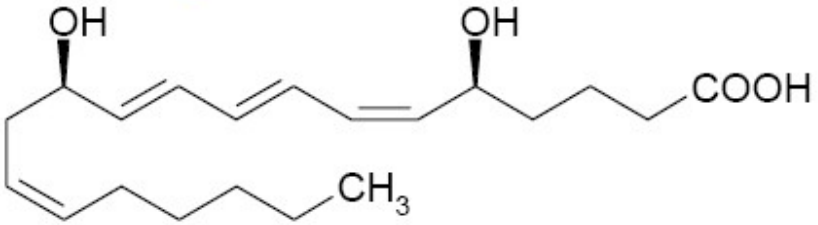

Acides Gras (20 C)
Enz
+ $O_2$
oxygénase
Médiateurs




Dérivés NON cycliques

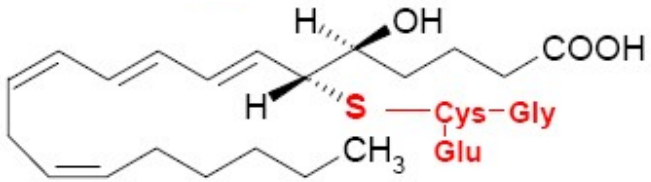



**LTA4**

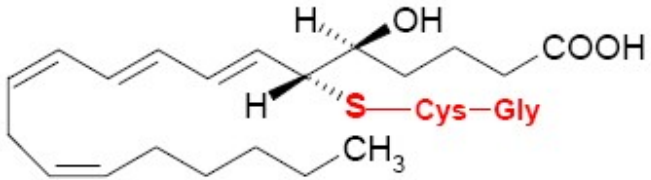



**LTB4**

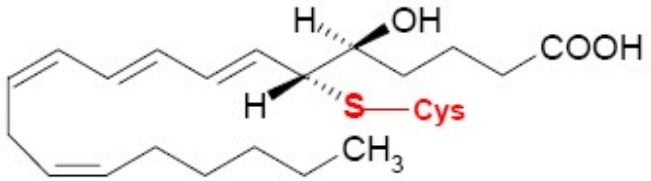
**LTC4**




**LTD4**




**LTE4**




# LT : Leucotriène

# Acides Gras (20 C)

i. **Acide arachidonique** **C 20:4 (n-6)**

# Acides Gras (20 C)

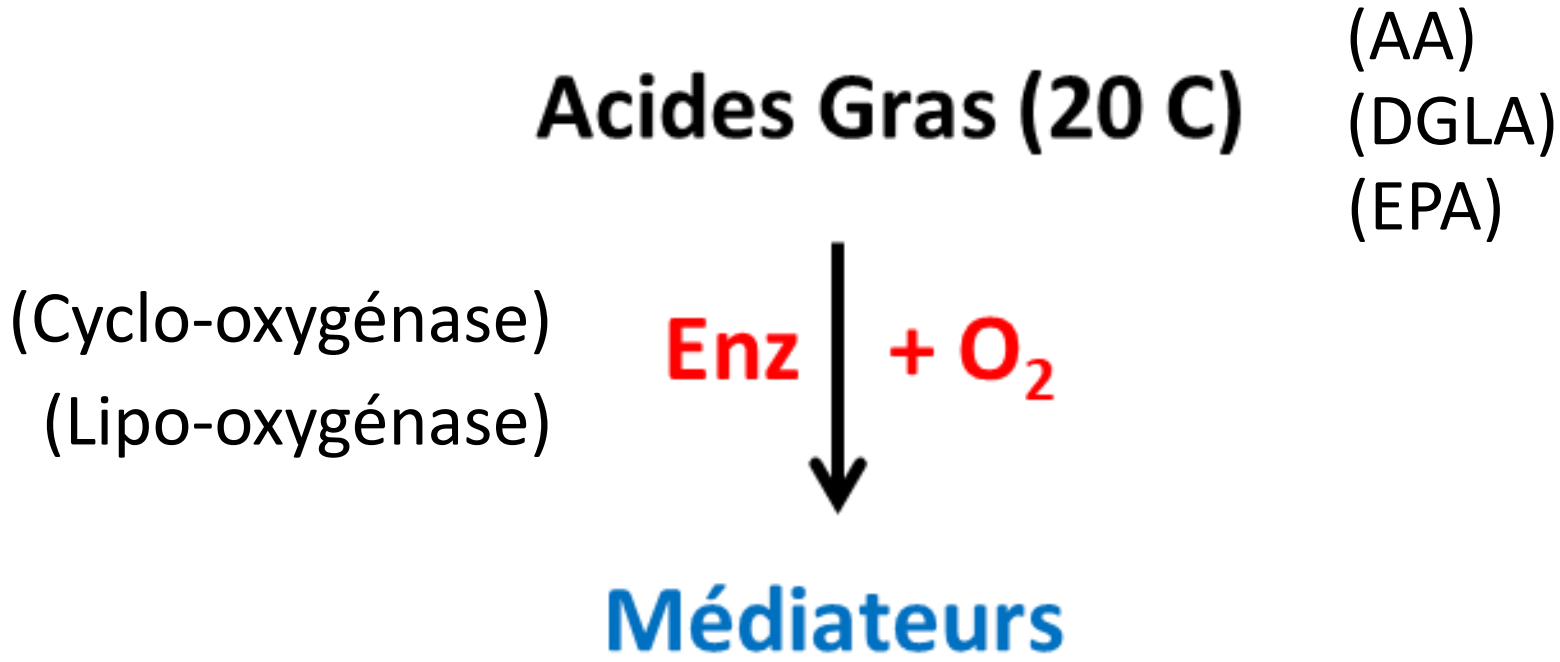
| | | |
|---|---|---|
| **i.** | **Acide arachidonique** | **C 20:4 (n-6)** |
| ii. | Acide dihomo-γ-linolénique | C 20:3 (n-6) |
| iii. | Acide eicosapentaénoïque | C 20:5 (n-3) |

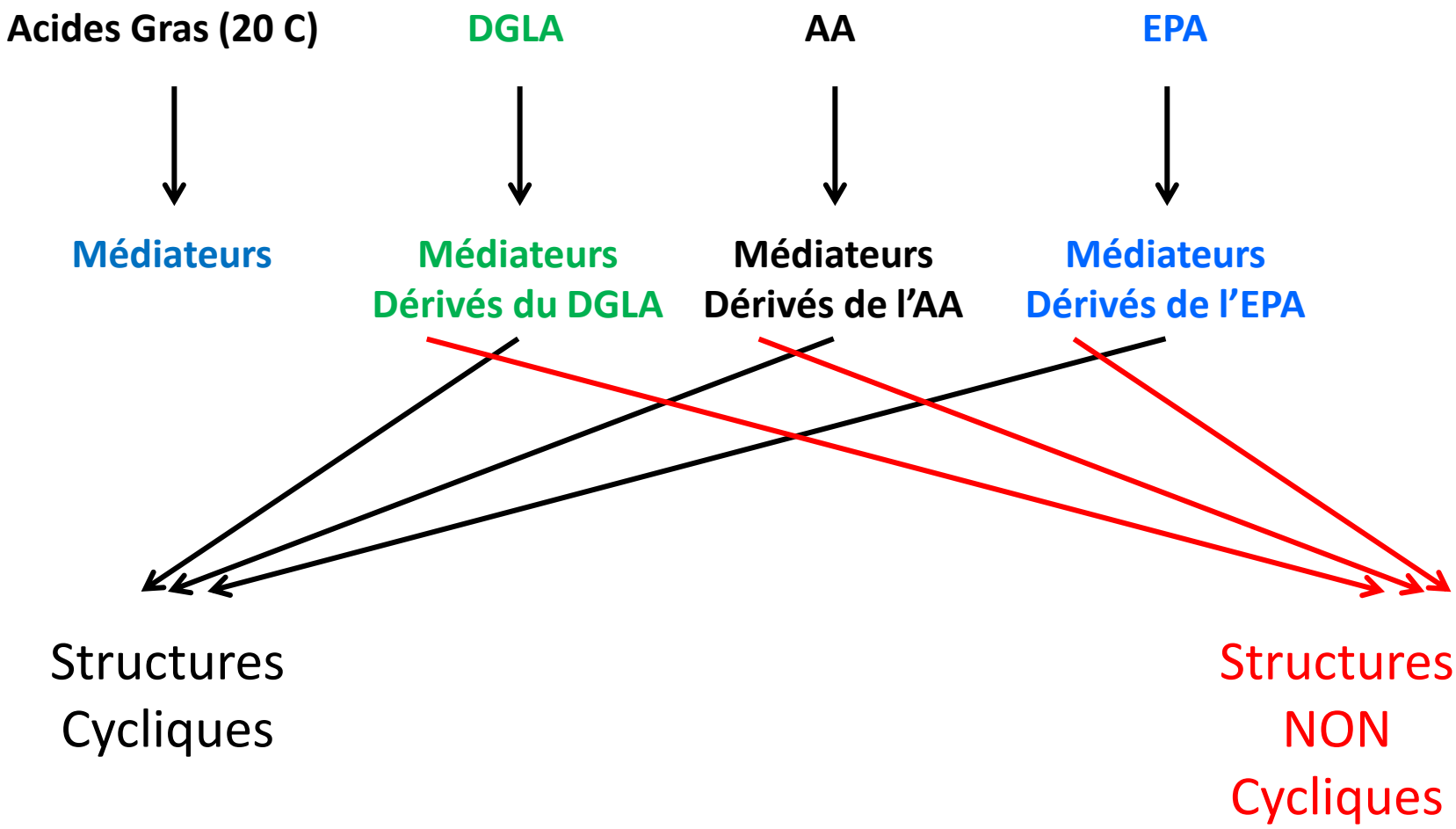
# Acides Gras (20 C)

