



Université Libre de Saint-Germain-en-Laye

Séminaires de Biologie 2023 -2024

Infection et Immunité

22 janvier 2024

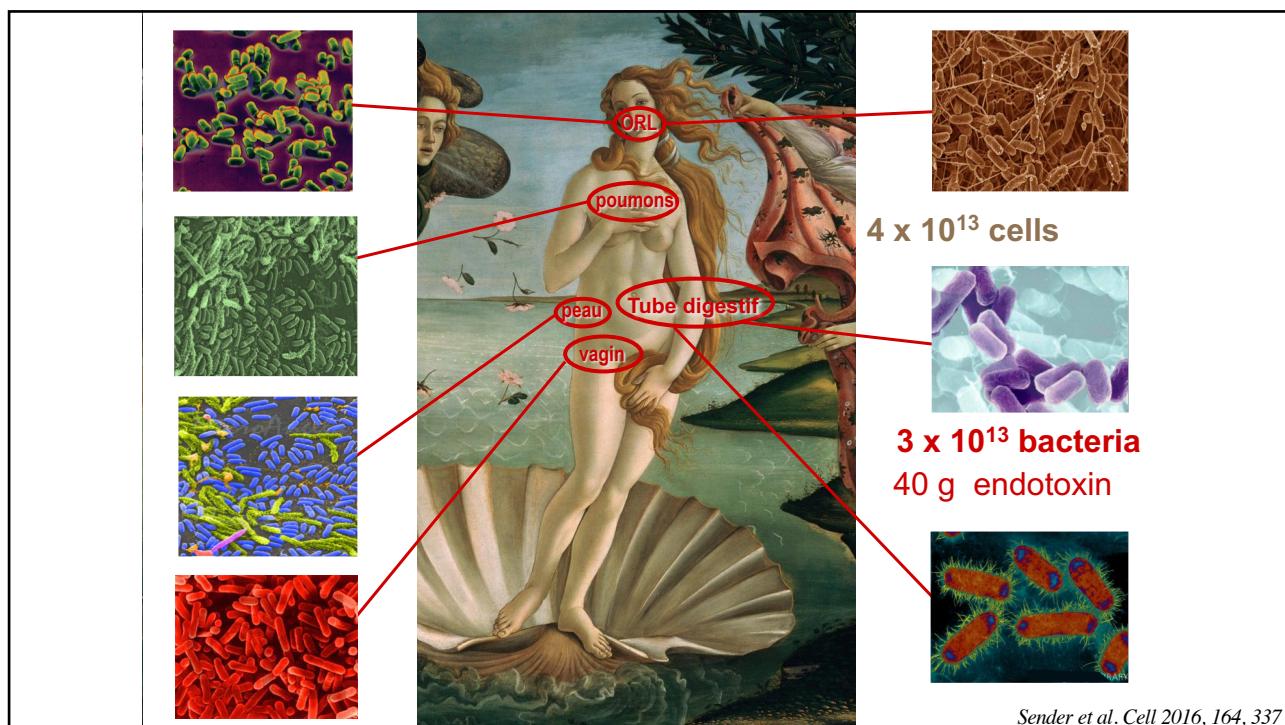


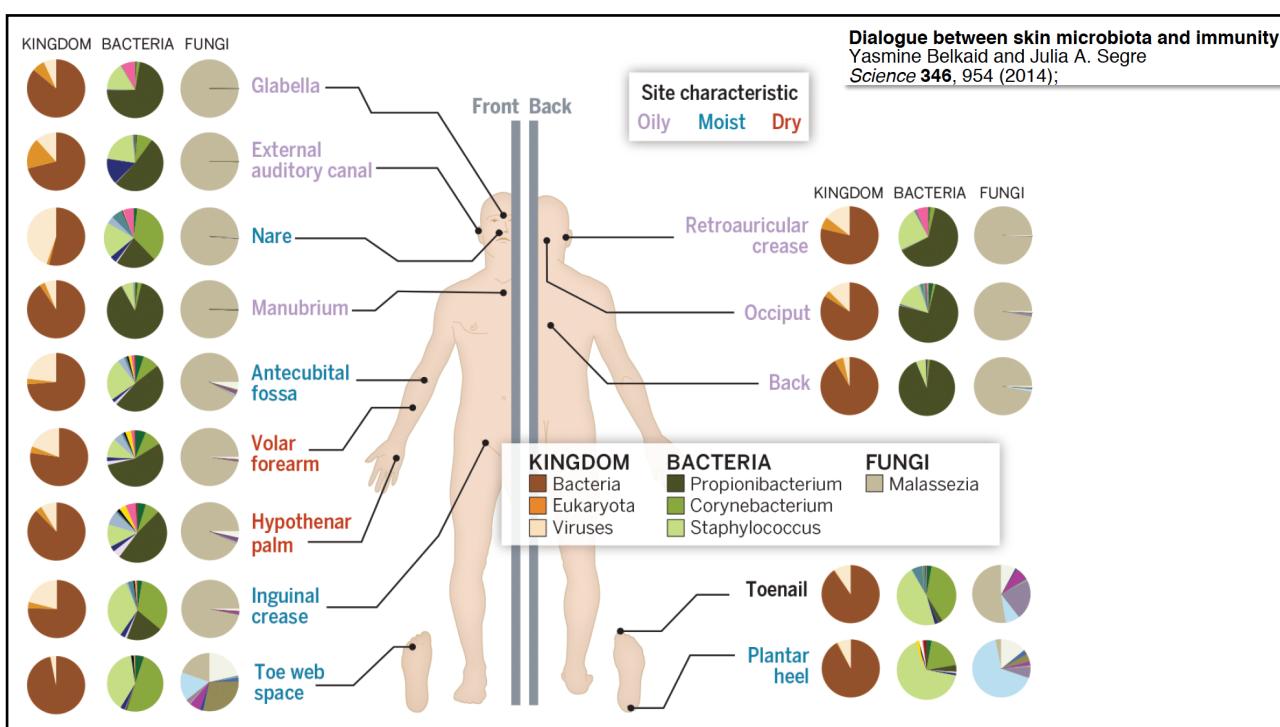
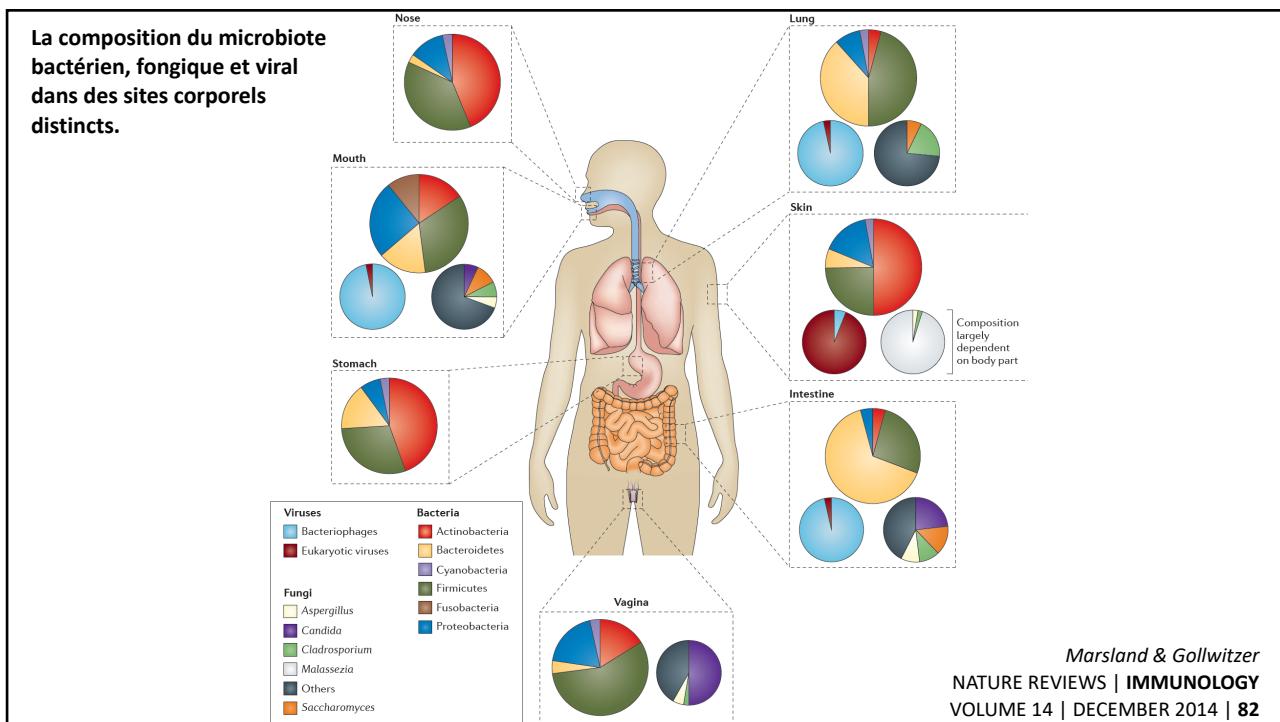
Les paramètres qui influencent le système immunitaire et son étude

