Implication polymorphismes gène MTHFR dans les fausses couches à répétition

SAMPIL
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Laboratoire CLEMENT

Pas de conflit d’intérêt à signaler

Fausse couche / Miscarriage / Recurrent Pregnancy Loss

Définition

Organisation Mondiale de la Santé (OMS)	American Congress of Obstetricians and Gynecologists (ACOG)
⊗ ⊗ ⊗	⊗ ⊗
3 fausse couches consécutives	2 fausses couche consécutives

Etiologies

- Génétiques : trisomie (21), polyploïdie, monotonie X
- Malformations utérines
- Maladie chronique non équilibrée : diabète, dysthyroïde, SOPK, lupus,
- Troubles de l'hémostase : SAPL
- Infections : toxoplasmose, rubéole, listériose

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MTHFR et Fausses couches

Jeddi-Tehrani et al., 2011
Iran
5 polymorphismes génétiques
Association de MTFR (C677T et A1298C) avec FC

Torabi et al., 2012
2 groupes :
- 100 femmes avec minimum 2 FC consécutives
- 100 femmes avec minimum 2 naissances vivantes et aucune FC

Comparaison sur 11 polymorphismes génétiques
Association de MTFR (A1298C) avec FC

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MTHFR et Fausses couches

Methylenetetrahydrofolate Reductase C677T and A1298C Polymorphisms in Male Partners of Recurrent Miscarriage Couples

Somayeh Sadat Tara [1], Fatemeh Ghaemimanesh [2], Saeed Zarei [2], Fakhreddin Reihani-Sabet [3], Zhamak Pahlevanzadeh [3], Mohammad Hosein Modarresi [4], Mahmood Jeddi-Tehrani [2*]

Tara et al., 2015

2 groupes :
- 100 couples avec minimum 2 naissances vivantes sans complications obstétricales
- 225 couples avec min 3 FC successives ayant comme critères d'exclusion : femmes avec
  - 1 des 2 mutations à l'état hétérozygote
  - Polymorphisme sauvage

Analyse MTHFR chez femmes et leurs conjoints

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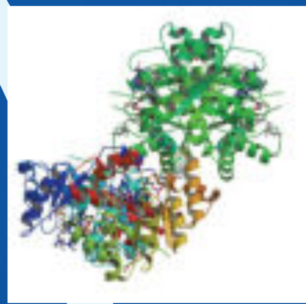
MTHFR



Enzyme codée par gène de 12 exons, sur chromosome 1
656 acides aminés
2 SNPs décrits —> ↘ 50% activité enzymatique
- C677T (Alanine en Valine)
- A1298C (Glutamate en Alanine)

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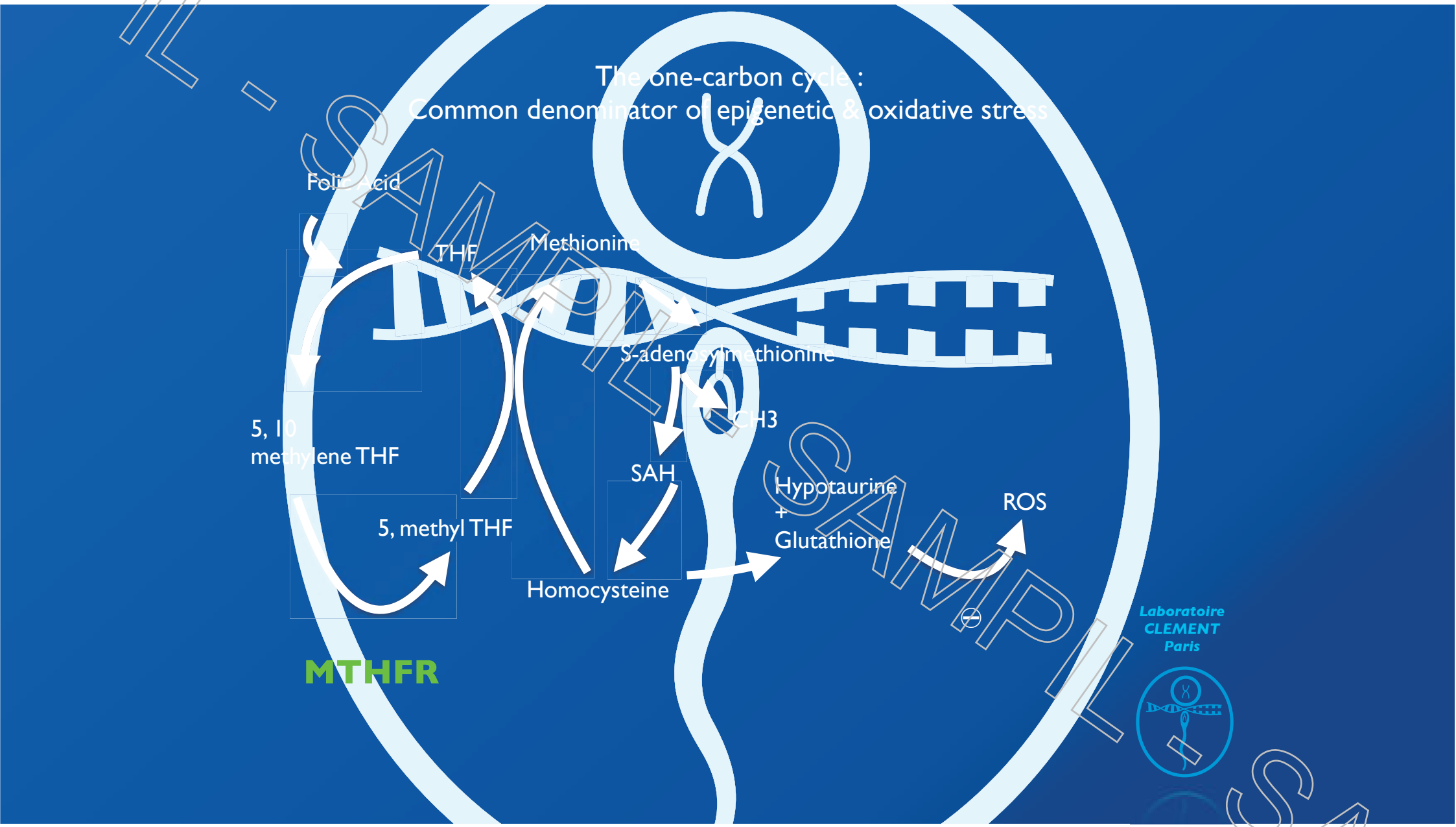

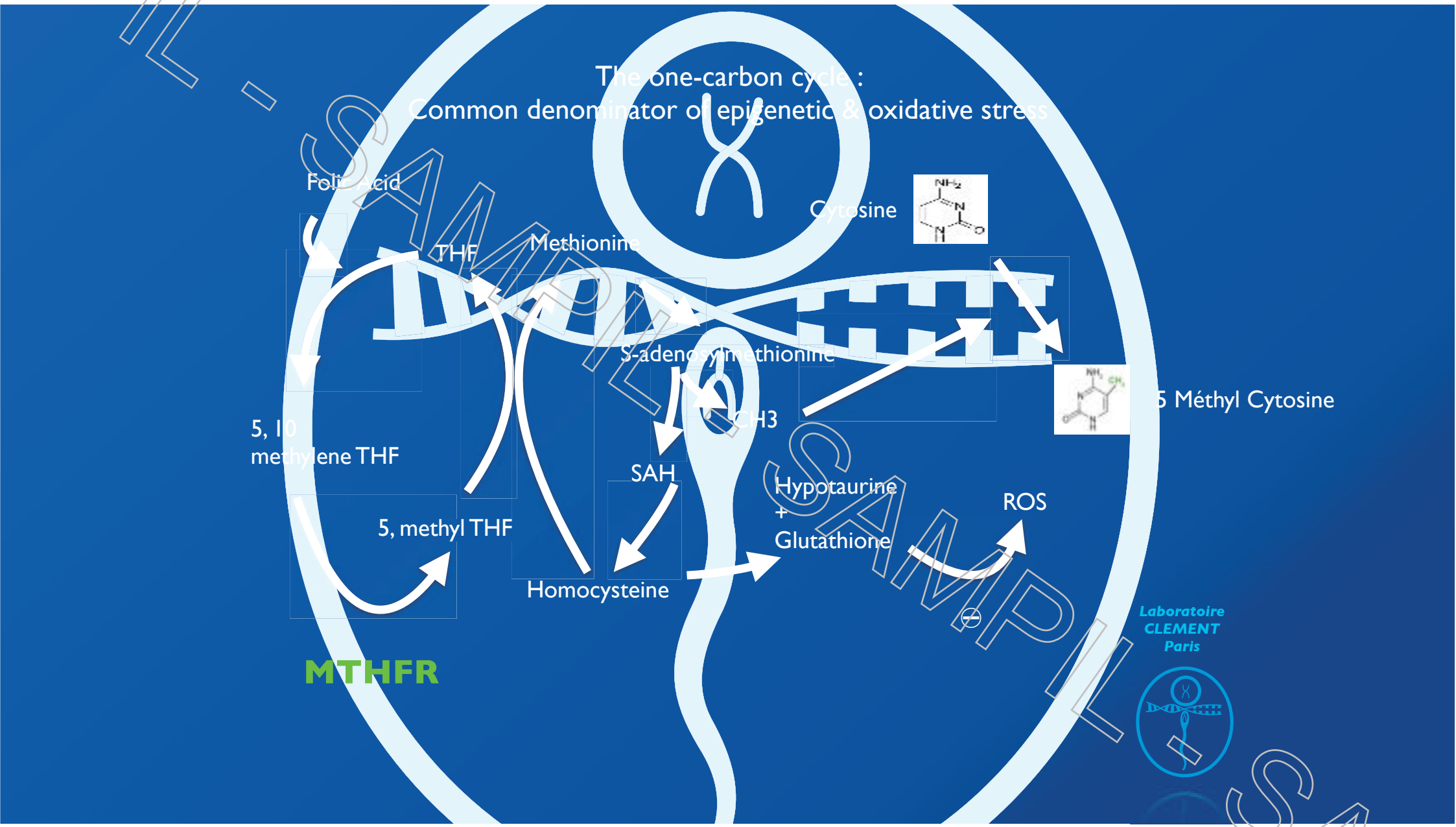
The one-carbon cycle :
Common denominator of epigenetic & oxidative stress
Folic Acid
THF
Methionine
Cytosine
S-adenosylmethionine
CH3
5 Méthyl Cytosine
5, 10
methylene THF
5, methyl THF
SAH
Homocysteine
Hypotaurine
+
Glutathione
ROS
MTHFR
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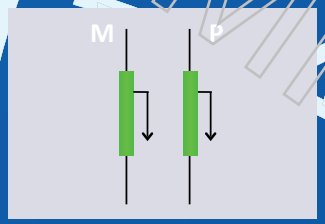
Genomic imprinting