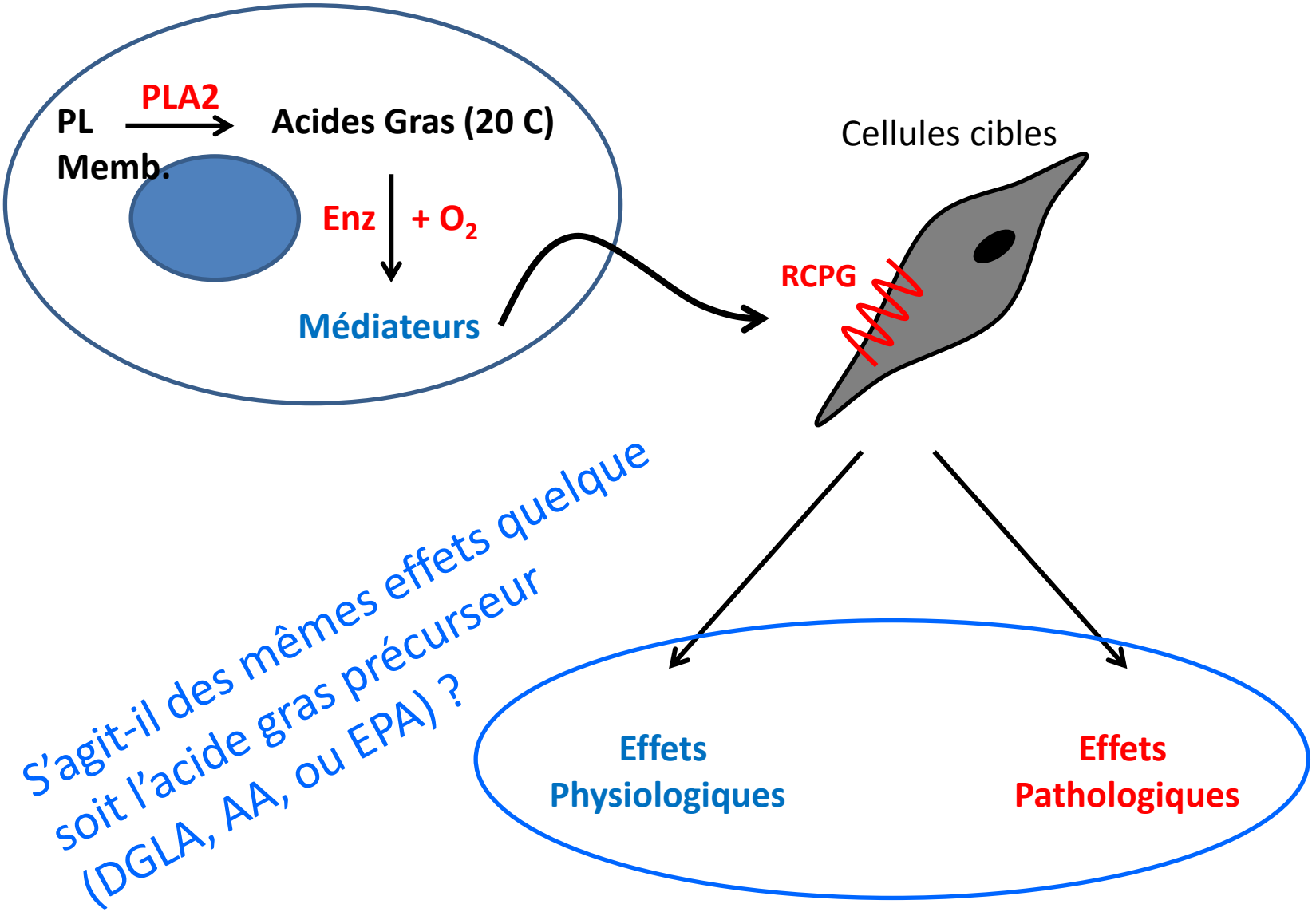
| | | |
|---|---|---|
| **i.** | **AA** | **C 20:4 (n-6)** |
| ii. | DGLA | C 20:3 (n-6) |
| iii. | EPA | C 20:5 (n-3) |

# Acides Gras (20 C)

| | | |
|---|---|---|
| **i.** | **AA** | **C 20:4 (ω 6)** |
| ii. | DGLA | C 20:3 (ω 6) |
| iii. | EPA | C 20:5 (ω 3) |


Acides Gras (20 C)
(AA)
(DGLA)
(EPA)
(Cyclo-oxygénase)
(Lipo-oxygénase)
Enz
+ $O_2$
Médiateurs


Acides Gras (20 C)
DGLA
AA
EPA
Médiateurs
Médiateurs
Dérivés du DGLA
Médiateurs
Dérivés de l'AA
Médiateurs
Dérivés de l'EPA
Structures
Cycliques
Structures
NON
Cycliques


PLA2
PL
Acides Gras (20 C)
Memb.
Enz
+ $O_2$
Médiateurs
Cellules cibles
RCPG
S'agit-il des mêmes effets quelque soit l'acide gras précurseur (DGLA, AA, ou EPA) ?
Effets Physiologiques
Effets Pathologiques

# PLASMA LIPID AND LIPOPROTEIN PATTERN IN GREENLANDIC WEST-COAST ESKIMOS

H. O. BANG J. DYERBERG
AASE BRØNDUM NIELSEN

*Department of Clinical Chemistry,*
*Aalborg Hospital North, Denmark*

***Summary*** The plasma-lipid pattern, including quantitative lipoprotein electrophoresis, was examined in 130 Eskimos (69 females, 61 males) — hunters and/or fishermen, and their wives — in the northern part of the west coast of Greenland, and consuming a predominantly meat diet rich in polyunsaturated fatty acids. Most types of lipid were decreased, compared with Danish controls and Eskimos living in Denmark. The most remarkable finding was a much lower level of pre-β-lipoprotein and consequently of plasma-triglycerides in Greenlandic Eskimos than in Danish controls. These findings may explain the very low incidence of ischæmic heart-disease and the complete absence of diabetes mellitus in Greenlandic Eskimos.

The NEW ENGLAND JOURNAL of MEDICINE

CURRENT ISSUE SPECIALTIES TOPICS

ORIGINAL ARTICLE

# Marine n–3 Fatty Acids and Prevention of Cardiovascular Disease and Cancer

**Authors**: JoAnn E. Manson, M.D., Dr.P.H., Nancy R. Cook, Sc.D., I-Min Lee, M.B., B.S., Sc.D., William Christen, Sc.D., Shari S. Bassuk, Sc.D., Samia Mora, M.D., M.H.S., Heike Gibson, Ph.D., +10 , for the VITAL Research Group* Author Info & Affiliations

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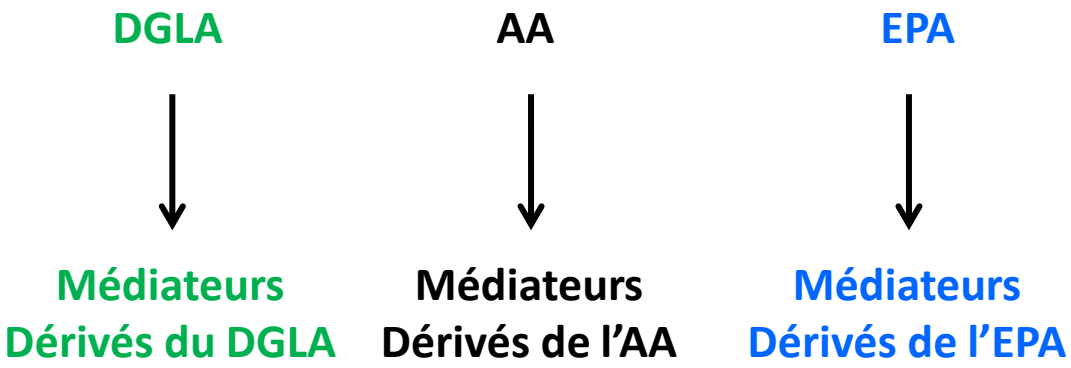
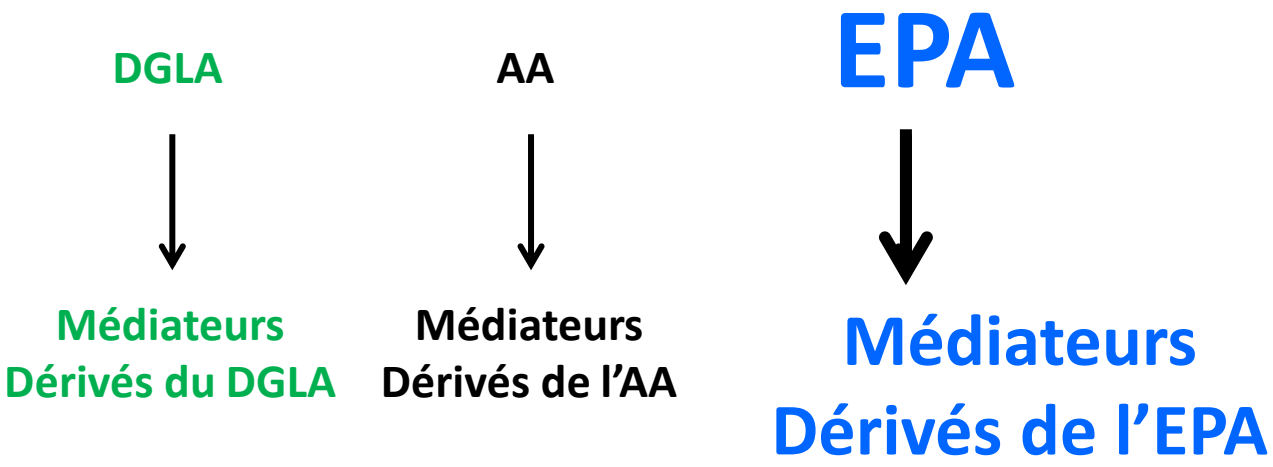
## CONCLUSIONS