Jean-Marc Cavaillon



MICROBIOTE





1902

**ZEITSCHRIFT
FÜR
KLINISCHE MEDICIN.**

1902, Vol. XLVIII, pp.413-444

Aus der medicinischen Klinik in Bonn (Director: Geh.-Rath Professor Dr. Fr. Schultze).

Untersuchungen über die Bakterienmenge in menschlichen Fäces.

von
Cell 164, January 28, 2016
Privatdozent, Assistenzarzt an der medicinischen Poliklinik.

JULIUS STRASBURGER
(1871-1934)

Cell 164, January 28, 2016

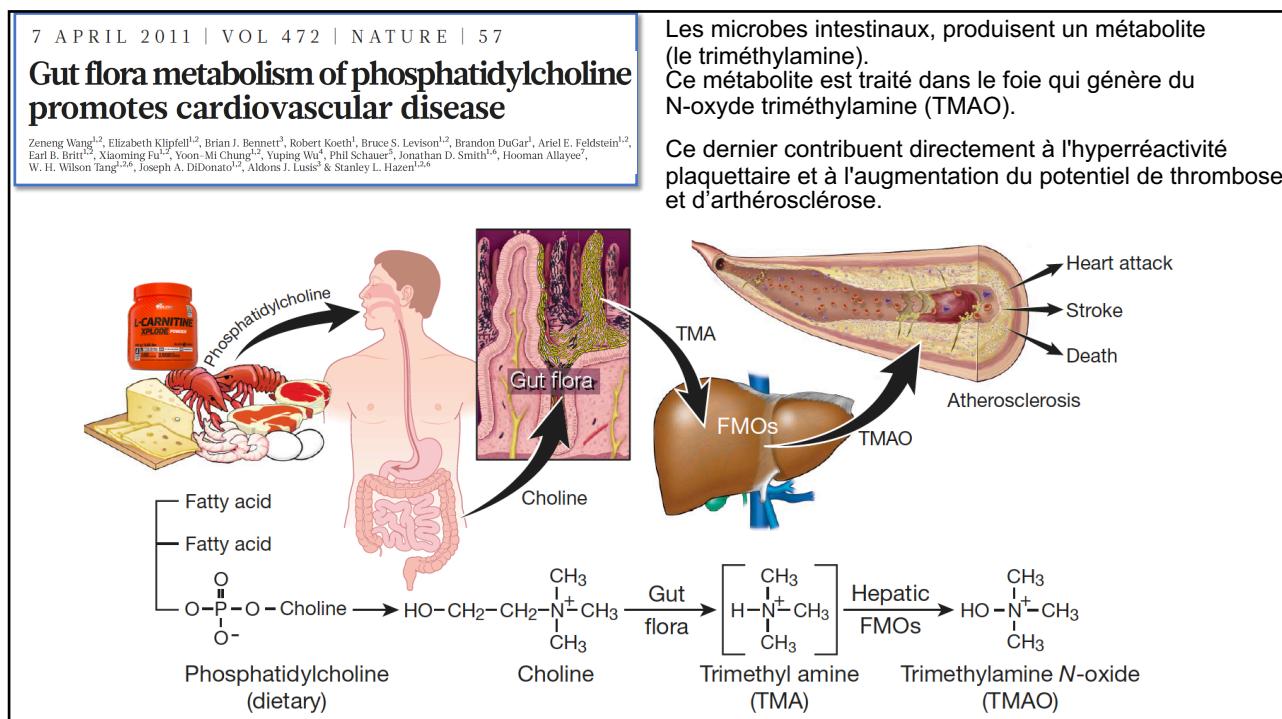
**Are We Really Vastly Outnumbered?
Revisiting the Ratio of Bacterial to Host Cells in Humans**