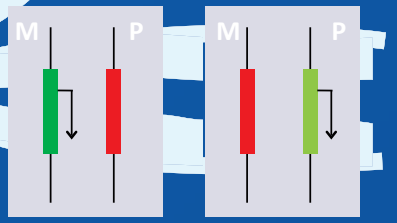
Non imprinted Genes

Biallelic Expression



Imprinted Genes

Monoallelic Expression



Maternally expressed

Paternally expressed

DNA Methylation

Cytosine

5 Methyl Cytosine

DNA methyl transferase adds a methyl group

Blocks transcription of that gene

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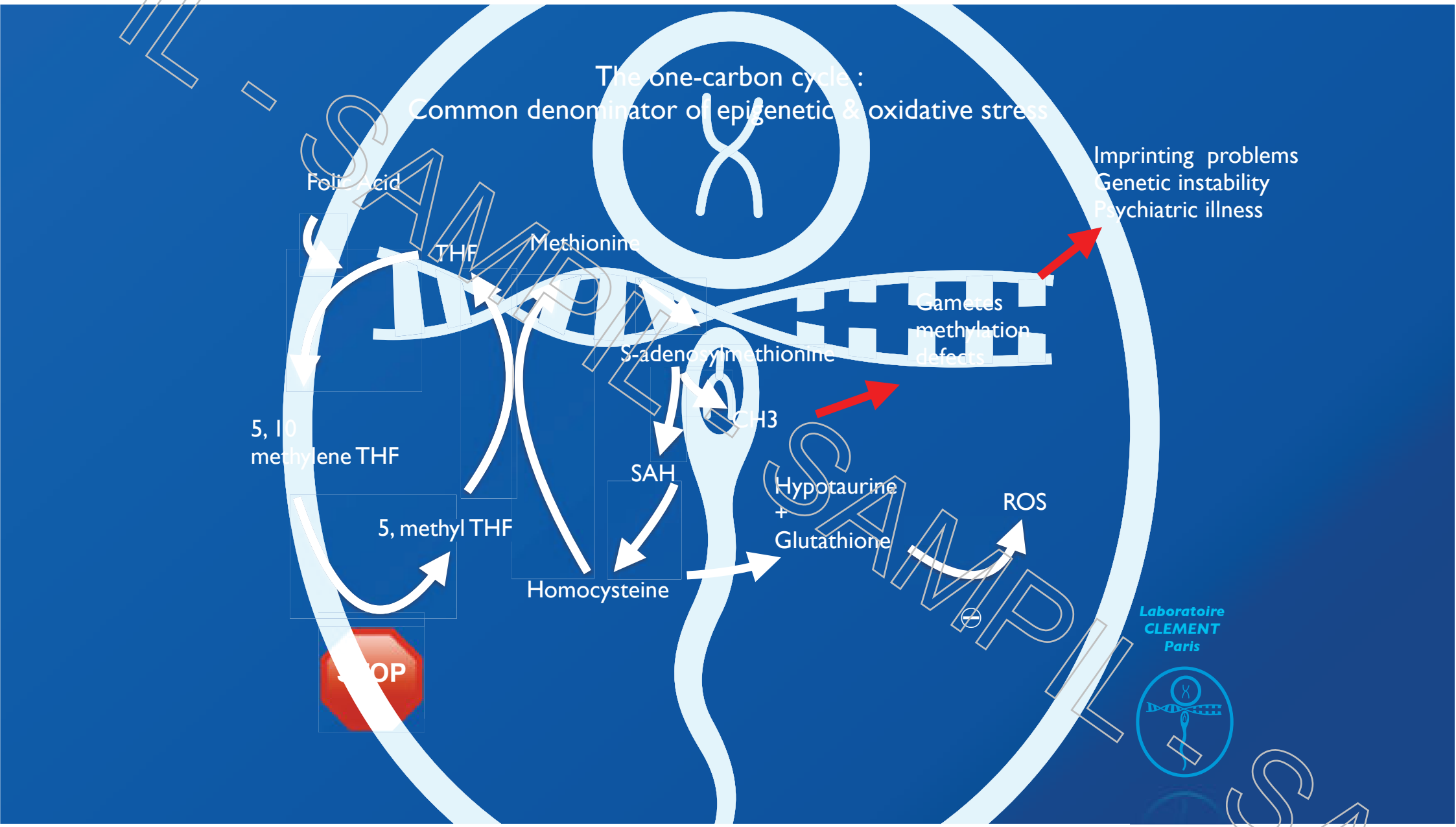
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Homocysteine
STOP
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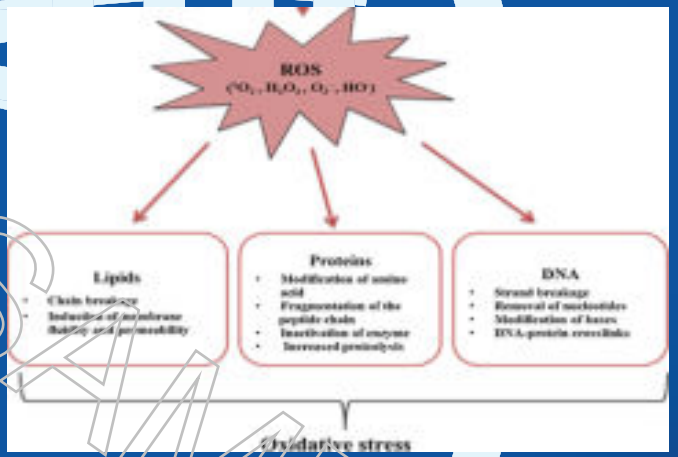
Oxidative Stress (OS)

Reactive Oxygen Species (ROS): natural byproduct of aerobic metabolism
- **important role in cellular signaling and homeostasis**
- **highly reactive free radicals – can cause oxidative damage to DNA & other molecules**

1. Antioxidant defense mechanisms provide protection from ROS : an imbalance between ROS and antioxidant defense mechanisms creates OS

2. *OS is linked to errors in methylation*: 'two sides of the same coin' *(Ménézo et al., 2016)*
   - Strong correlation between oxidative stress and DNA methylation, via an influence on the 1-CC
   - Guanine is highly sensitive to oxidation: 8-oxoG
     - Significant effect on CpG islands (and telomeres)

3. OS disturbs important zones of gene expression/ regulation linked to epigenetic homeostasis



Environmental endocrine disruptor chemicals (EDCs) exacerbate OS
Xenobiotics: mimic natural hormones and occupy hormone receptors
Negative effects on methylation processes, transgenerational effect

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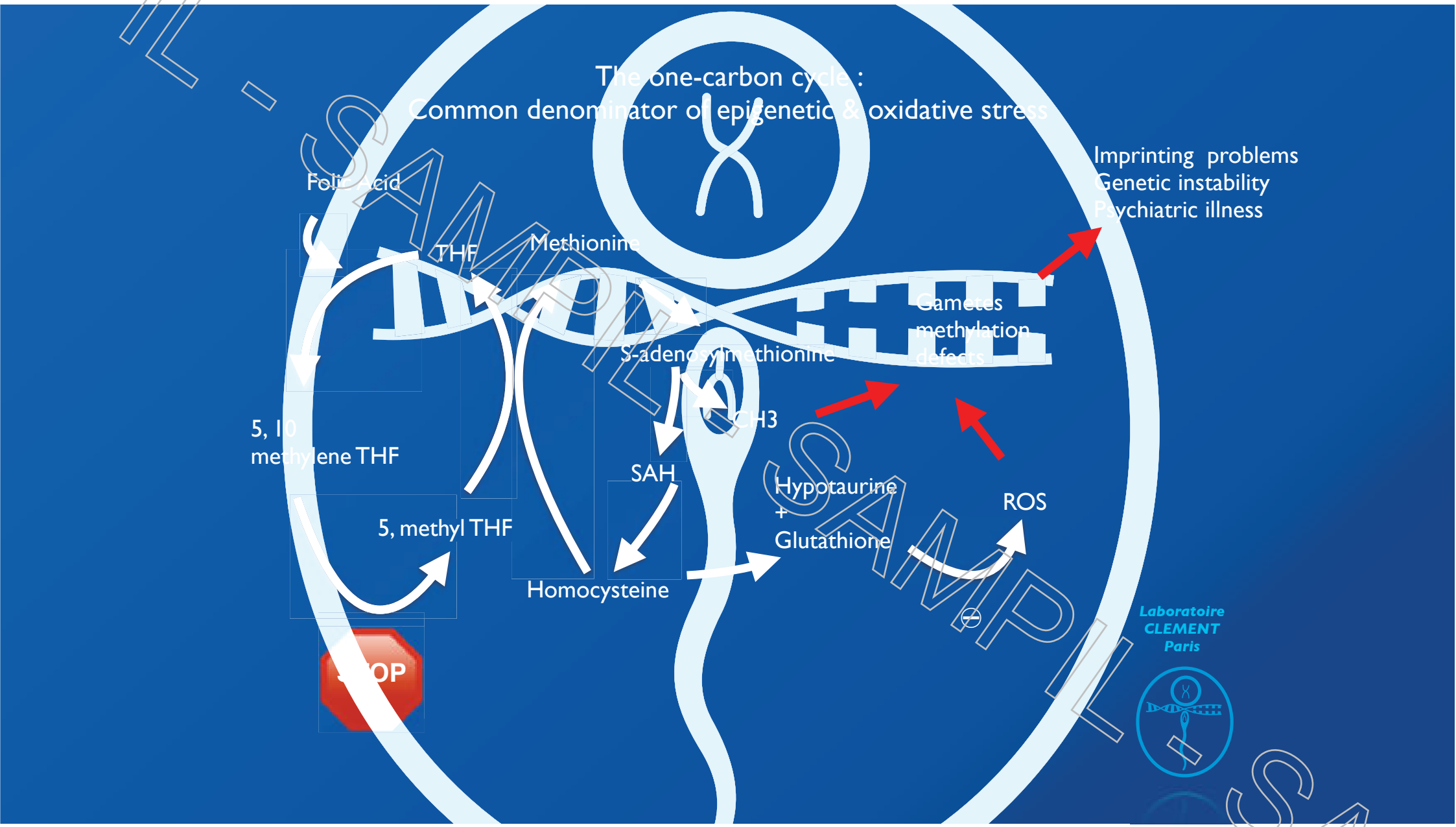
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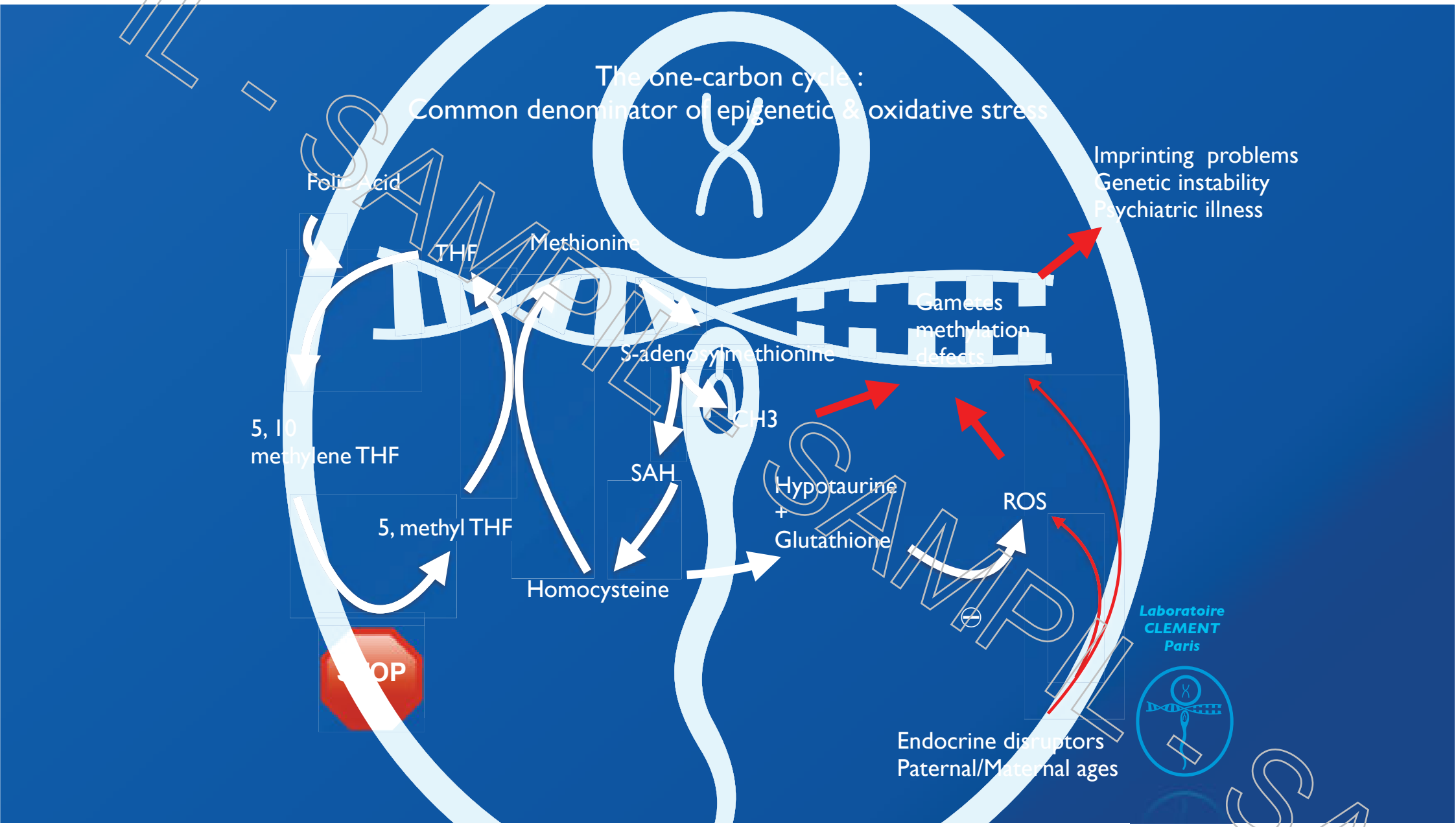
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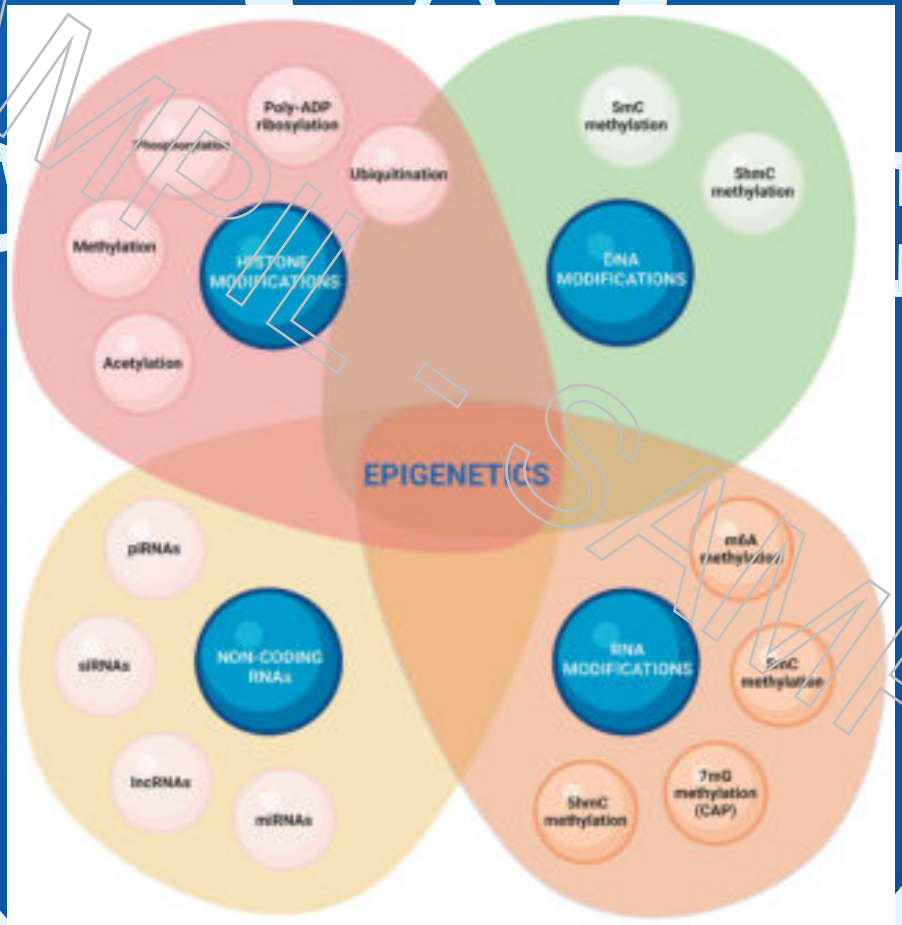
Epigénétique et développement embryonnaire précoce