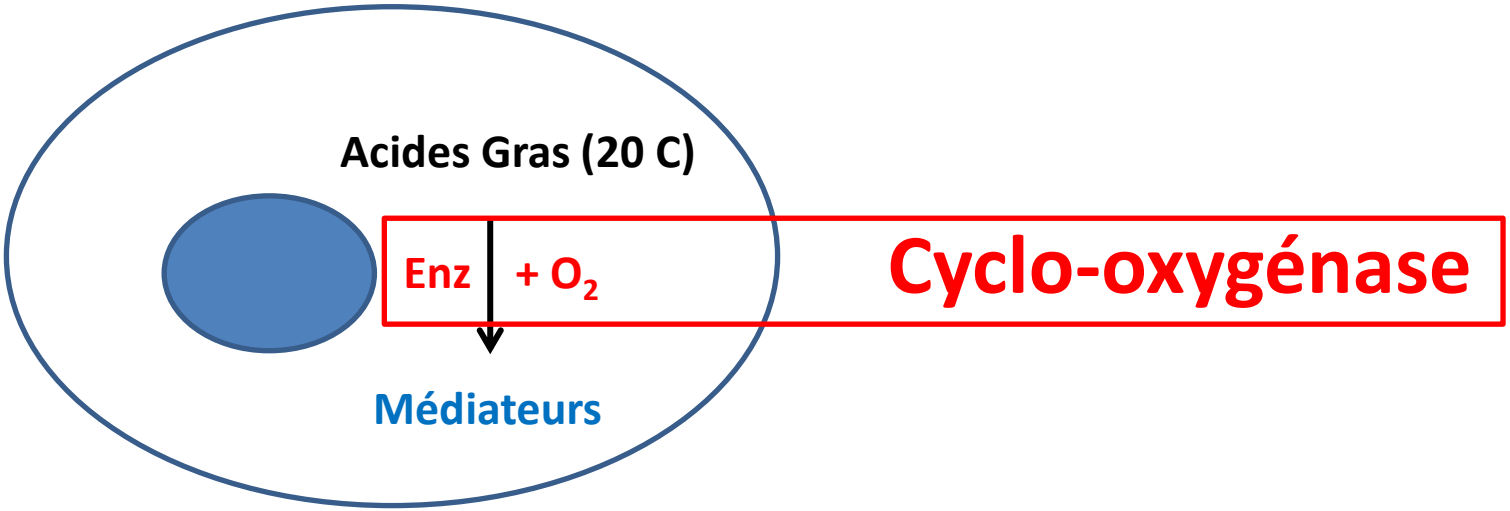
Supplementation with n–3 fatty acids did not result in a lower incidence of major cardiovascular events or cancer than placebo.

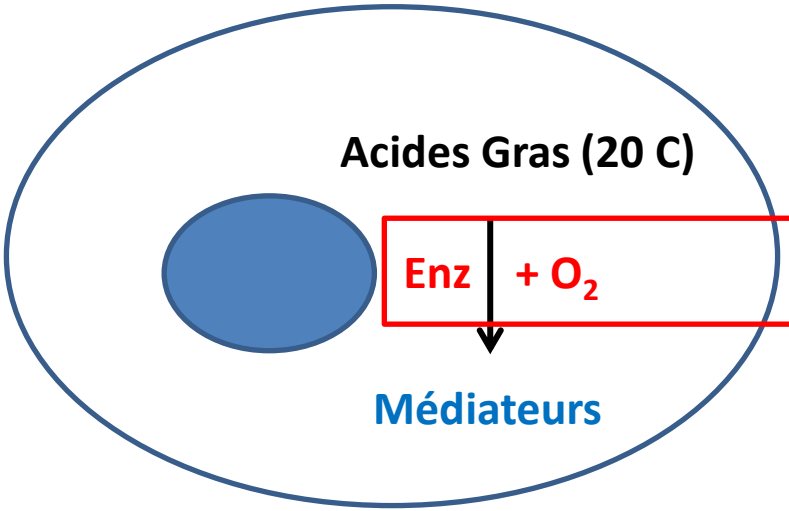
# Le biais de confirmation

Tendance naturelle à privilégier et à retenir les informations qui confirment nos croyances, tout en ignorant celles qui les contredisent


DGLA
AA
EPA
Médiateurs
Dérivés du DGLA
Médiateurs
Dérivés de l'AA
Médiateurs
Dérivés de l'EPA


DGLA
AA
EPA
Médiateurs
Dérivés du DGLA
Médiateurs
Dérivés de l'AA
Médiateurs
Dérivés de l'EPA


Acides Gras (20 C)
Enz
+ $O_2$
Cyclo-oxygénase
Médiateurs

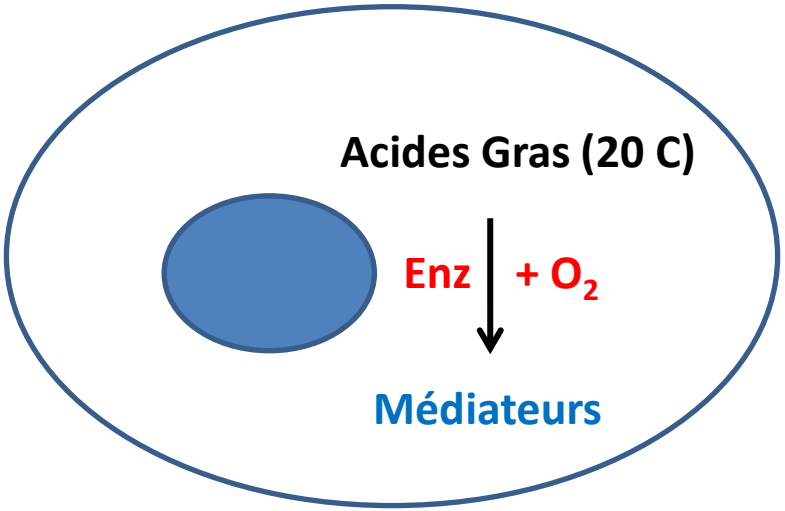



**Cyclo-oxygénase**

**=**

**COX**

**PGH synthase**




**Cyclo-oxygénases**

**=**

**COX**

**PGH synthases**

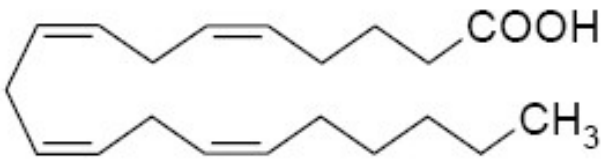
## ISOENZYMES

- COX-1
- COX-2

- COX-3 (Variant de cox-1)

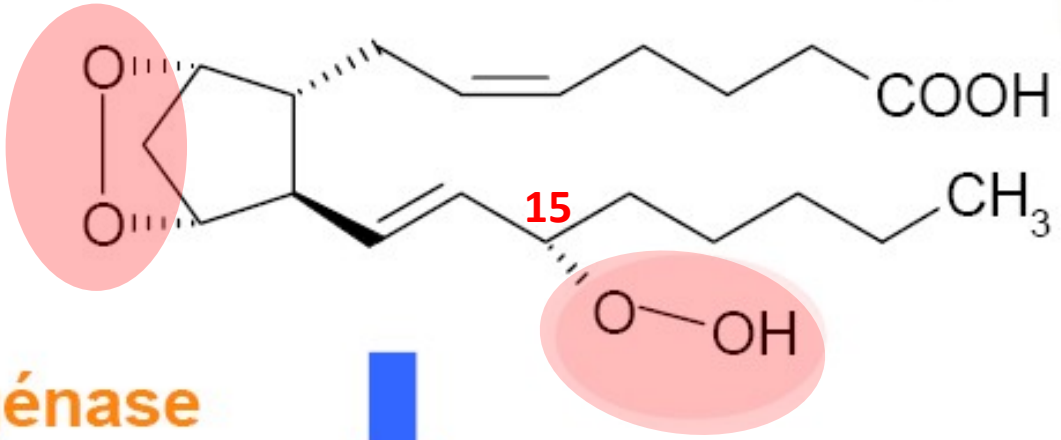
| Isoenzyme | Expression | Tissus majeurs | Rôle dominant |
|---|---|---|---|
| **COX-1** | Constitutive | Estomac, plaquettes, rein | Homéostasie |
| **COX-2** | Inductible + constitutive | Cellules inflammatoires, rein, SNC | Inflammation, douleur |
| **COX-3** | SNC | Cerveau | Douleur / fièvre |