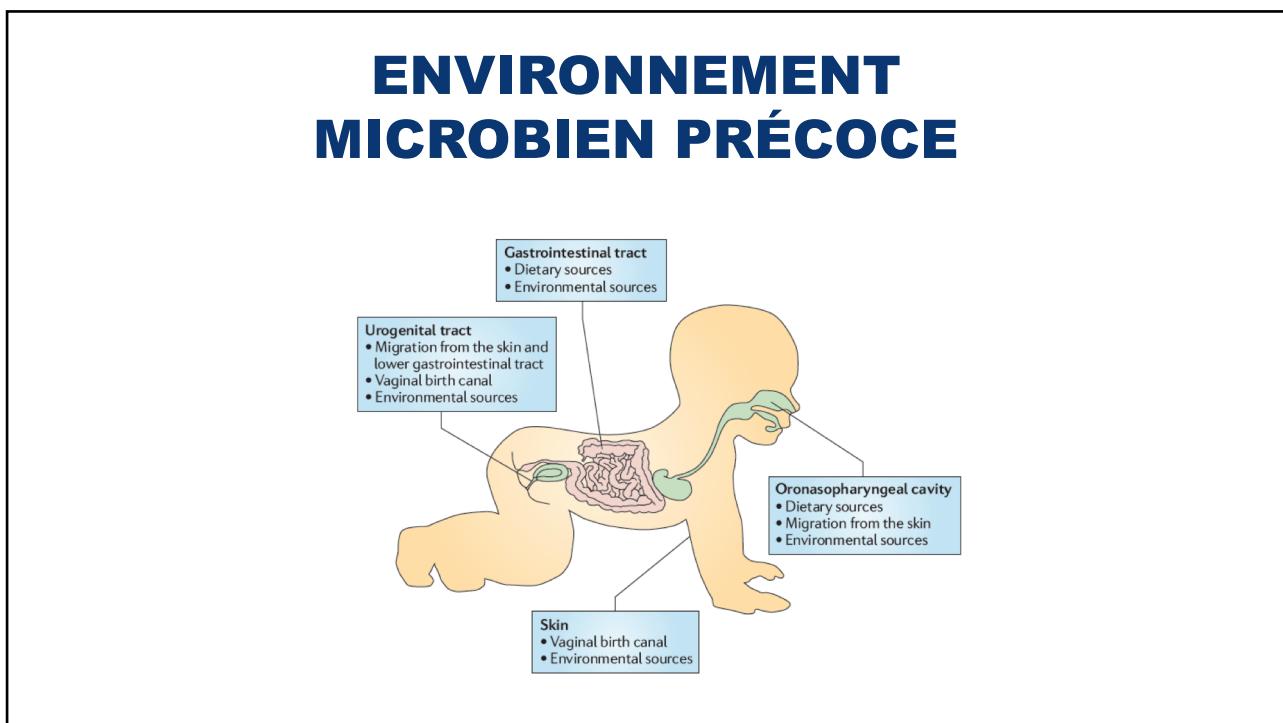
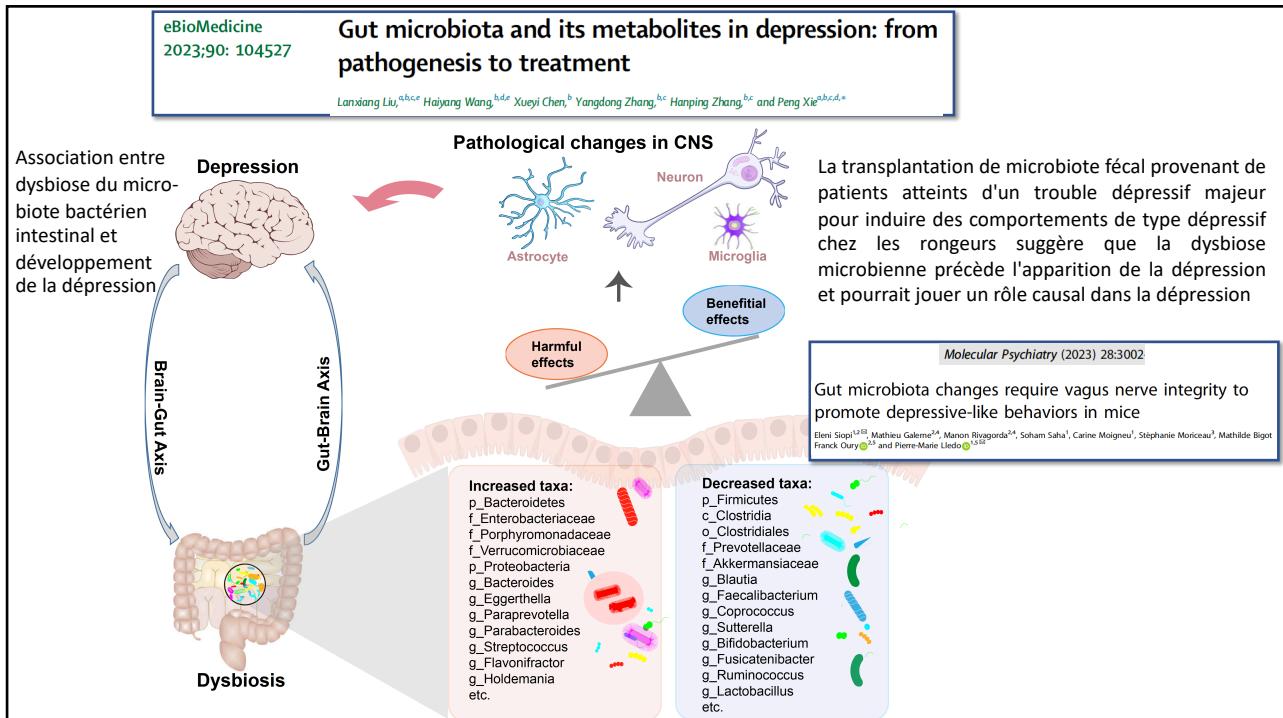
Ron Sender,¹ Shai Fuchs,^{2,3,*} and Ron Milo¹

**1902 → 1.28 × 10¹⁴
1972 → 1 × 10¹⁴
2016 → 3 × 10¹³**

Bakterien im Koth.
Der Zahl der Bakterien, die er bei Antheil der Mikroorganismen an der Da meine Methode ließen letzteren ich jetzt den umgekehrten Weg einubstanz der Bakterien ihre Anzahl be mit der von Alex. Klein verglichen er Bakterien wird im Koth durch Baet. geht daher keinen wesentlichen Fehler, schätigt und bei Berechnung seines Volumens die Formel für einen Cylinder zu Grunde legt, dessen Länge und Durchmesser im Mittel 2,0 und 0,5 μ betragen¹. Unter Zugrundeliegung des spezifischen Gewichtes von 1,05²) findet man für ein Milligramm frisch 2 410 000 000 Bakterien. Nehme ich den Gehalt an Trockensubstanz in Übereinstimmung mit Klein³) zu 15 pCt. an, so ergeben sich trockene Bakterien auf 1 mg 16 000 000 000. Bei einer täglichen Ausscheidung von 8 g trockenen Bakterien berechnet sich somit, dass die Fäces eines erwachsenen Menschen normalerweise täglich 128 000 000 000 000, d. h. 128 Billionen Bakterien enthalten.