(Dvoran et al., 2022)



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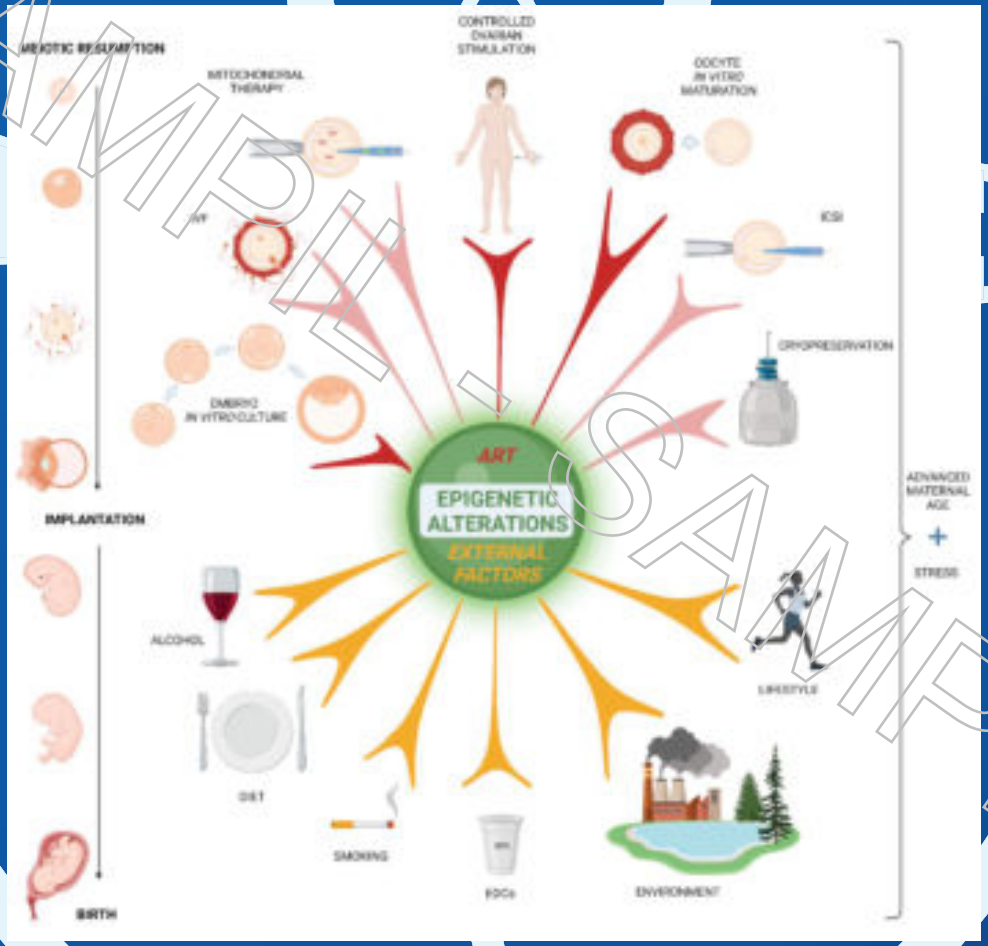

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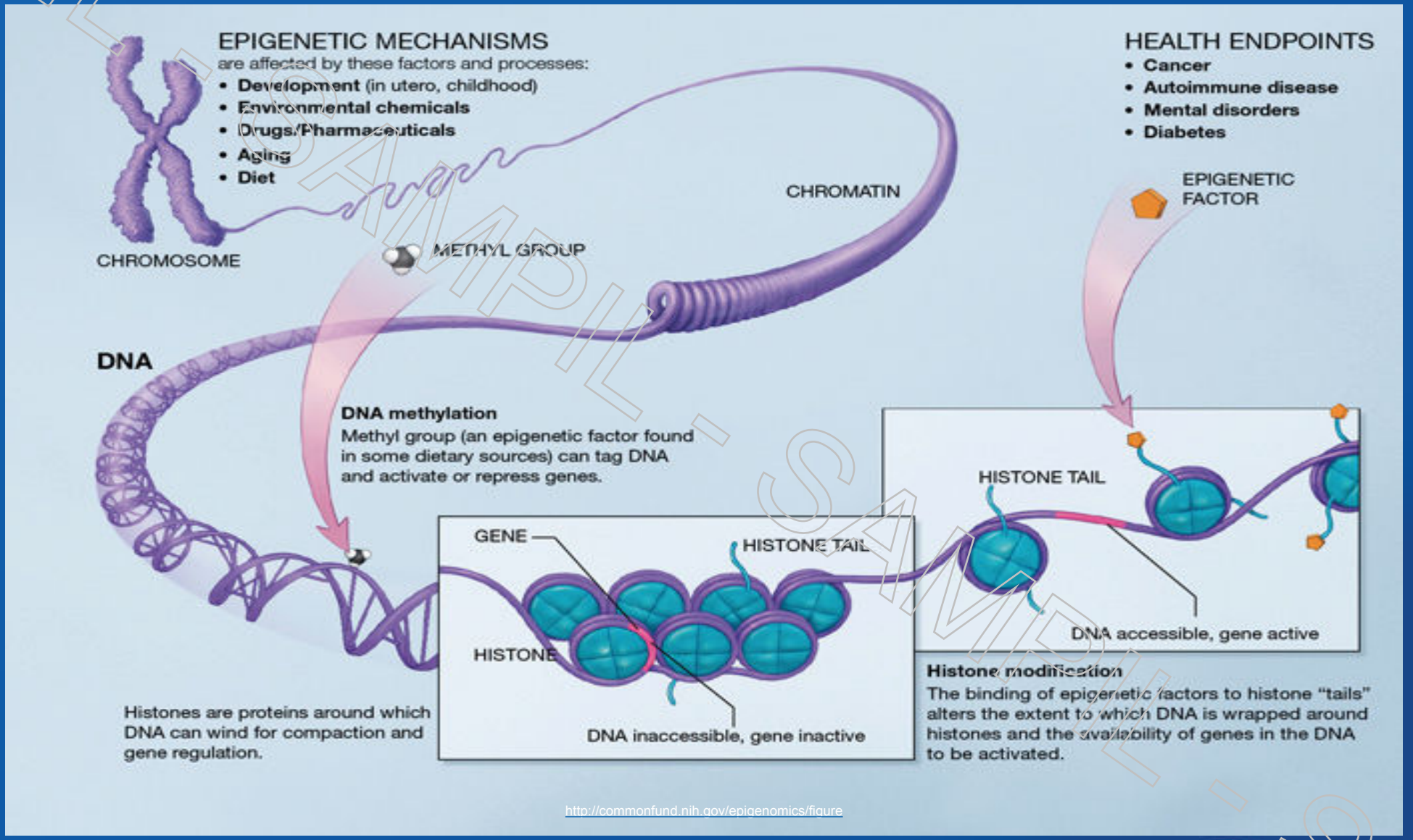
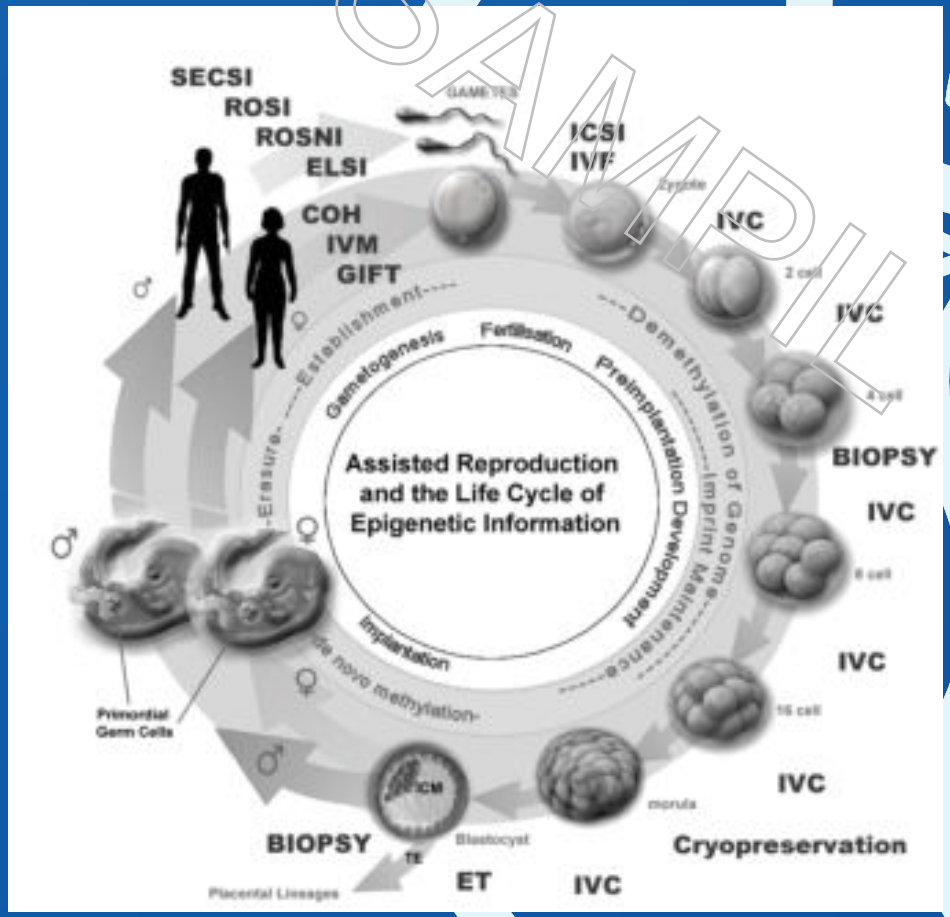


http://commonfund.nih.gov/epigenomics/figure

Imprinting evolution during the cycle of life



adapted from: Nature Reviews G[illegible] 21-32 (January 2001)