**AA**



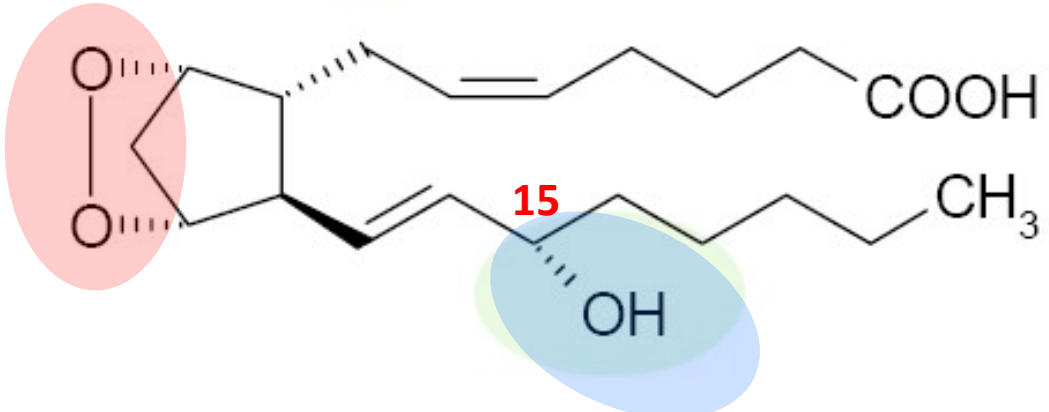

cyclo-oxygénase

**PG $G_2$**

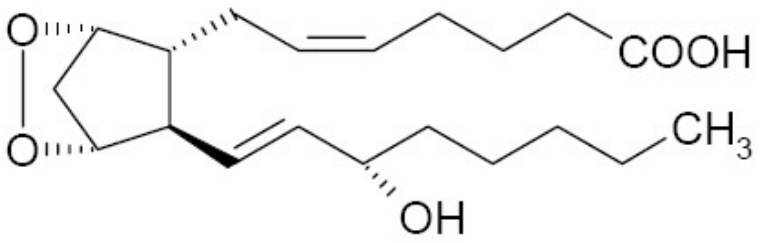



cyclo-oxygénase

**PG $H_2$**



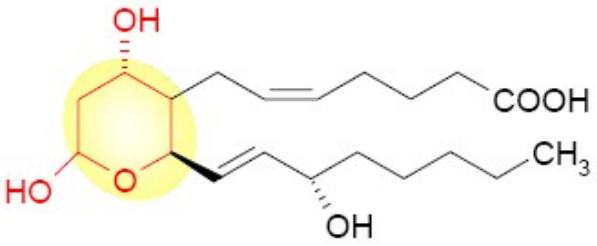
**PG $H_2$**



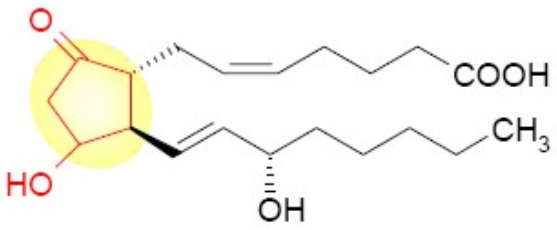

Thromboxane synthase

Prostaglandine synthase

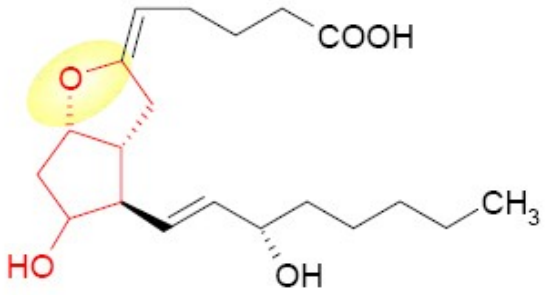
Prostacycline synthase



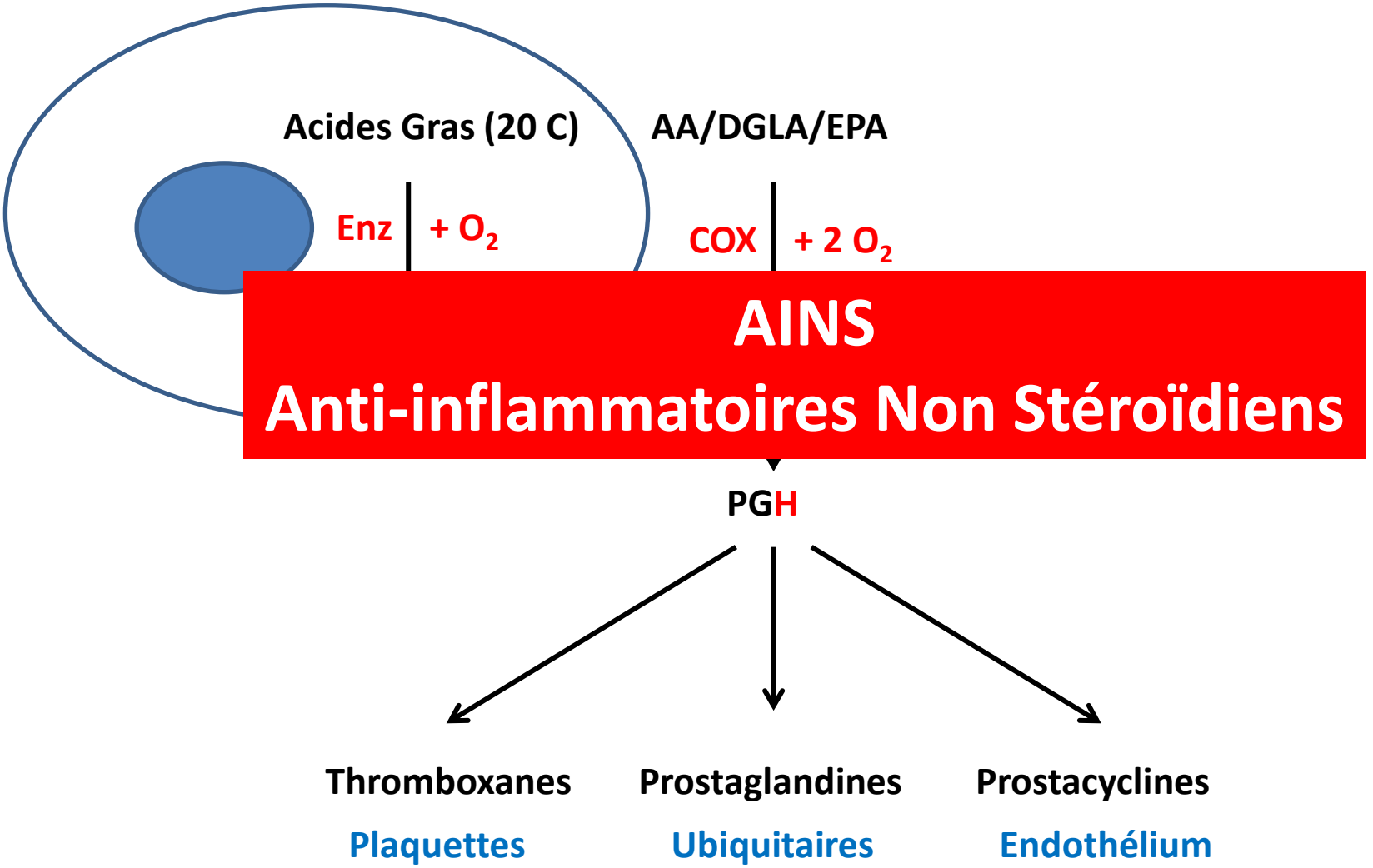

**Thromboxane $B_2$**

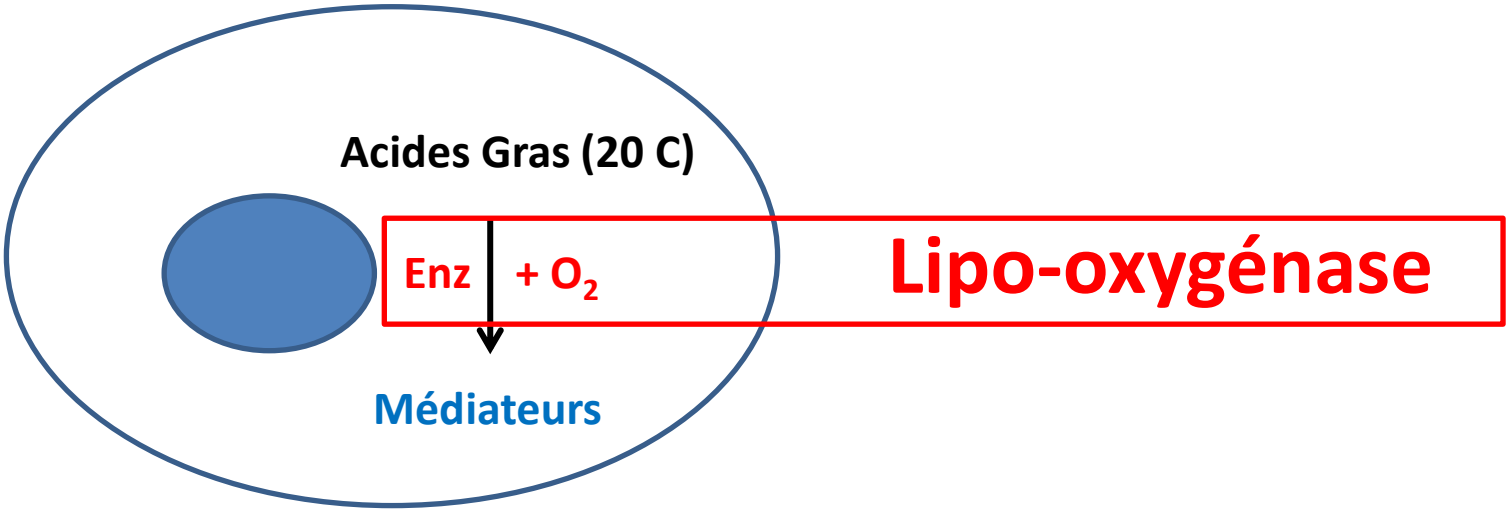



**Prostaglandine $E_2$**

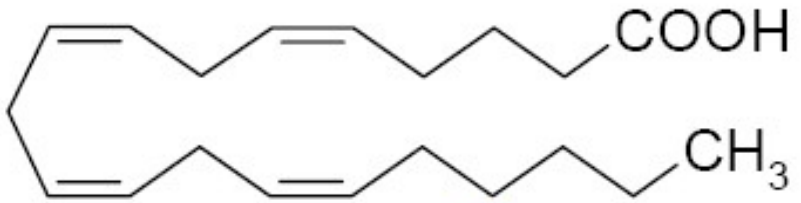



**Prostacycline $I_2$**

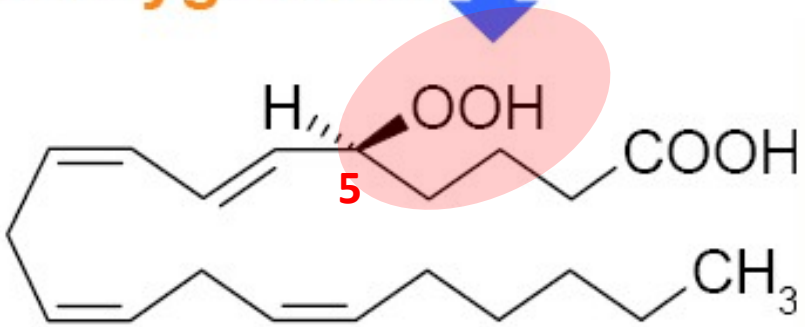

Acides Gras (20 C)
AA/DGLA/EPA
Enz
+ $O_2$
COX
+ 2 $O_2$
AINS
Anti-inflammatoires Non Stéroïdiens
PGH
Thromboxanes
Plaquettes
Prostaglandines
Ubiquitaires
Prostacyclines
Endothélium