Klein, dessen Zahl bereits alle früheren Angaben erheblich übertrifft, fand nur 8,8 Billionen⁴), das ist der 14,5. Theil von meiner Zahl.

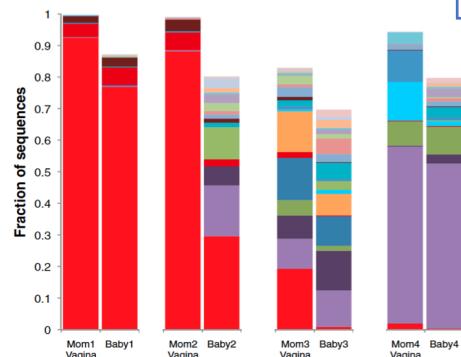




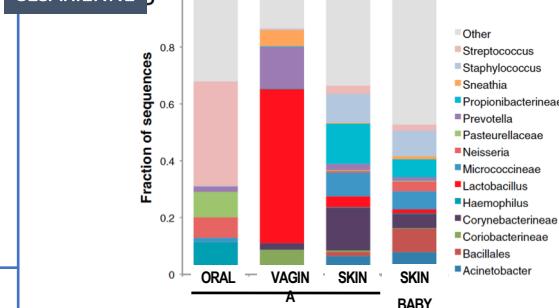
Delivery mode shapes the acquisition and structure of the initial microbiota in newborns

Dominguez-Bello et al. PNAS 2010, 107, 11971-5

ACCOUCHEMENT PAR LES VOIES NATURELLES



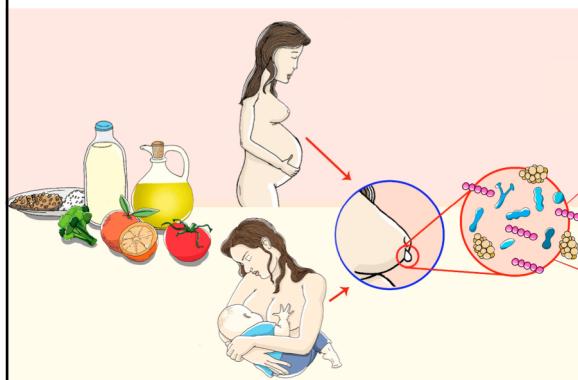
CÉSARIENNE



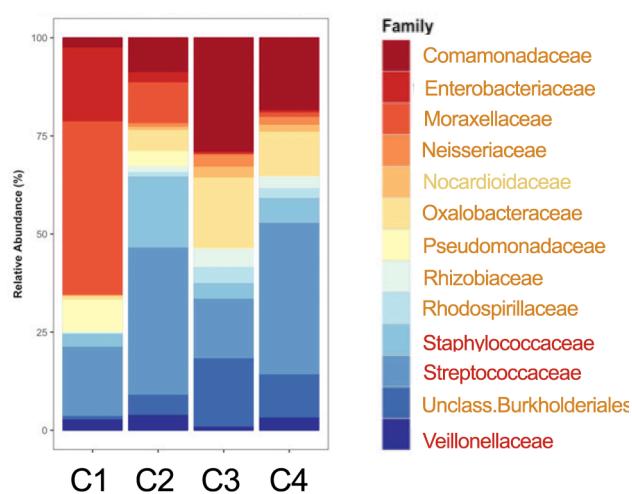
Composition and variation of the human milk microbiota are influenced by maternal and early-life factors

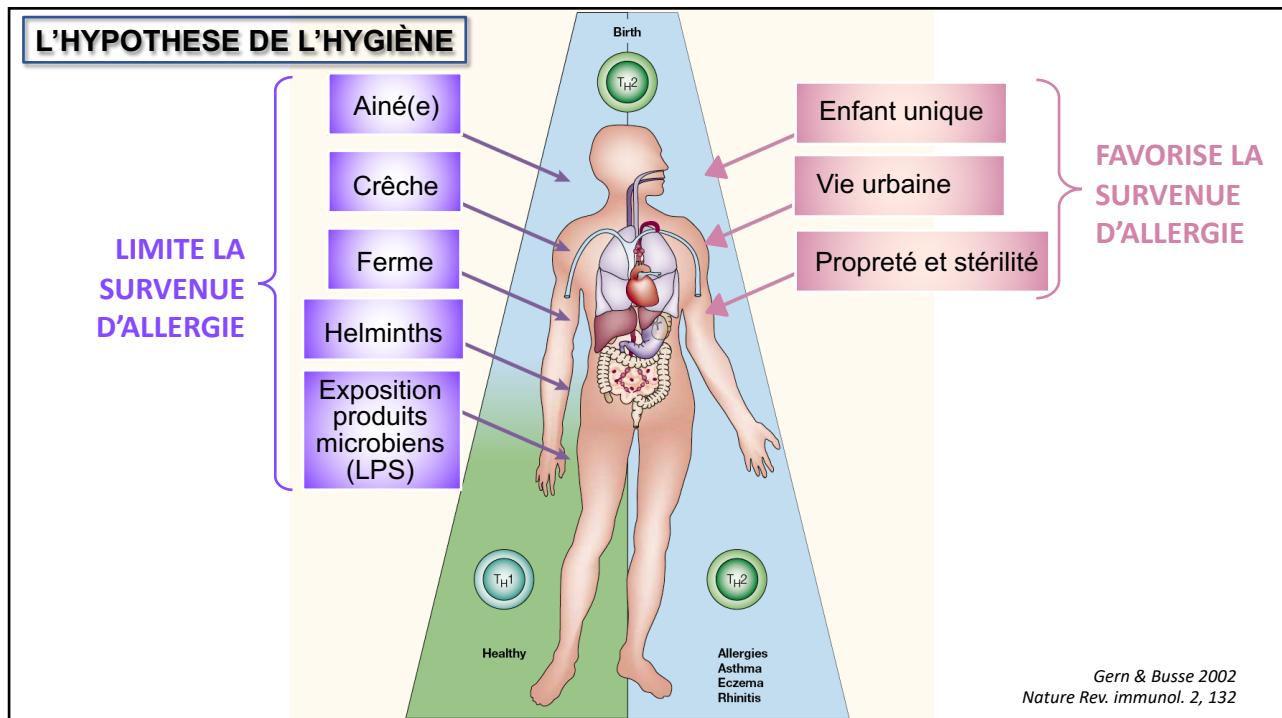
Moossavi et al., 2019, Cell Host & Microbe 25, 324–335

Les profils du microbiote du lait sont très variables entre les femmes



Le régime alimentaire maternel influe le microbiote du lait maternel, en particulier pendant la grossesse, ce qui peut contribuer à façonner le microbiote intestinal.