1. D[illegible]g fetal development, DNA methyl[illegible]n patterns are erased in [illegible]mordial germ cells (PGCs)
2. [illegible]esta[illegible]hed [illegible]ing g[illegible]neto[illegible]nesis or a[illegible] fertilization
3. S[illegible]cific[illegible]NA/h[illegible]ne r[illegible]hylati[illegible]n occurs at [illegible]ilization
   - ✓ Mate[illegible]dleti[illegible]are acqui[illegible]during oocyte growth
   - ✓ Paternal genes: paternal pronucleus und[illegible]oes extensive epigenetic reprogramming in zygotes
4. Global demethylation takes place during pre[illegible]lantation development: Post MZT
   - Silenced (imprinted) alleles must be reco[illegible]zed and protected so that the imprinted mark can be propa[illegible]ed and the correct allele expressed
   - *de novo* methylation as differentiation o[illegible]rs

A dynamic balance between global demethylation and focused methylation must be maintained during gametogenesis and development

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Epigénétique et développement embryonnaire précoce

(Dvoran et al., 2022)

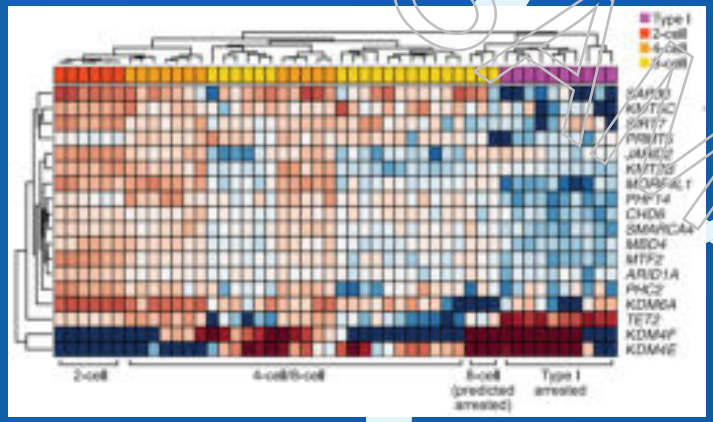
Stressor	Species	Genes Affected	Main Findings	Reference
		Oxidative stress		
Presence of reactive oxygen species	human	NE	Sperm originated changes to epigenetic regulation of human embryo development	[178]
Culture under 20% of oxygen	bovine	*CAT, GLRX2, HSP90AA1, KEAP1, NFR2, PRDX1, PRDX3, SOD1, TXN, TXNRD1, H2AFZ, H3F3B*	Increase of transcript of genes associated with epigenetic remodelling, oxidative stress and cellular stress response in blastocysts	[179]
Culture under 20% of oxygen	bovine	*DNMT3A*	Elevated *DNMT3A* expression and increase of global DNA methylation in 4-cell embryos and blastocysts	[180]
Oxidative stress (palmitic acid)	bovine	*PRDX3, HADHB, UQCRB, CYCS*	Upregulation of PRDX3 protein. Elevation of the mitochondrial HADHB, UQCRB and CYCS proteins in oocytes	[181]
Oxidative stress (H_2O_2)	mouse	NE	Decrease in mitochondria-derived ATP and disassembly of spindles in in vitro cultured MII oocytes	[87]
		In vitro techniques		
Oocyte in vitro maturation	human	*HDAC1*	Compromised deacetylation in oocytes. Residual acetylation linked to aneuploidy	[182]
Oocyte in vitro maturation	bovine	*SIRT2*	Faulty mitochondria	[183]
Cytoplasmic transfer	human	Not tested yet	10–15% cytoplasm transfer into aged oocytes produced healthy offspring	[95]
Suboptimal culture media	rabbit	NE	Alteration of DNA methylation reprogramming in paternal pronuclei of zygotes	[184]
In vitro fertilization & ICSI	human	H19	ART caused demethylation resulted in the changes of genomic imprinting	[185]
Embryo in vitro culture	human	NE	miRNAS detected in spent culture medium downregulate embryonic mRNAs	[186]
Cryopreservation	human	*LINE1*	Differently methylated placental DNA between fresh and frozen embryotransfers	[187]
Suboptimal culture media	mouse	NE	Higher methylation disturbances in embryos from superovulated females and IVF	[188]
Intracytoplasmic sperm injection	mouse	*H19, Snrpn, Peg3, Igf2*	Imprinting defects in somatic tissues	[189]

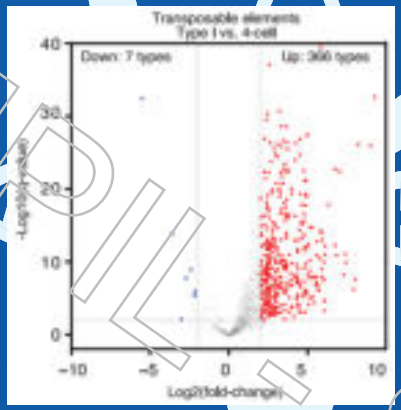
Stressor	Species	Genes Affected	Main Findings	Reference
		Ovarian Stimulation		
Controlled ovarian stimulation	human	NE	Chromosomal aneuploidy	[168]
Superovulation	mouse	*Dnmt1, Dnmt3A, Dnmt3B*	Affected expressin of methyltransferases in GV, MII oocytes, in one-cell and two-cell embryos	[169]
Superovulation	mouse	*Eprb, Pabc1*	Altered expression of translational regulators *mRNA* in mouse GV and MII oocytes and in zygots	[170]
Superovulation	mouse	*Snrpn, Peg3, Kcnqlot1, H19*	Disrupted methylation of imprinted genes in blastocysts	[171]
Superovulation	mouse	*Gbn2, Fem3, Crl94, Syf2*	In oocytes, altered methylation of genes involved in glucose metabolism, nervous system development, cell cycle, cell proliferation, and mRNA processing	[172]
Superovulation	mouse	*H19*	Altered *H19* methylation in mouse blastocysts after in vivo fertilization	[173]
Superovulation	mouse	*Fasn, Dgat1, Dgat2*	Decreased fatty acid content in mice 2-cell embryos by reducing the *Fasn* and increasing the *Dgat1* and *Dgat2 expression.*	[174]
Repeated superovulation	mouse	*Cox1, Cytb, Nd2, Nd4*	Altered expression of mitochondrial genes in mouse cumulus cells	[175]
Repeated superovulation	mouse	NE	Abnormalities in mitochondrial structure and distribution in mouse oocytes	[176]
Superovulation	mouse	NE	Decrease of mitochondrial activity and ATP production in mouse oocytes	[177]
Superovulation	bovine	*TXN2, PDX3*	Decline of mtDNA copy number in bovine oocytes., decreased expression of antioxidant genes in bovine cumulus cells	[93]

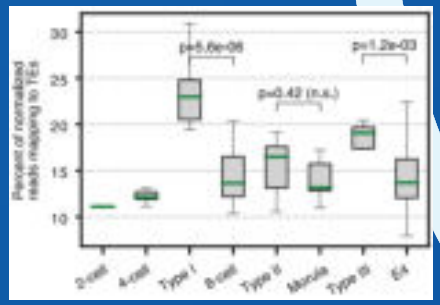
Les facteurs épigénétiques et les mécanismes de régulation de la transcription et de la traduction qui en découlent influencent la maturation méiotique, la fécondation, le développement et la qualité embryonnaire.

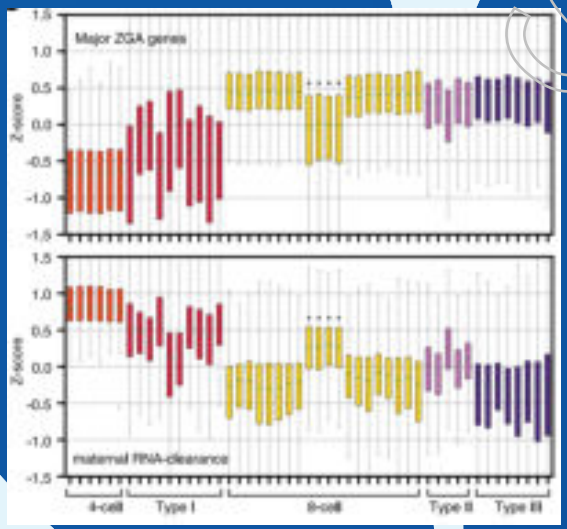
Epigénétique et développement embryonnaire précoce

(Yang et al., 2022)









Arrêt de développement embryonnaire = phénomène de sénescence avec arrêt du cycle cellulaire marqué par :

- la down regulation des ribosomes, des histones et des facteurs de traduction
- la up regulation de MYC et p53

Les embryons qui ne se développent pas peuvent être divisés en 3 types :

- Type I qui ne passent pas l'activation génome embryonnaire = période active épigénétique ==> défauts épigénétiques altèrent cette phase
- Type II / III qui ont de faibles niveaux de glycolyse avec un niveau élevé (type II) ou faible (type III) de phosphorylation oxydation

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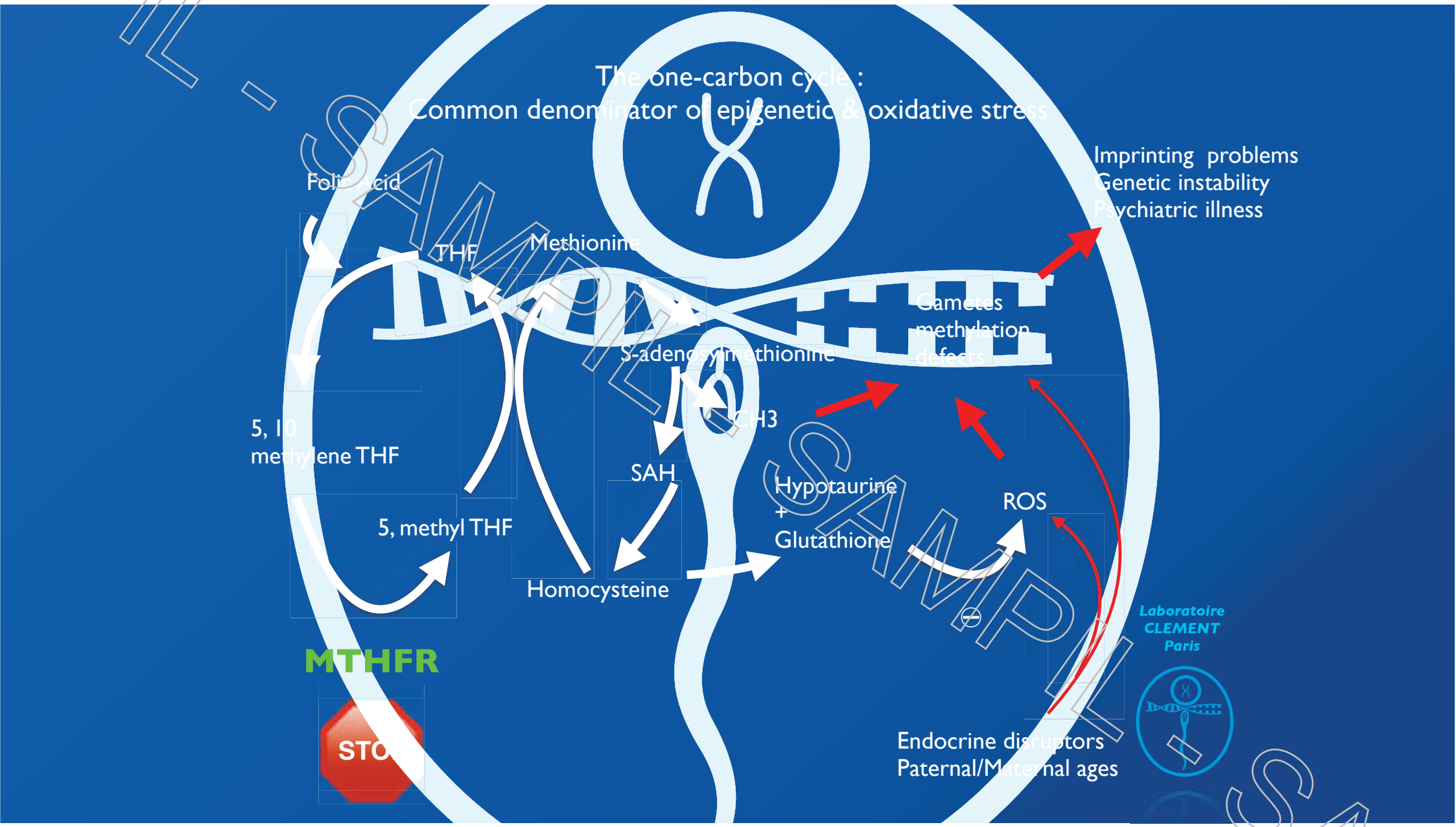
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Distribution of MTHFR SNPs among infertile patients