Acides Gras (20 C)
Enz
+ $O_2$
Lipo-oxygénase
Médiateurs

**AA**

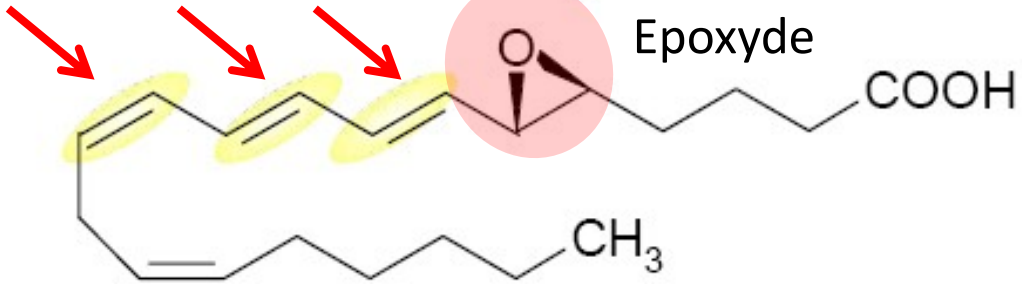



5-lipo-oxygénase

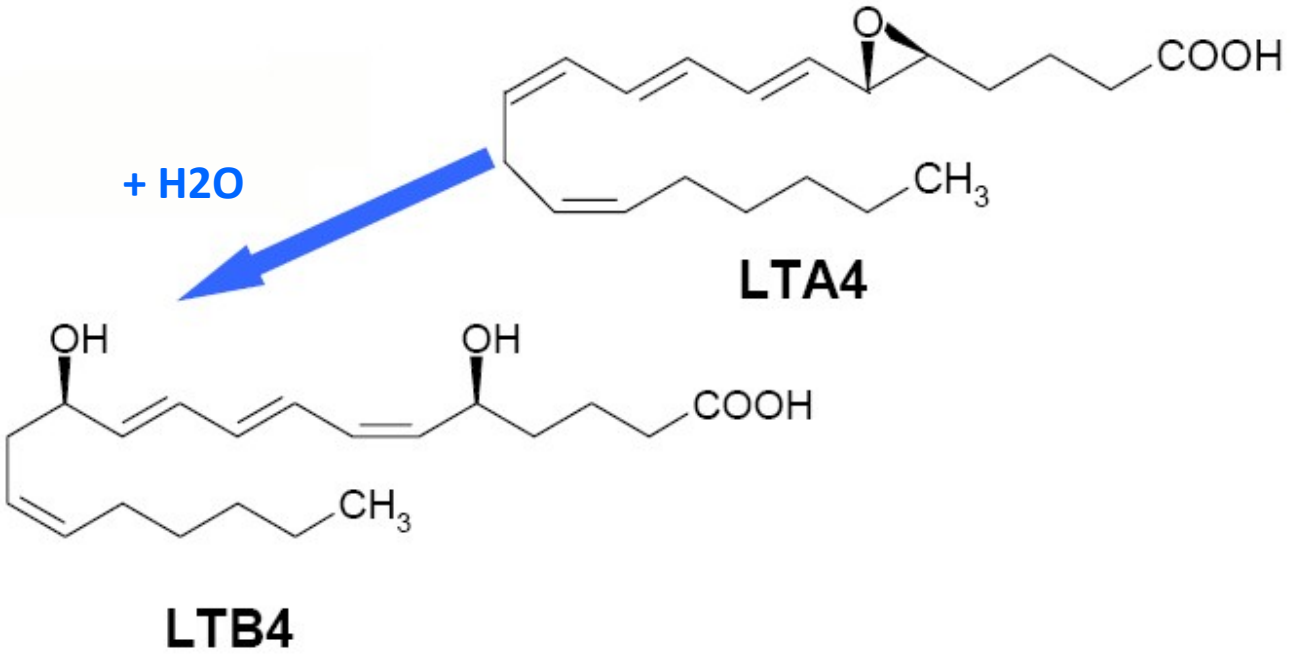


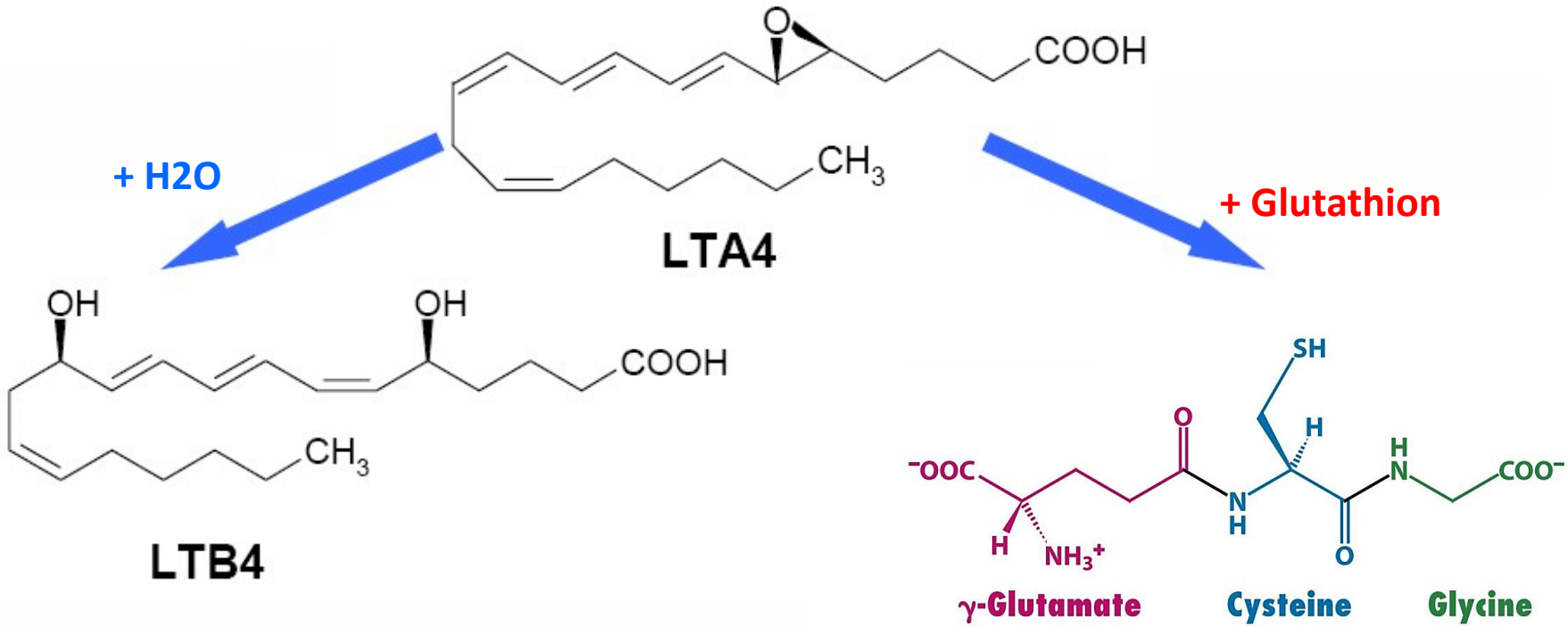

**5-HPETE**

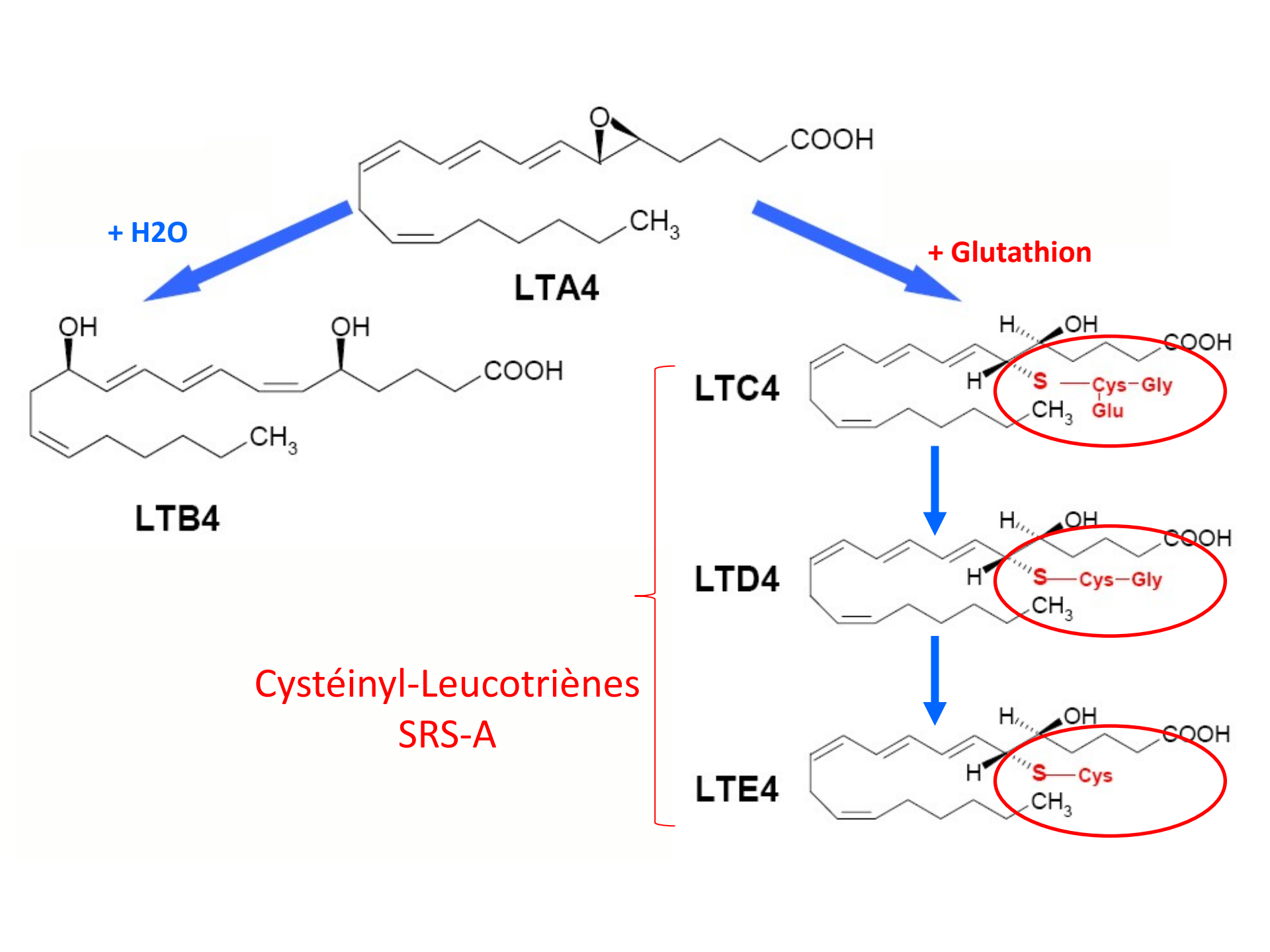
5-lipo-oxygénase