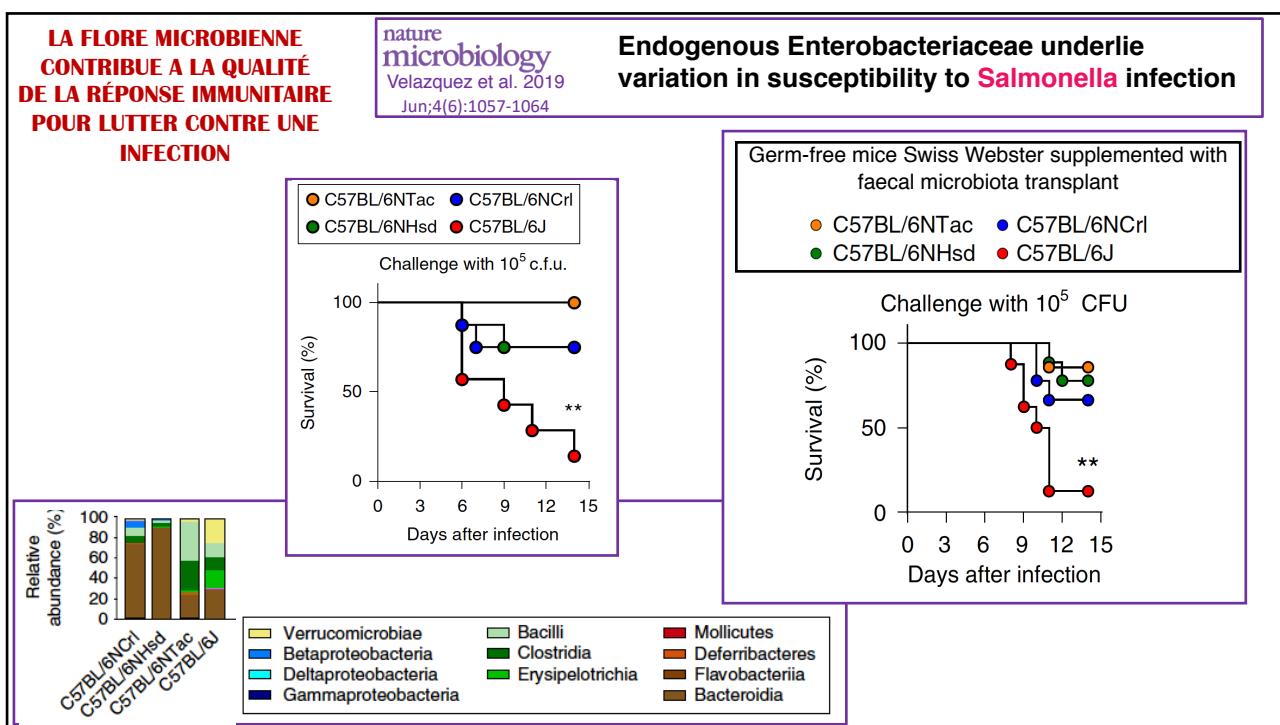
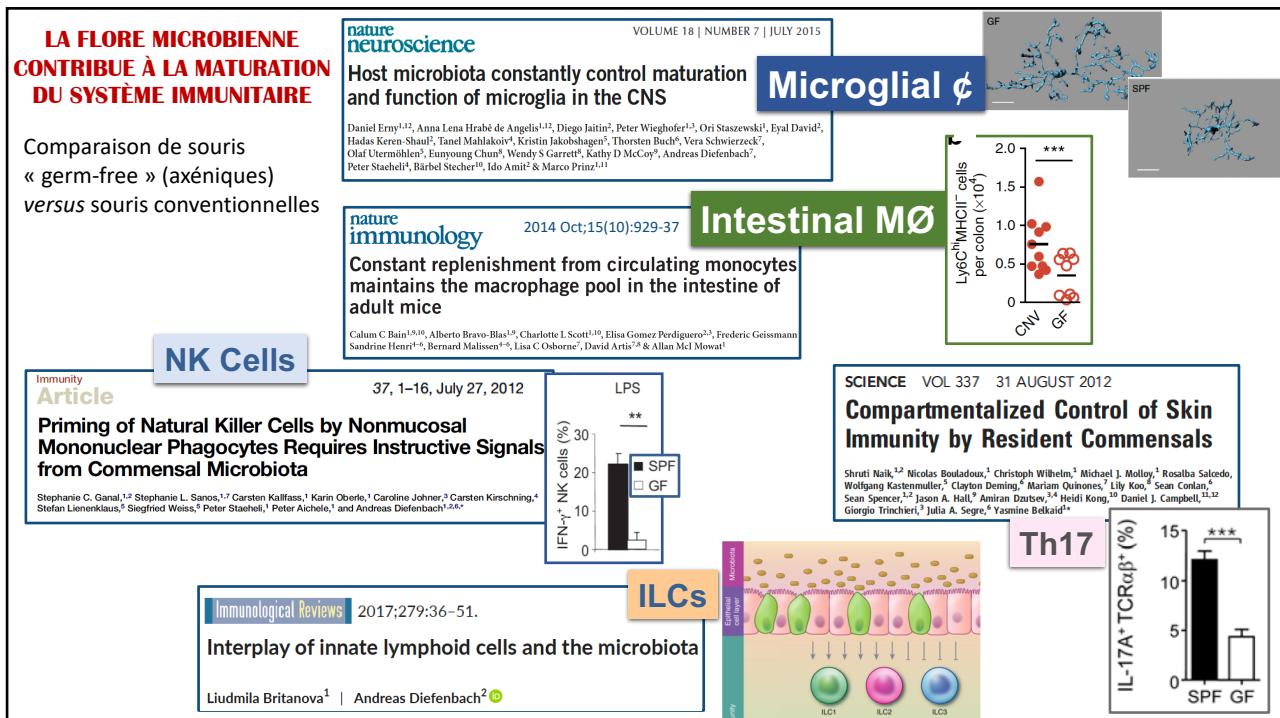