Male and female partners
7710 patients
Inclusion criteria :
- Unexplained infertility
- Recurrent implantation failure
- Recurrent pregnancy loss

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Distribution of MTHFR SNPs among infertile patients

	Number of MEN	Percentage
TOTAL	3536	

	Number of WOMEN	Percentage
TOTAL	4174	

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7710 patients
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Distribution of MTHFR SNPs among infertile patients

	Number of MEN	Percentage
wt/wt	512	14,5
TOTAL	3536	

	Number of WOMEN	Percentage
wt/wt	637	15,3
TOTAL	4174	

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Distribution of MTHFR SNPs among infertile patients

	Number of MEN	Percentage
wt/wt	512	**14,5**
HT 677	830	**23,5**
HM 677	438	**12,4**
HT 1298	711	**20,1**
HM 1298	286	**8,1**
HT compo	755	**21,4**
HM/HT HT/HM	7	**0,2**
HM/HM	0	**0,0**
TOTAL	3536	100,0

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wt/wt	637	**15,3**
HT 677	960	**23,0**
HM 677	490	**11,7**
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85%

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MTHFR carriers		
	Infertile population	85 %
	General population (Zappacosta, 2014)	70 %

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Very few numbers of HM/HT + HT/HM
No HM/HM

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7710 patients
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MTHFR carriers	Infertile population	85 %
	General population (Zappacosta, 2014)	70 %

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	Tara et al., 2015		
	Groupe contrôle	Groupe FC	
Population	100	225	
wt/wt	36,0	/	
HT 677	19,0	/	
HM 677	4,0	20,9	
HT 1298	26,0	/	
HM 1298	8,0	27,5	
HT compo	16,0	50,6	
HM/HT HT/HM	1,0	0,9	
HM/HM	0,0	0,0	

	Tara et al., 2015		
	Groupe contrôle	Groupe FC	
Population	100	225	
wt/wt	25,0	12,4	
HT 677	28,0	20,4	
HM 677	3,0	6,2	
HT 1298	18,0	24,4	
HM 1298	9,0	12,0	
HT compo	14,0	23,1	
HM/HT HT/HM	3,0	1,3	
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HM 1298	8,0	27,5	
HT compo	6,0	50,6	
HM/HT HT/HM	1,0	0,9	
HM/HM	0,0	0,0	

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HM/HT HT/HM	1,0	0,9	0,3
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	Tara et al., 2015		Population Laboratoire Clement
	Groupe contrôle	Groupe FC	
Population	100	225	4174
wt/wt	36,0	/	15,3
HT 677	19,0	/	23,6
HM 677	4,0	20,9	11,7
HT 1298	26,0	/	20,0
HM 1298	8,0	27,5	9,4
HT compo	6,0	50,6	20,4
HM/HT HT/HM	1,0	0,9	0,3
HM/HM	0,0	0,0	0,0

	Tara et al., 2015		Population Laboratoire Clement
	Groupe contrôle	Groupe FC	
Population	100	225	3536
wt/wt	25,0	12,4	14,5
HT 677	28,0	20,4	23,5
HM 677	3,0	6,2	12,4
HT 1298	18,0	24,4	20,1
HM 1298	9,0	12,0	8,1
HT compo	14,0	23,1	21,4
HM/HT HT/HM	3,0	1,3	0,2
HM/HM	0,0	0,0	0,0

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Laboratoire CLEMENT Paris

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HM/HT HT/HM	1,0	0,9	0,3
HM/HM	0,0	0,0	0,0

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HM/HM	0,0	0,0	0,0

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RPL : Homocysteine +++

Authors	Experimental group	Control group	Results	Conclusions
RPL				
Nelen et al. [69]	123 RPL patients	104 normal women	Increased fasting Hct (≥18.3 mmol/L) and afterload Hct (≥61.5 mmol/L) were both associated with RPL.	Increased Hct was a risk factor for RPL.
Raziel et al. [35]	36 nonpregnant RPL patients	40 parous women	HHct was found in 31% of the RPL patients.	Patients with RPL were more likely to have HHct.
Zammiti et al. [34]	350 RPL patients	200 normal women	The tHct levels were similar between the two groups.	There was no association between the risk of RPL and tHct levels.
Creus et al. [36]	60 RPL patients	30 fertile females	There was no significant difference in the Hct levels between the two groups.	RPL was not associated with HHct.
Chakraborty et al. [68]	126 RPL patients with PCOS	117 normal women without PCOS	There was a significant difference in Hct expression between the experimental group and the control group (70.63% vs. 57.26%; $P < 0.05$).	HHct could increase the possibility of RPL.
Zarfeshan Fard et al. [70]	50 RPL patients	50 women having at least two normal pregnancies	The expression of Hct was higher in the experimental group ($P = 0.002$) compared to the control group. Increased Hct tended to be more common in women with the T allele.	The 677CT genotype may be a risk marker for abortion, and the C allele protected women from RPL.
Lin et al. [71]	403 RPL patients	342 normal females	The expression of Hct was higher in the experimental group relative to that in the control group.	MTHFR 677CT and MTRR 66AG gene mutations increased Hct expressions.
PE				
Raijmakers et al. [72]	20 PE patients	10 healthy nonpregnant females and 10 normotensive pregnant females	PE patients had higher Hct levels than normotensive pregnant women (13.3 vs. 8.4 nmol/L, $P < 0.05$).	Mild HHct may not be a risk marker for PE. HHct in PE was related to the changes of plasma volume instead of MTHFR gene mutation.
Mao et al. [40]	62 PE patients	30 normal pregnant women	Both the mild and severe PE patients exhibited higher Hct-levels compared to controls.	The Hct-ADMA-NO pathway was involved in the cause of PE and associated with the severity of PE.
Kulkarni et al. [73]	49 PE patients	57 normotensive pregnant women	Despite there being no difference in folic acid and vitamin B_{12} levels between the two groups, the Hct levels were higher in the experimental group.	The reduction of DHA in PE was related to HHct.
Laskowska et al. [41]	62 early-onset PE and 53 late-onset PE patients	65 normotensive pregnant women	There were increased expressions of Hct in the serum of patients with PE, especially in the early-onset PE population.	The expression level of Hct was related to the severity of PE and could indicate early symptoms of PE.
Şarlıkan et al. [74]	30 severe PE and 24 mild PE patients	60 normal pregnant women	Hct levels in the control group were lower compared to those in the experimental group. A significant difference did not exist in Hct expression between the mild and severe PE patients.	Hct was significantly increased in PE patients, but it was not related to the severity of this disease.
Wadhwani et al. [75]	62 PE patients	126 normotensive pregnant women	PE patients had higher Hct levels compared with controls in the second trimester, third trimester, and during delivery.	Increased Hct expressions occurred in PE patients from the first trimester to delivery.
Maru et al. [76]	64 mild PE, 50 severe PE, and	68 healthy pregnant women	Hct greater than 8 mmol/L was associated with severe PE, and maternal	Hct was usable as one of the predictors for PE.

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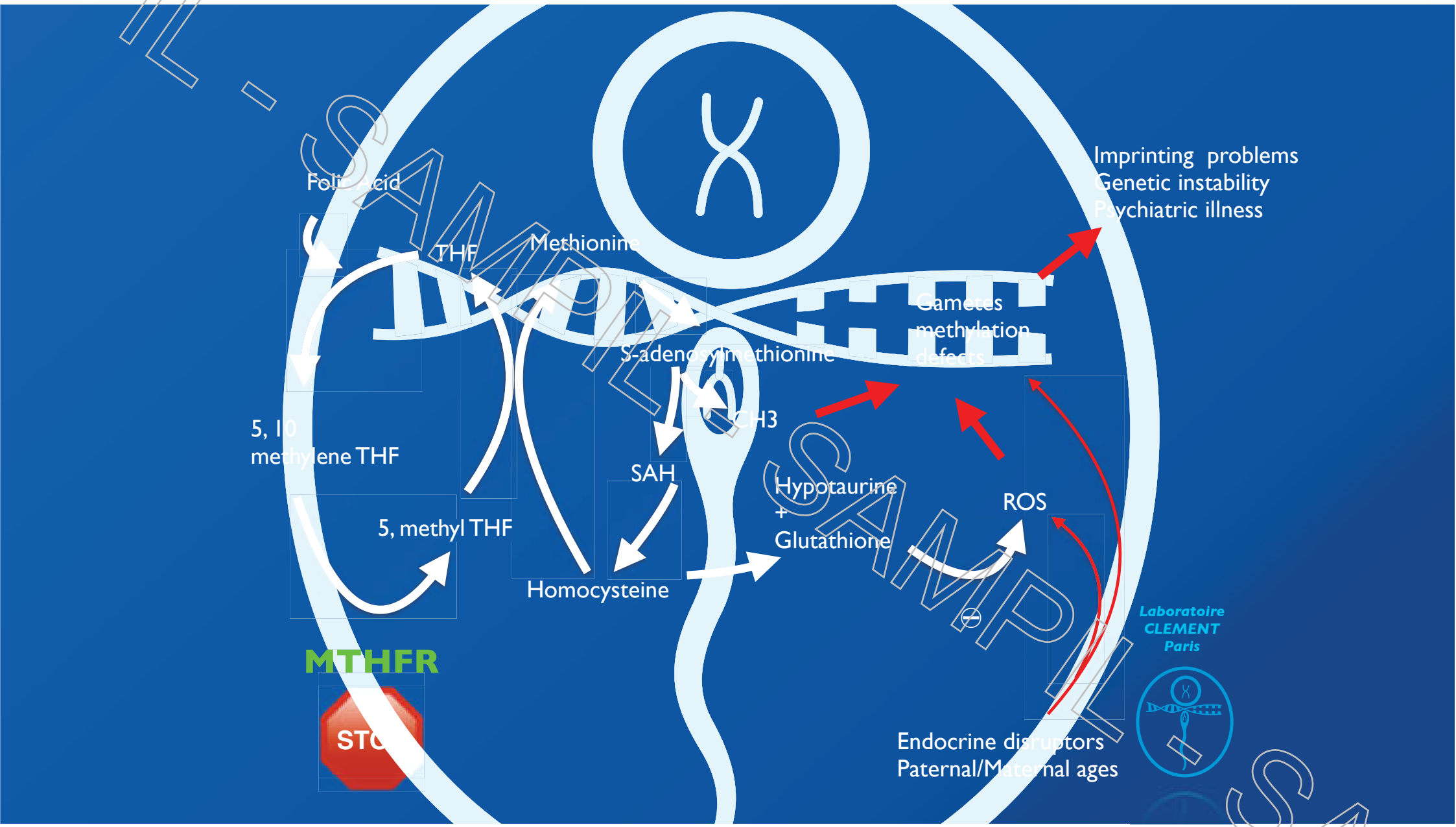
Folic Acid
THF
Methionine
Imprinting problems
Genetic instability
Psychiatric illness
Gametes
methylation
defects
S-adenosylmethionine
CH3
5, 10
methylene THF
SAH
Hypotaurine
+
Glutathione
ROS
5, methyl THF
Homocysteine
MTHFR
STO
Endocrine disruptors
Paternal/Maternal ages
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Homocysteine value & MTHFR profile

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Homocysteine value & MTHFR profile

Homocysteine levels seems correlated with reported MTHFR activities (van der Put, 1998)

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Homocysteine value & MTHFR profile

Clement et al., 2021 (JARG)