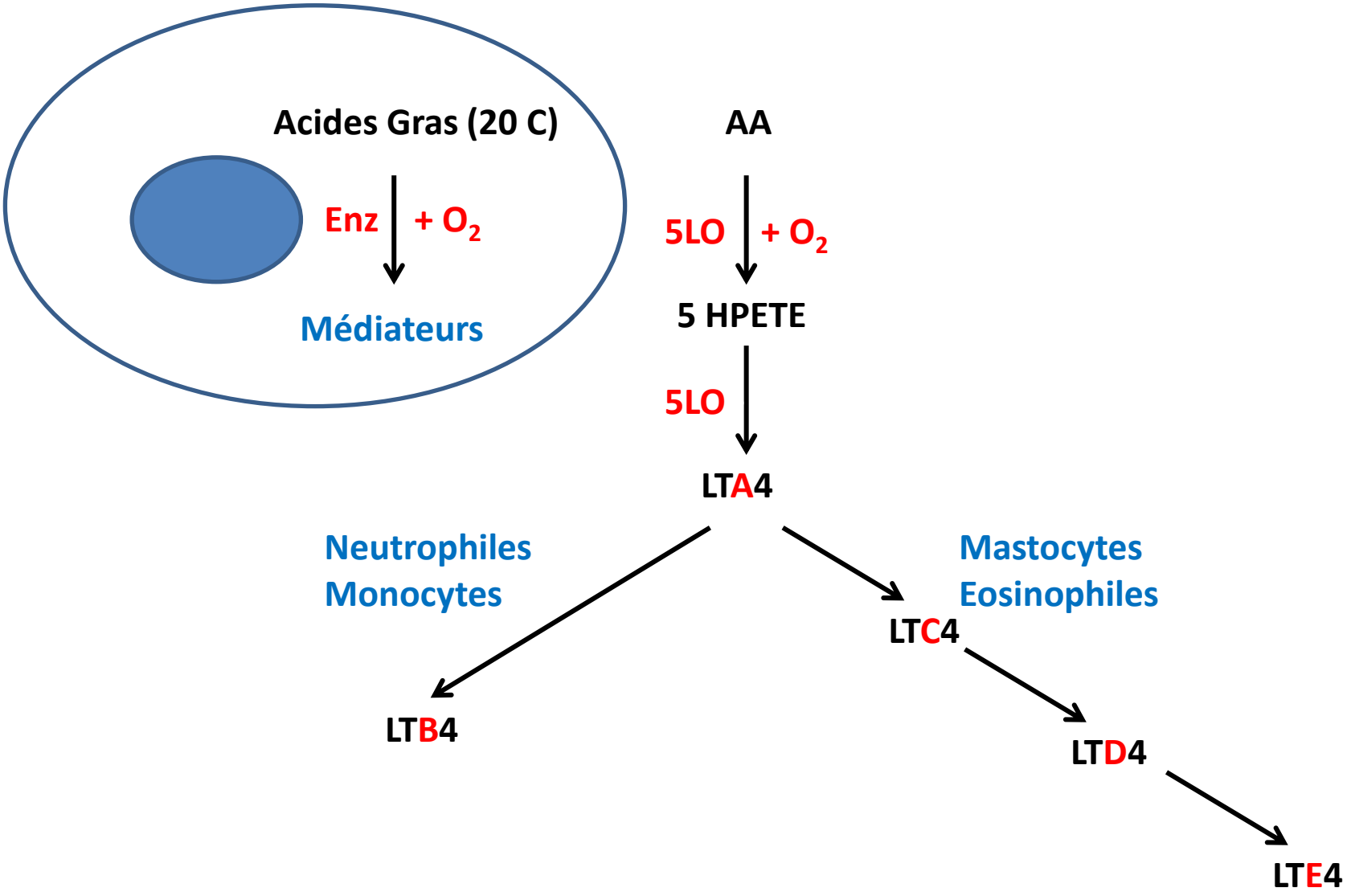



**LeucoTriene A4** **LTA4**

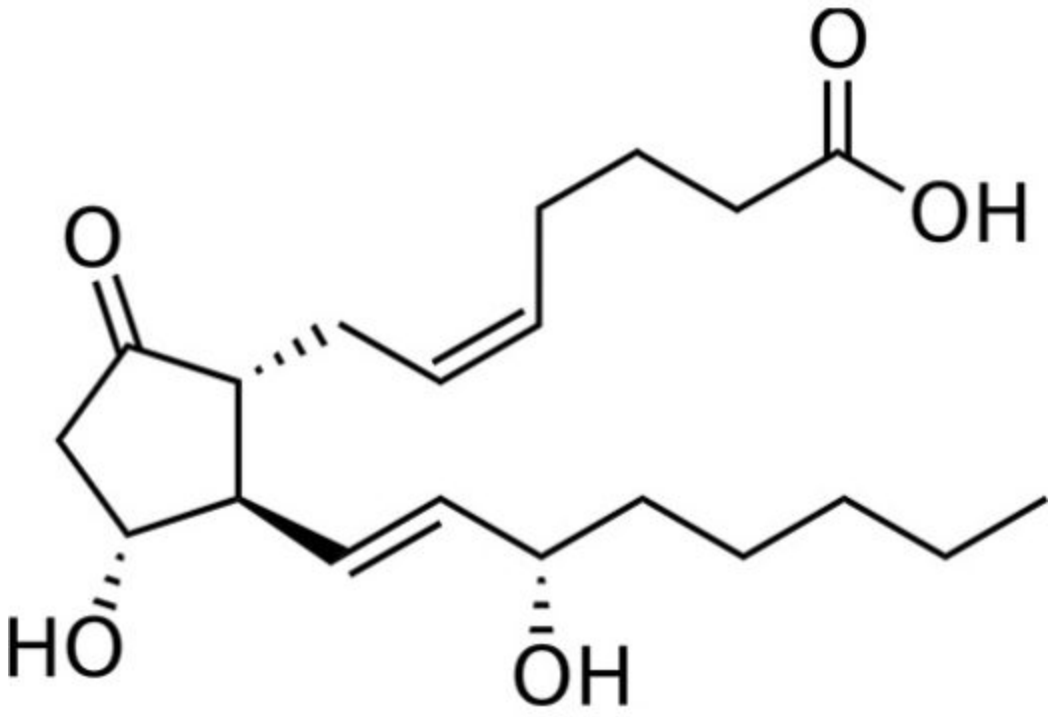

+ H2O
O
COOH
CH3
LTA4
OH
OH
COOH
CH3
LTB4


O
COOH
CH3
LTA4
+ H2O
+ Glutathion
OH
OH
COOH
CH3
LTB4
SH
O
H
H
N
COO⁻
⁻OOC
N
H
H
NH3+
O
γ-Glutamate
Cysteine
Glycine