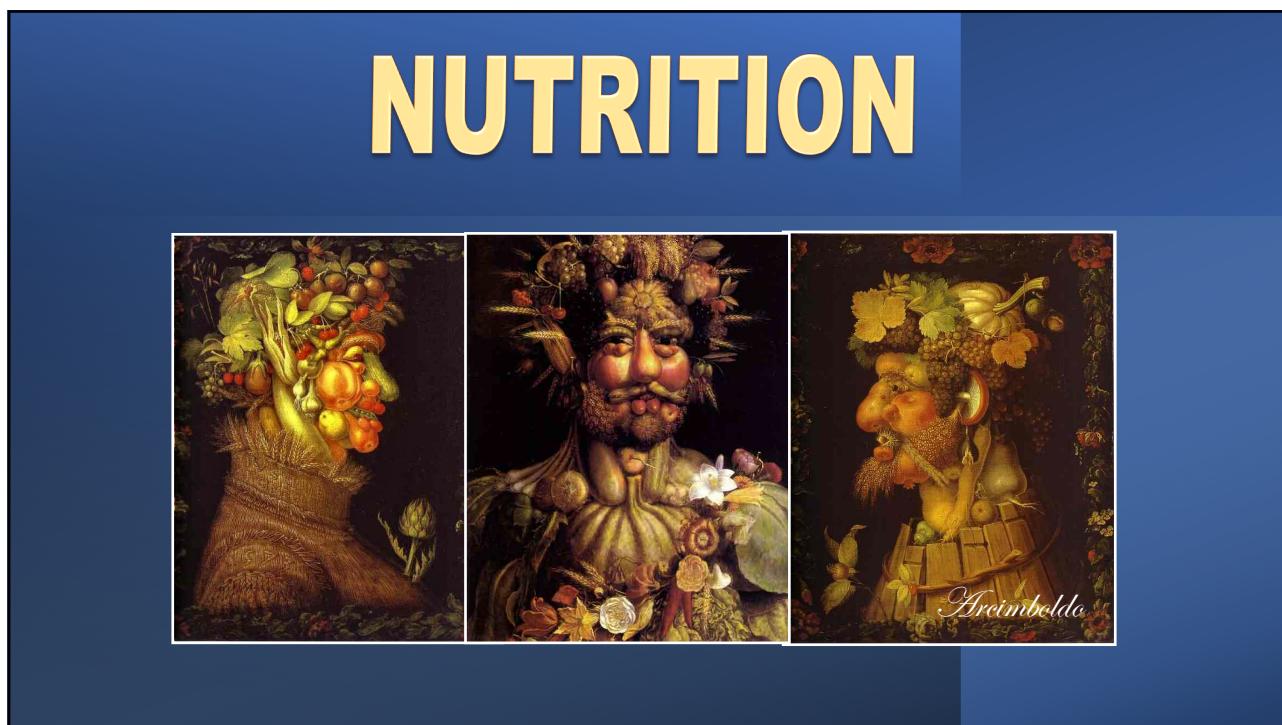
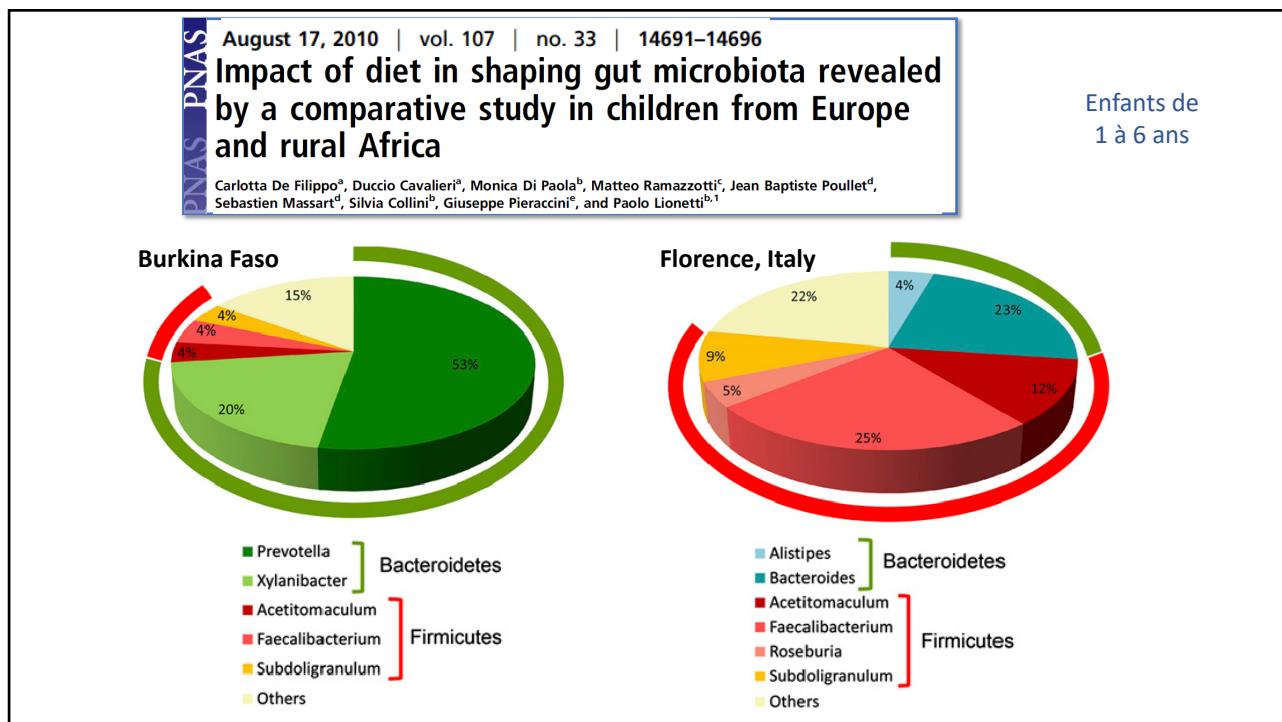


Exposition aux travaux de la ferme au début de la vie et développement de l'asthme et des allergies