Statut mutationnel 677/1298	Hcy < 10 microM	Hcy > 10 microM	**Total**
Het/wt	190	149	**339**
Wt/het	152	123	**275**
Het/het	164	163	**327**
Hom/het + Het/hom	2	9	**11**
Wt/wt	107	78	**185**
Hom/wt	83	97	**180**
Wt/hom	88	47	**135**
Hom/hom	0	0	**0**
Total	786	666	1452

Corrélation entre valeur homocysteine & statut mutationnel
(p=0.002, Chi-square)

Homocysteine value & MTHFR profile

Clement et al., 2021 (JARG)

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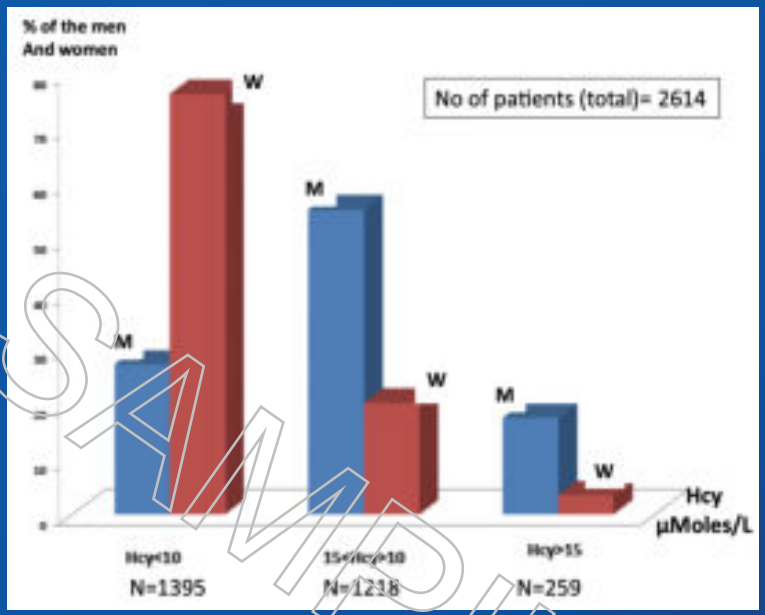

Impact plus important des polymorphismes
chez l'homme que chez la femme
(p<0,05, Chi-square)

Homocysteine value & MTHFR profile

872 infertile patients (455 MTHFR + homocysteine)

Homocysteine (µmol/	<10	10-15	>15	>20
1298 HT	21,5	20,7	10	0
1298 HM	11,8	3,69	2,5	0
677 HT	24,8	24,4	17,5	0
677 HM	9,3	11,6	42,5	100
HT composite	17,5	23,8	22,5	0
wt	15,0	13,4	5	0
HT/HM - HM/HT	0	2,4	0	0
Total	100	100	100	100

With increasing homocysteine levels :

- decreasing proportion of wt
- increasing proportion of composite HT, 677 HM (100% of the patients with homocysteine > 20 µmol/L were 677 HMZ)

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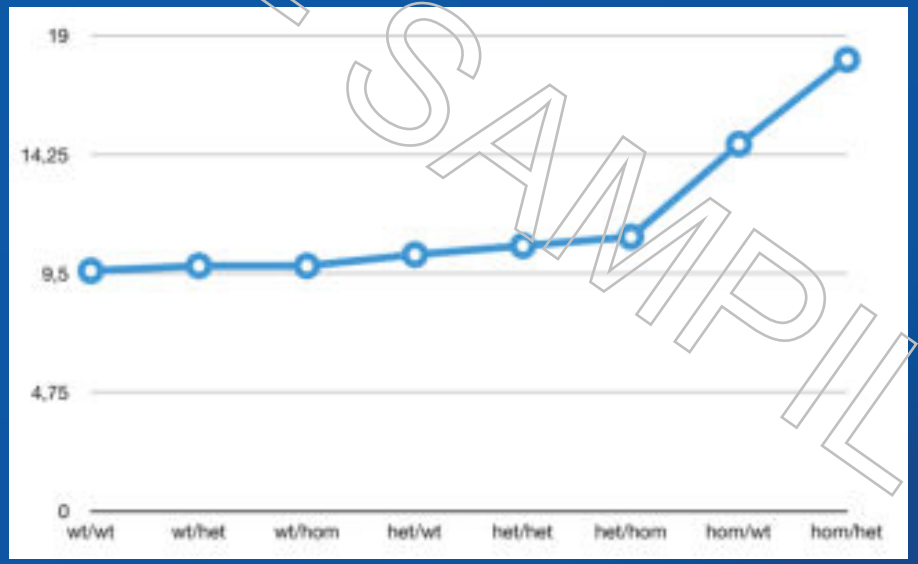
MTHFR et homocystéine

2103 patients
Février 2018-Juin 2019

Mutation	Nombre	Homocy moyenne	ET
Wt/wt	275	9,6	3,0
Het/wt	506	10,25	0,9
Hom/wt	256	14,66	11,49
wt/het	423	9,80	3,02
het/het	439	10,60	3,72
wt/hom	183	9,80	3,07
hom/het	2	18,04	2,42
het/hom	4	10,96	2,02
hom/hom	0		
Total	2088		



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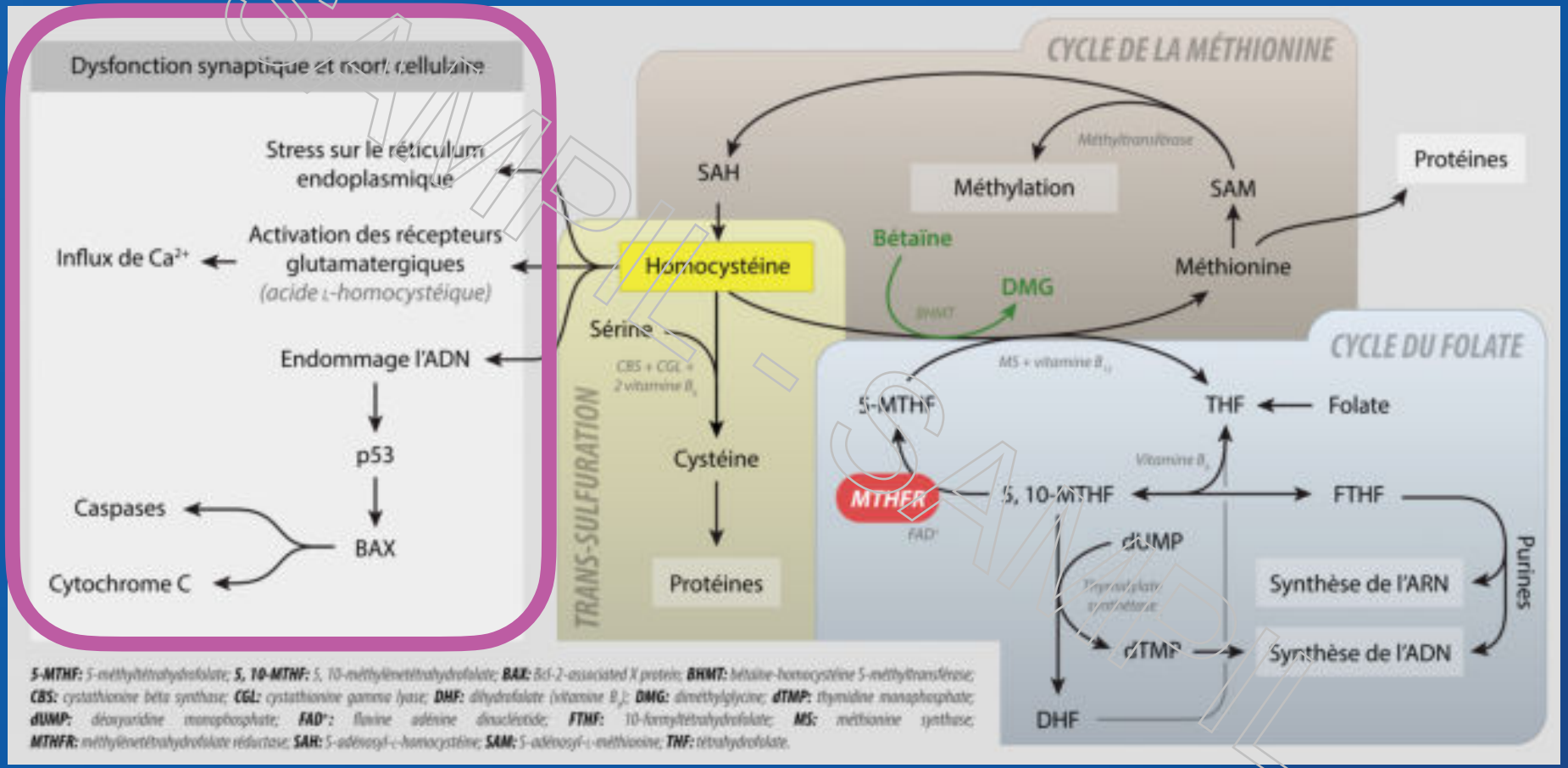
Dysfonction synaptique et mort cellulaire
Stress sur le réticulum endoplasmique
Influx de Ca2+
Activation des récepteurs glutamatergiques
(acide L-homocystéique)
Endommage l'ADN
p53
Caspases
BAX
Cytochrome C
CYCLE DE LA MÉTHIONINE
SAH
Méthyltransférase
Méthylation
SAM
Protéines
Bétaïne
Homocystéine
DMG
BHMT
Méthionine
Sérine
CBS + CGL + 2 vitamine B6
TRANS-SULFURATION
Cystéine
Protéines
CYCLE DU FOLATE
MS + vitamine B12
5-MTHF
THF
Folate
Vitamine B2
MTHFR
FAD+
5, 10-MTHF
FTHF
dUMP
Purines
Synthèse de l'ARN
dTMP
Synthèse de l'ADN
DHF
5-MTHF: 5-méthyltétrahydrofolate; 5, 10-MTHF: 5, 10-méthylènetétrahydrofolate; BAX: Bcl-2-associated X protein; BHMT: bétaïne-homocystéine S-méthyltransférase; CBS: cystathionine bêta synthase; CGL: cystathionine gamma lyase; DHF: dihydrofolate (vitamine B9); DMG: diméthylglycine; dTMP: thymidine monophosphate; dUMP: désoxyuridine monophosphate; FAD+: flavine adénine dinucléotide; FTHF: 10-formyltétrahydrofolate; MS: méthionine synthase; MTHFR: méthylènetétrahydrofolate réductase; SAH: S-adénosyl-L-homocystéine; SAM: S-adénosyl-L-méthionine; THF: tétrahydrofolate.

Cut-off pour définir l'hyperhocystéinémie?

Pas de valeur basale "normale" pour l'homocystéine
Cut-off retenu pour définir l'hyperhomocystéinémie n'est pas consensuel.

Différentes valeurs sont retenues dans la littérature :
- **AVC : 15.45 µmol/L pour Evers (1997)**
- **Accidents coronariens :**
  - **14.0µmol/L - Hoogeveen (1998)**
  - **14.5µmol/L - Moustapha (1998)**
  - **15.67µmol/L - Blacher (1997)**
  - **18.2µmol/L - Mendis (2002)**

Augmentation de 1µmol/L est associée avec une augmentation de 5% du risque d'accident coronarien (Klerk, 2002).

Quel que soit la valeur d'homocystéine de départ, après ajustement pour le tabac, la pression artérielle et le taux de cholestérol, chez les patients mutés pour MTHFR, une diminution de la valeur d'homocystéine de 25% entraine une diminution de 19% du risque ischémique (Clarke, 2002).