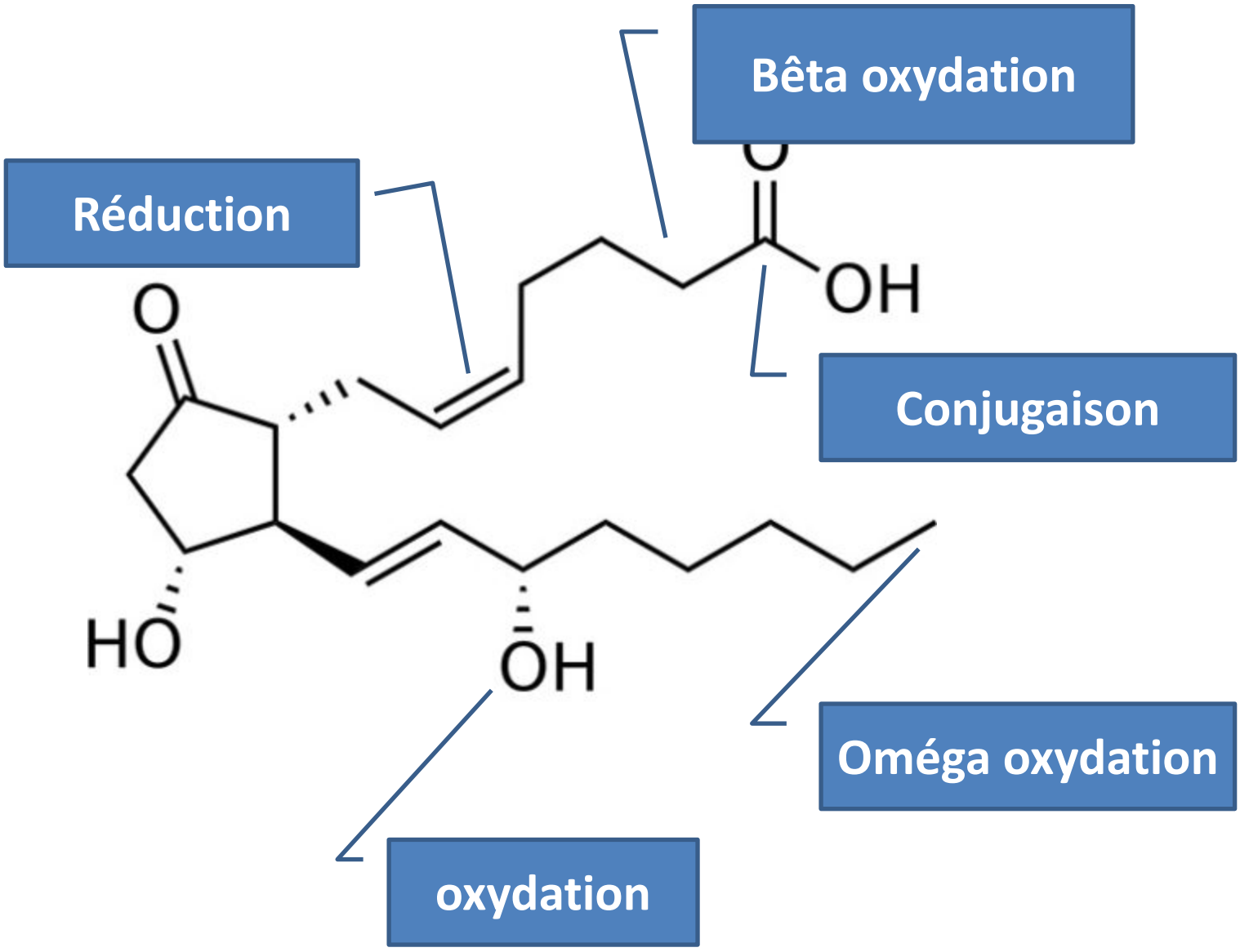

+ H2O
+ Glutathion
LTA4
LTB4
LTC4
LTD4
LTE4
Cystéinyl-Leucotriènes
SRS-A

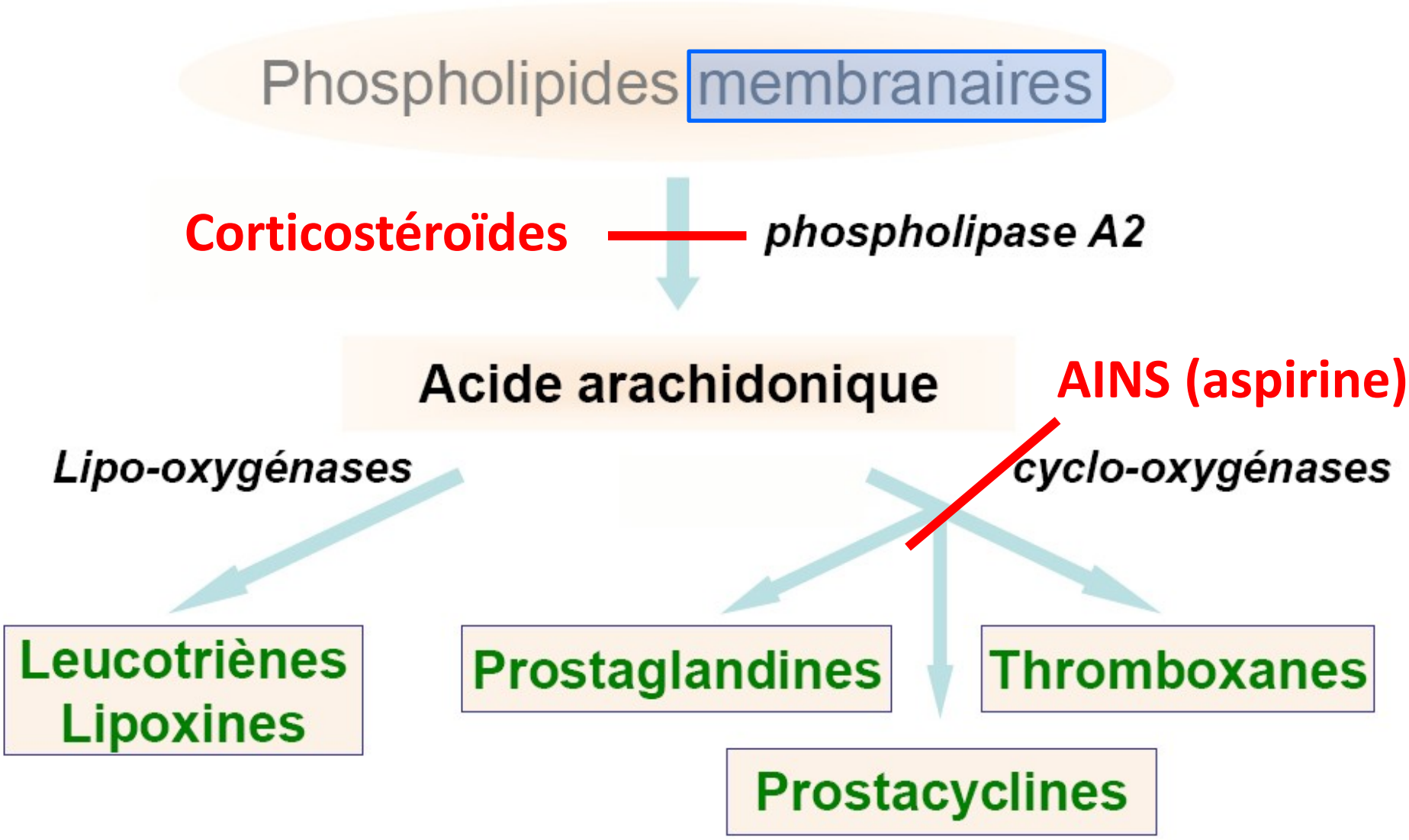

Acides Gras (20 C)
Enz
+ $O_2$
Médiateurs
AA
5LO
+ $O_2$
5 HPETE
5LO
LTA4
Neutrophiles
Monocytes
Mastocytes
Eosinophiles
LTC4
LTB4
LTD4
LTE4

# Catabolisme



# Catabolisme

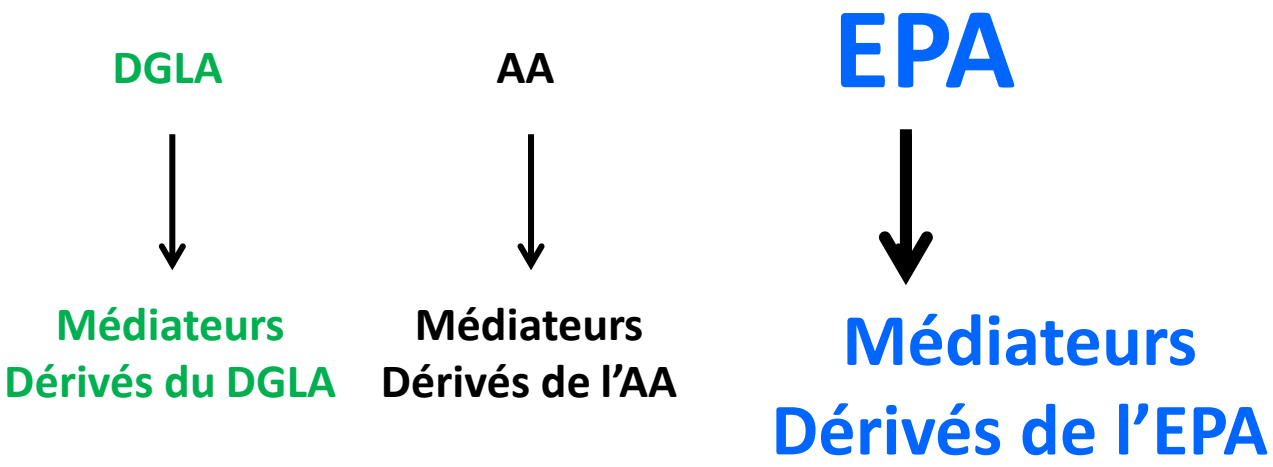



Phospholipides membranaires
Corticostéroïdes
phospholipase A2
Acide arachidonique
AINS (aspirine)
Lipo-oxygénases
cyclo-oxygénases
Leucotriènes
Lipoxines
Prostaglandines
Thromboxanes
Prostacyclines

Action
anti-inflammatoire

**Effets indésirables**

| Isoenzyme | Expression | Tissus majeurs | Rôle dominant |
|---|---|---|---|
| **COX-1** | Constitutive | Estomac, plaquettes, rein | Homéostasie |
| **COX-2** | Inductible + constitutive | Cellules inflammatoires, rein, SNC | Inflammation, douleur |
| **COX-3** | SNC | Cerveau | Douleur / fièvre |

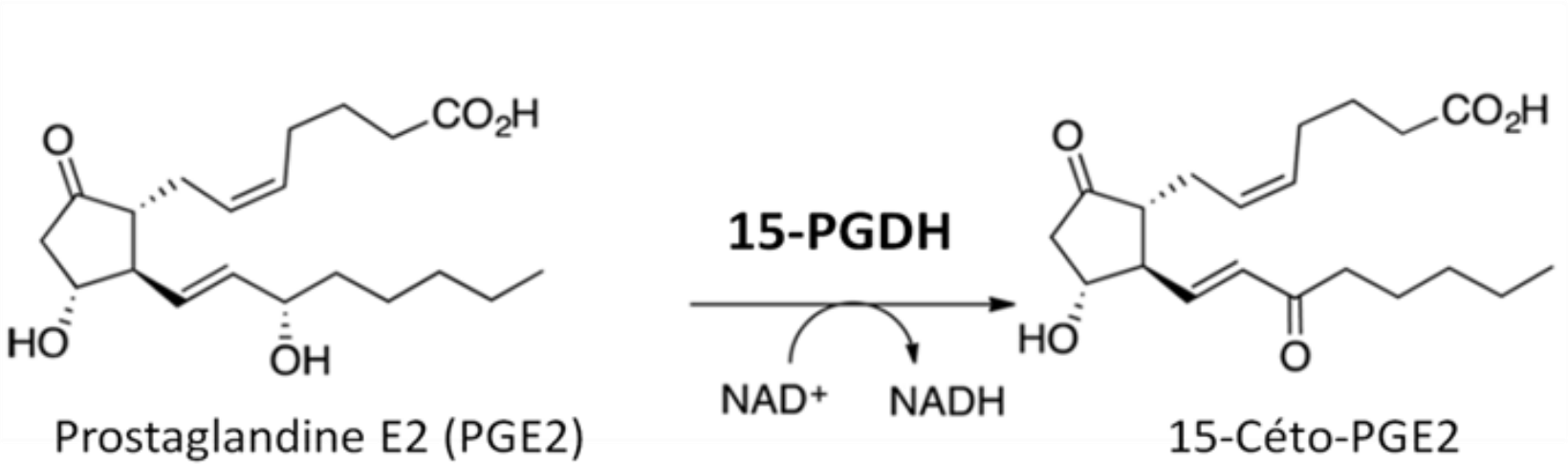

DGLA
AA
EPA
Médiateurs
Dérivés du DGLA
Médiateurs
Dérivés de l'AA
Médiateurs
Dérivés de l'EPA

# Exercice

1. La prostaglandine E2 (PGE2), en plus de son action inflammatoire, peut exercer un effet favorisant la multiplication des cellules (effet prolifératif)