Riedler et al. Lancet 2001, 358, 1129

Enquête menée dans les zones rurales d'Autriche, d'Allemagne et de Suisse. 2 618 parents d'enfants de 6 à 13 ans		Écuries + lait de ferme dans la première année de vie (n = 218)	Écuries, lait de ferme ou les deux APRÈS la première année de vie (n=138)	exposition NI aux écuries, NI au lait de ferme (n = 170)
Asthme		1%	11%	12%
Rhume des foins		3%	13%	16%
Sensibilisation atopique		12%	29%	33%
		Mère enceinte active quotidiennement à la ferme (n = 119)	Mère enceinte non active quotidiennement à la ferme et enfant non exposé aux écuries ni au lait de ferme au cours de la 1ère année de vie (n = 28)	
Asthme		0%	14%	
Rhume des foins		1%	11%	
Sensibilisation atopique		8%	39%	

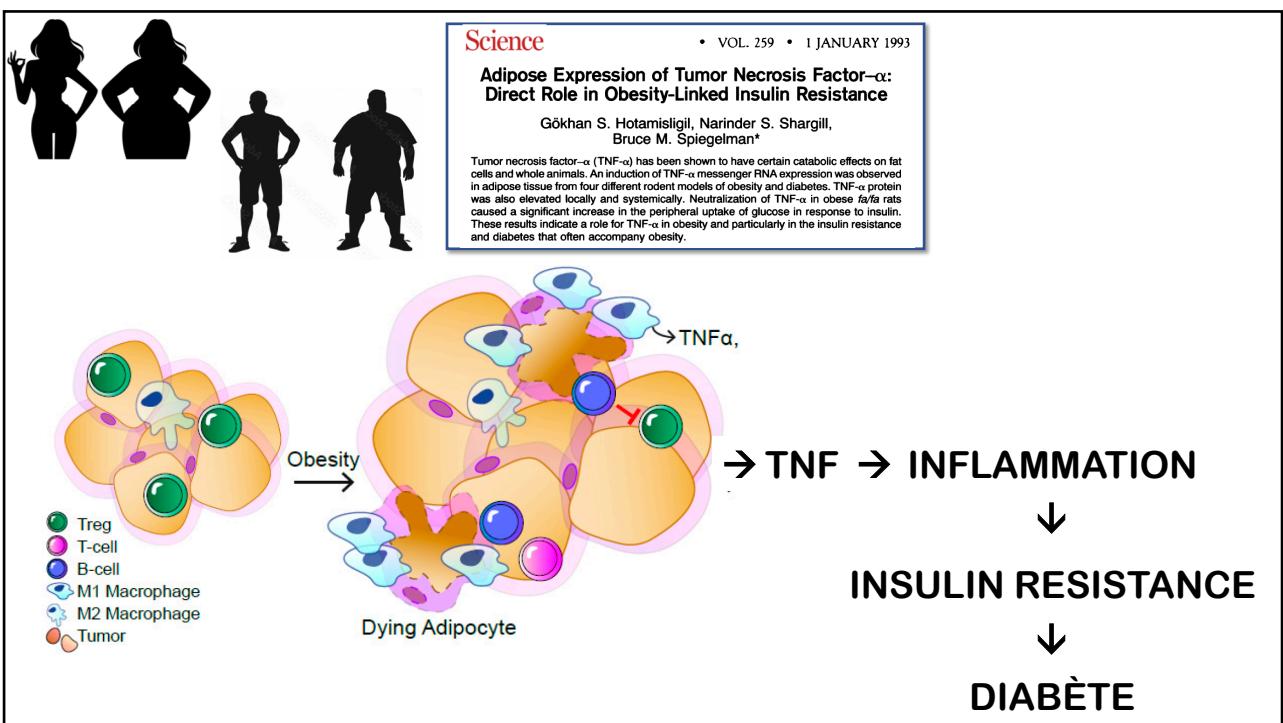


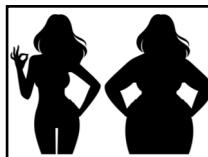


LES DÉBATS DE LA FONDATION DE L'ACADEMIE DE MÉDECINE
Évolution de l'alimentation : du chasseur-cueilleur au supermarché



Novembre 2023





Transcriptome analysis of human adipocytes implicates the NOD-like receptor pathway in obesity-induced adipose inflammation

Yin et al. Mol. Cell Endocrinol. 2014 Aug 25;394(1-2):80-7

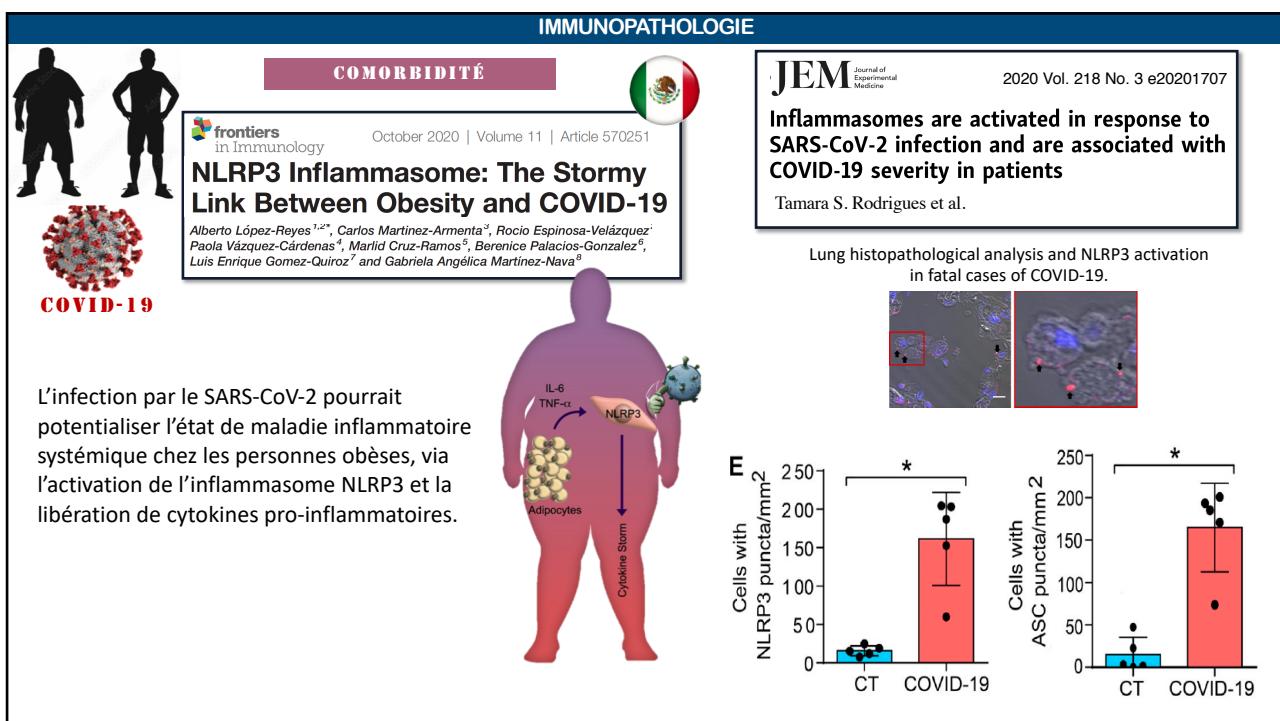
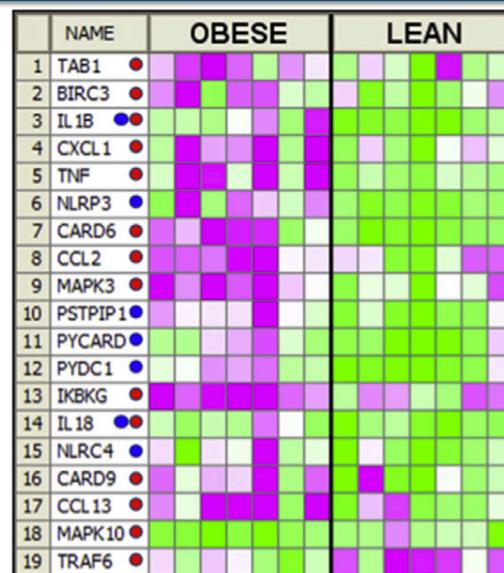
ADIPOCYTES DE FEMMES