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Hyperhomocysteinemie - implication transversale

Cardiovasculaire (Klerk meta-analysis, 2002) :
AIC
Maladies CV précoces x 3 si MTHFR 677 homozygote

Prénatal : Défaut de fermeture du tube neural

Obstétricales :
- FCS à répétition (Wen, 2008)
- SOPK (Ziong)
- Anomalie de fermeture du tube neural (Yu, 2019)
- Croissance embryonnaire (Rubini, 2022)

Oncologique (Hasan, 2019)Sm : sein, adénocarcinome pulmonaire, carcinome hépatocellulaire
- Tumeur gastrique (Xu, 2016)

Autres:
- Fente labiopalatine : incidence x 3 quand 677 homozygote
- Neurotoxique (agoniste pour les récepteurs au glutamate) : démence (Smith, 2016)
- Désordres psychiatriques : troubles bipolaires, dépression (Zhao, 2022)
- Ophtalmologiques : rétinoblastome (Bisht, 2018)
- Néphrologiques
- Osseuses : ostépoporose (Refsum, 2006)
- Gastrointestinaux : maladie de Crohn, RCH, infarctus mésentériques

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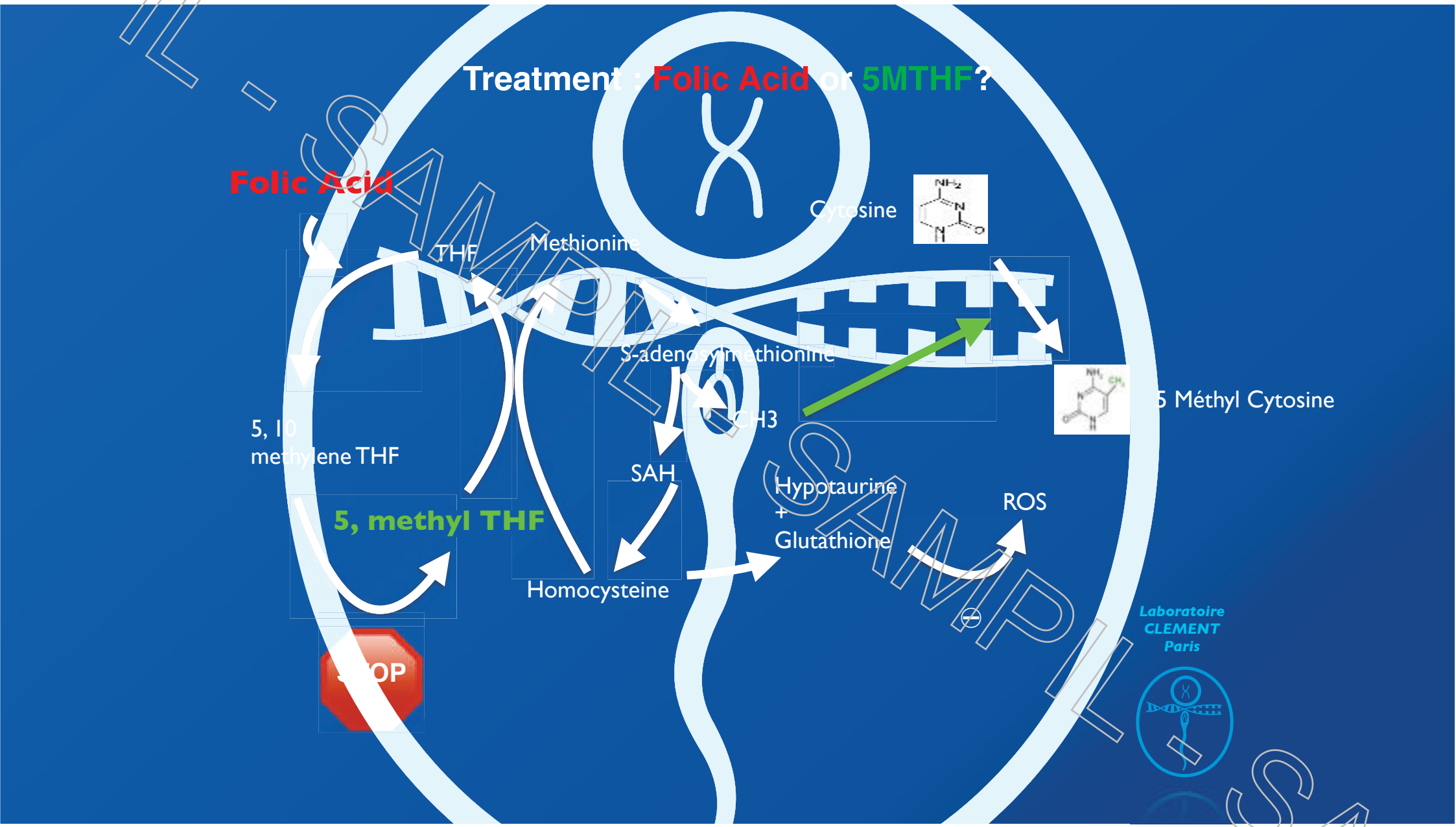
Treatment : Folic Acid or 5MTHF?
Folic Acid
THF
Methionine
Cytosine
S-adenosylmethionine
CH3
5 Méthyl Cytosine
5, 10
methylene THF
5, methyl THF
SAH
Hypotaurine
+
Glutathione
ROS
Homocysteine
STOP
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UMFA : Unmetabolized Folic Acid Syndrom

High concentrations of folate and unmetabolized folic acid in a cohort of pregnant Canadian women and umbilical cord blood

Folic Acid Food Fortification—Its History, Effect, Concerns, and Future Directions

Raising Concerns About Unmetabolized Folic Acid

Clinical Obstetrics, Gynecology and Reproductive Medicine

oat

Review Article ISSN: 2059-4828

The Methylene Tetrahydrofolate Reductase (MTHFR) isoform challenge. High doses of folic acid are not a suitable option compared to 5 Methyltetrahydrofolate treatment

Clinical Obstetrics, Gynecology and Reproductive Medicine

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Mini Review ISSN: 2059-4828

The hazards of excessive folic acid intake in MTHFR gene mutation carriers: An obstetric and gynecological perspective

High-dose folic acid supplementation alters the human sperm methylome and is influenced by the *MTHFR* C677T polymorphism

High doses of folic acid induce a pseudo MTHFR syndrome in a Wild type patient: a case report

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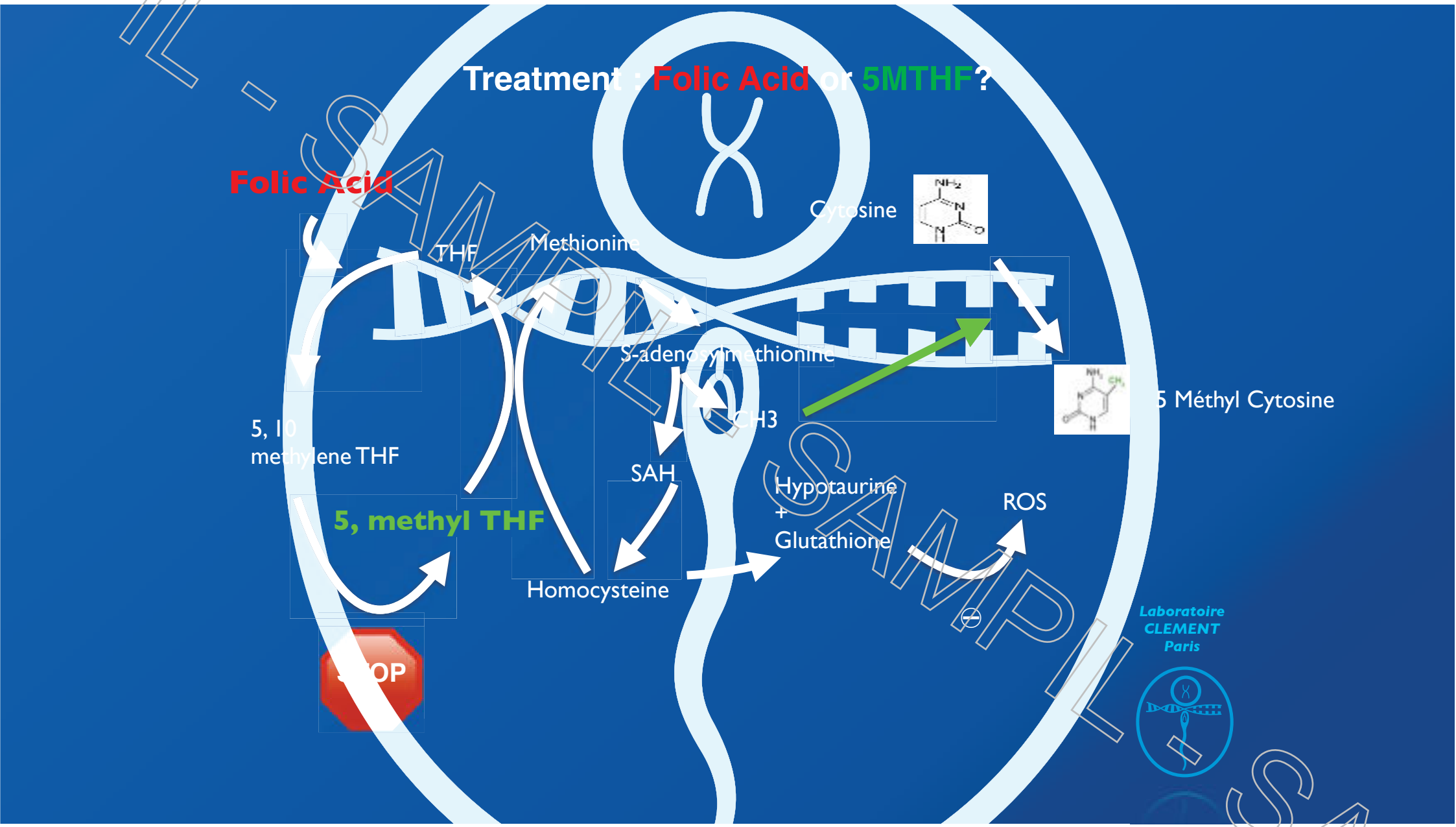
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+
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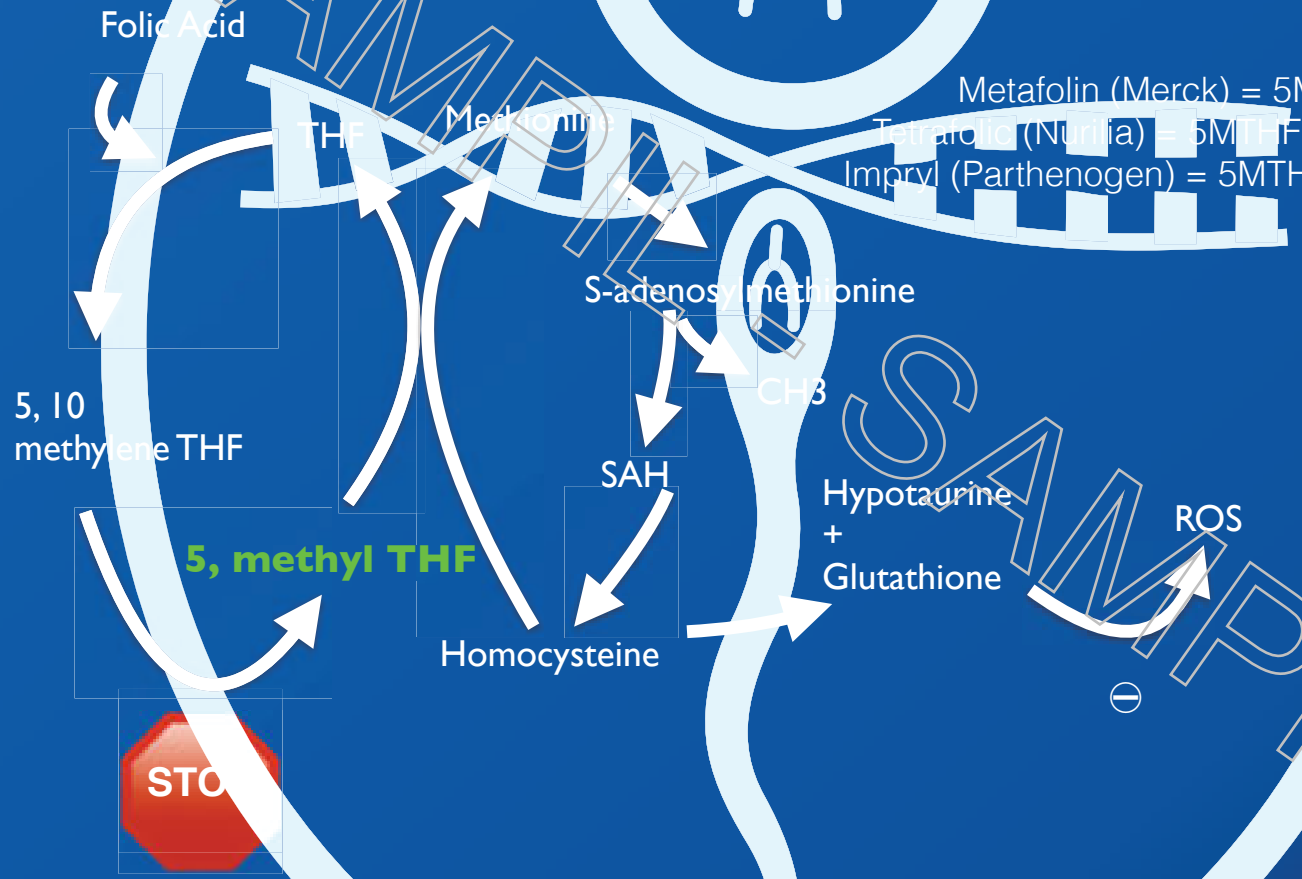
Treatment available for MTHFR carriers : 5MTHF

Bypass the problems linked to MTHFR impaired activity.
Allows a correct efficacy of the one carbon cycle.