1. La prostaglandine E2 (PGE2), en plus de son action inflammatoire, peut exercer un effet favorisant la multiplication des cellules (effet prolifératif)

2. La PGE2 peut être transformée en 15-Céto-PGE2 par la 15-prostaglandine déshydrogénase (15-PGDH) selon la réaction ci-dessous




Prostaglandine E2 (PGE2)

15-Céto-PGE2

3. Dans certains cancers nous avons constaté une augmentation de l'expression d'une isoenzyme de la cyclo-oxygénase (COX-2) concomitante avec une baisse de l'expression de la 15-PGDH.

Expliquez le lien éventuel de ces données avec le développement tumoral

La 15-PGDH transforme la PGE2 en un dérivé inactif en raison de l'absence de l'OH en position 15.

L'enzyme COX-2 permet la synthèse des prostaglandines Selon la donnée 3, cette situation aura pour résultante une augmentation de la production de PGE2 avec une baisse de son inactivation. La concentration de PGE2 va donc augmenter.

Comme nous savons que la PGE2 possède un effet « prolifératif », nous pouvons supposer que l'augmentation des concentrations de la PGE2 va favoriser la prolifération tumorale.


BONUS


Paracétamol 1000 mg
COMPRIMÉS
Antalgique et antipyretique
16 Comprimés
PCEM1LABS

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|---|---|---|---|
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# MERCI !