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MTHFR et homocystéine

Couples screened for MTHFR status and homocysteine levels (n=125)

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Clement, submitted 2018

MTHFR et homocystéine

Couples screened for MTHFR status and homocysteine levels (n=125)

Clement, submitted 2018

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MTHFR et homocystéine

Couples screened for MTHFR status and homocysteine levels (n=125)
Treatment for MTHFR mutations carriers with 5MTHF during 4 months

Clement, submitted 2018

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MTHFR et homocystéine

Couples screened for MTHFR status and homocysteine levels (n=125)
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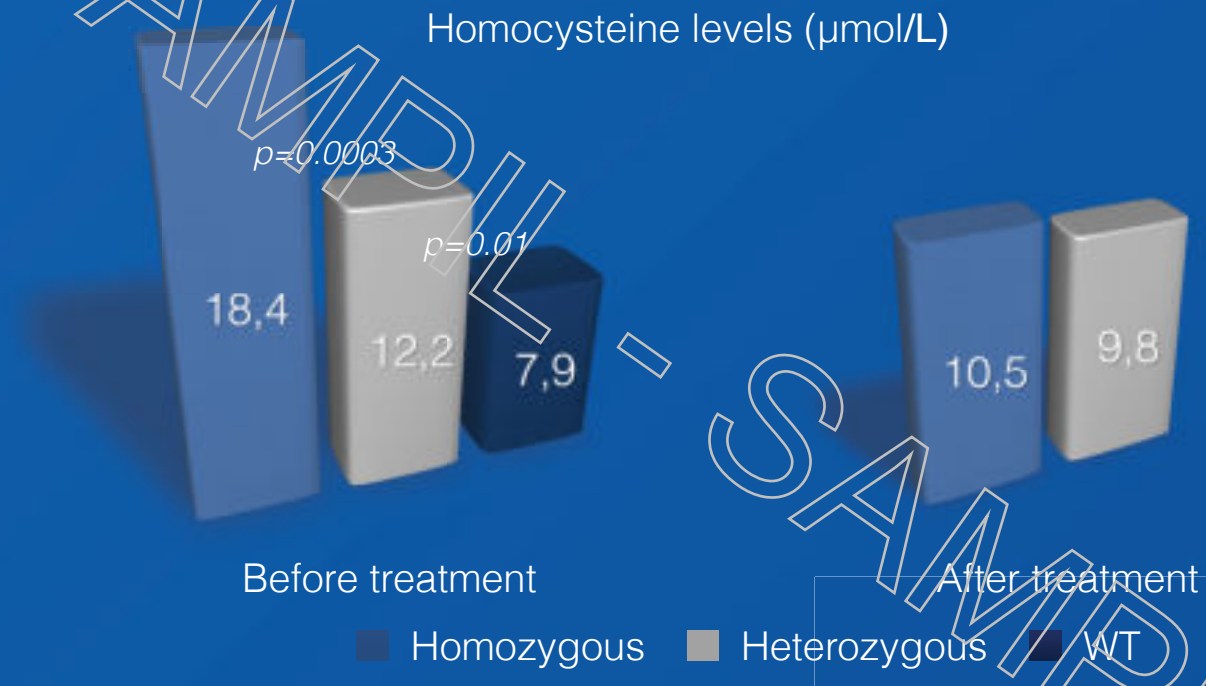

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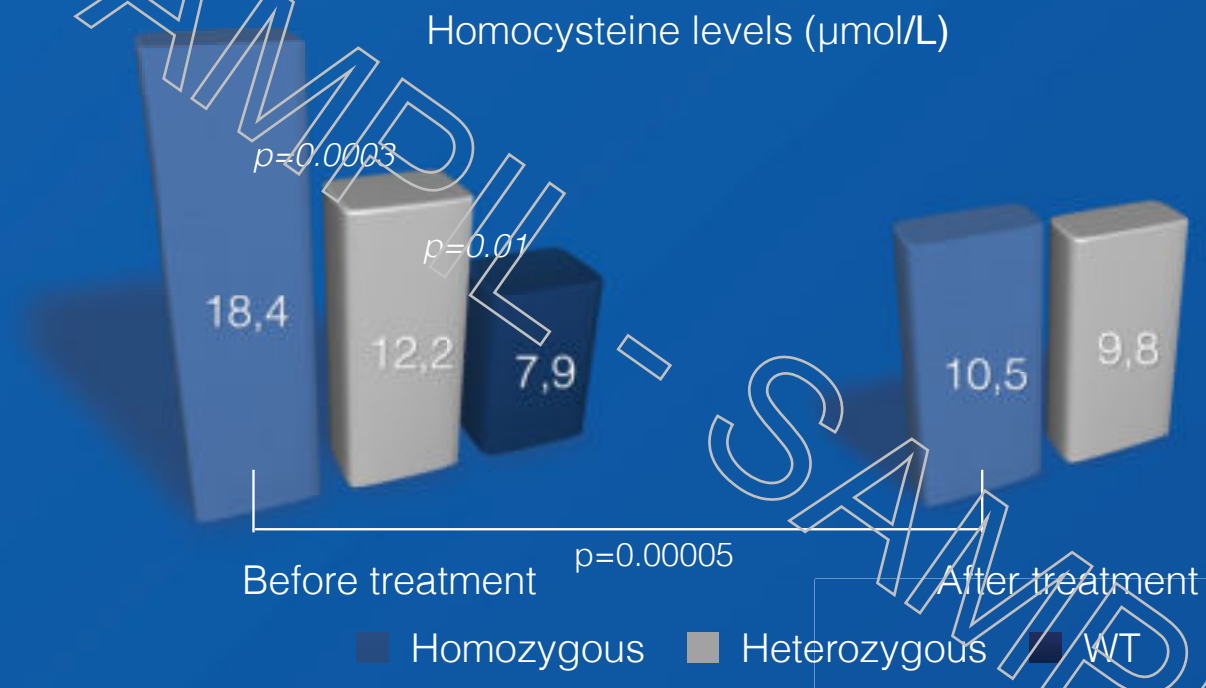

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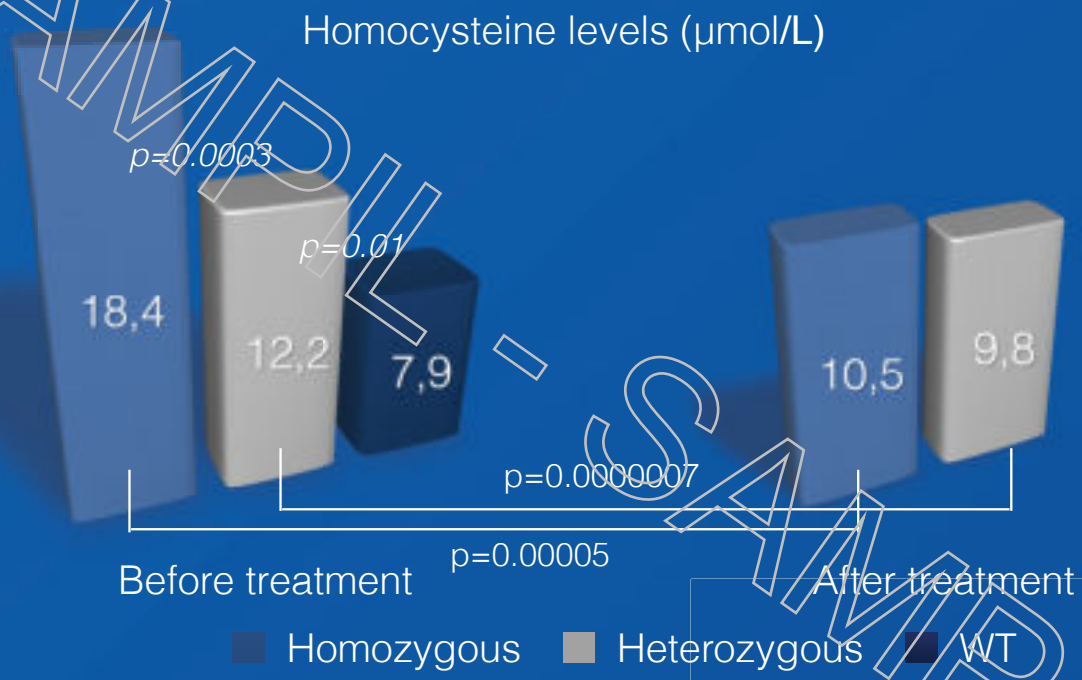

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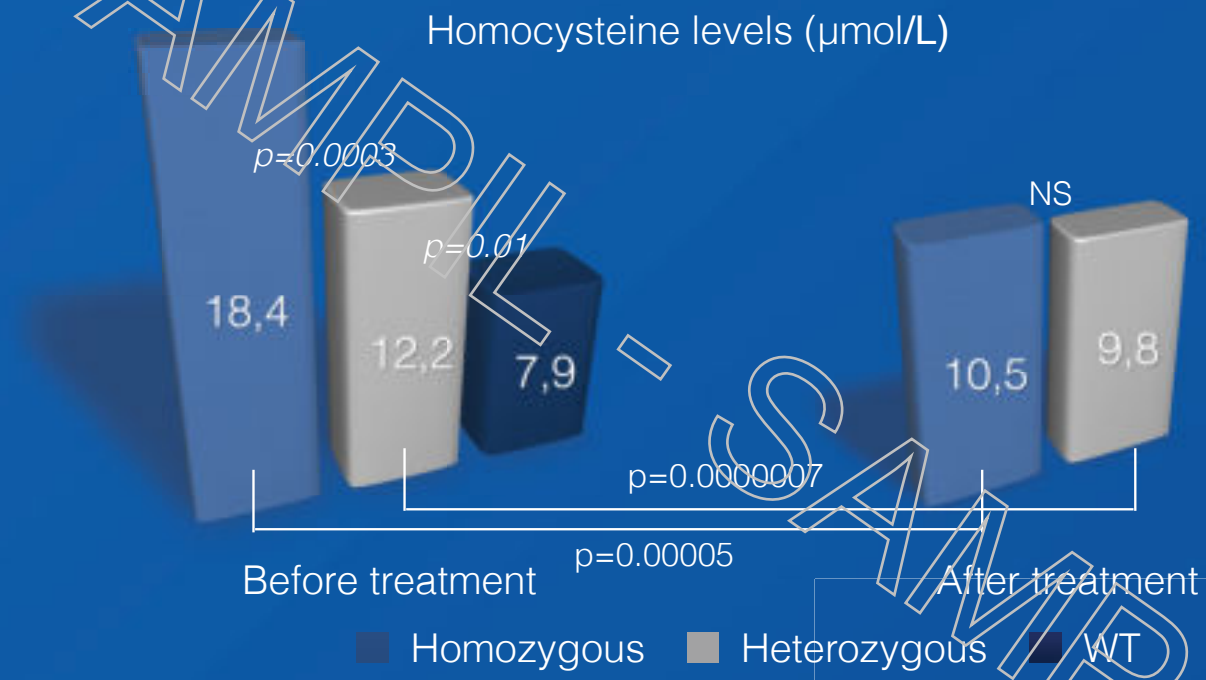

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Take-home messages

Impact des mutations MTHFR
Corrélation MTHFR & homocystéinémie
Atteintes transversales de l'hyperhomocystéinémie

Chez couples infertiles :
Rechercher les mutations MTHFR (677 et 1298)

Traitement diminue les hyperhomocystéinémies
Traitement améliore les paramètres gamétiques et embryonnaires

Chez les porteurs de mutations avec hyperhomocystéimies
Intérêt de traiter par 5MTHF

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Implication polymorphismes gène MTHFR dans les fausses couches à répétition

SAMPIL
13/06/23

Dr. Arthur CLEMENT
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