"Heat map"

AUGMENTÉ - (violet) and
DIMINUÉ (vert)

Signalisation NOD-signaling-
(points rouges)

Gènes liés à l'inflammasome
(points bleus)



PROBIOTICS



**GENEVA
1905**

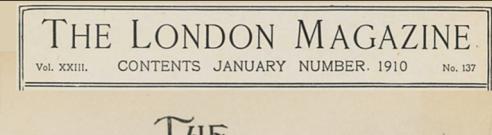
LÉON MASSOL
(1838-1909)



1910

STAMEN GRIGOROV
(1878 – 1945)

Bulgarian Yoghurt



THE LONDON MAGAZINE
Vol. XXIII. CONTENTS JANUARY NUMBER. 1910 No. 137

ELIE METCHNIKOFF
(1845 – 1916)

The Man who prolongs life

Lactobacillus bulgaricus

PROBIOTICS

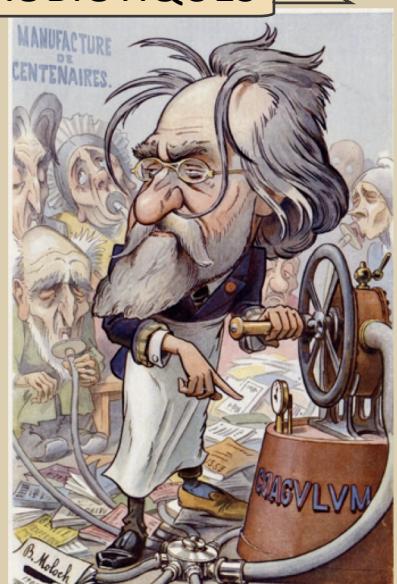


**COMPRIMÉS DE LACTOBACILLINE
LE FERMENT**
SEUL FOURNISSEUR DU PROFESSEUR METCHNIKOFF
LABORATOIRES DARRASSE, NANTERRE, Seine, FRANCE
Louis Darrasse, Pharmacien

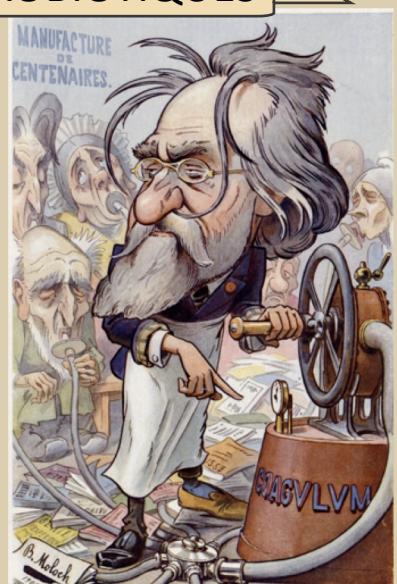
Boîte de 8 Tubes de 5 Comprimés
Dose minima 3 à 6 Comprimés par jour
MARQUE **FL** DÉPOSÉE

PROBIOTIQUES

Prononcé en 1915 lors de son Jubilé



"Persuadé de la nocivité de notre flore intestinale, j'ai institué depuis plus de 18 ans, dans l'intention de combattre son action néfaste, une expérience sur moi-même, je m'abstiens de toute nourriture crue et, de plus, j'ai introduit dans mon régime des microbes lactiques capables d'empêcher la putréfaction intestinale. Ce n'est bien entendu que le premier pas"



MANUFACTURE DE CENTENAIRE.

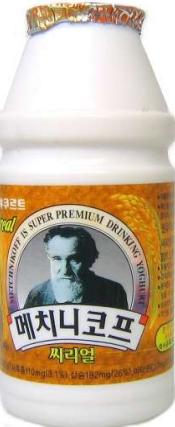
Le Professeur METCHNIKOFF

PROBIOTICS

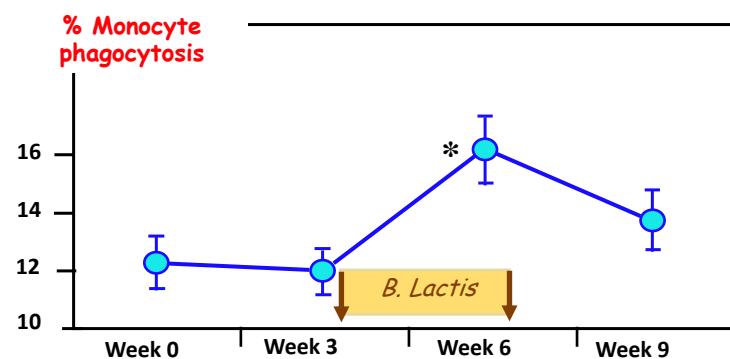


Enhancement of innate immunity by probiotics
Gill et al. Am. J. Clin. Nutr. 2001, 7: 833-839

Study design
30 Elderly subjects (63 - 84 yrs)
Given milk supplemented with *Bifidobacterium lactis* HN019
 5×10^9 organisms/day for 3 weeks



% Monocyte phagocytosis



PROBIOTICS

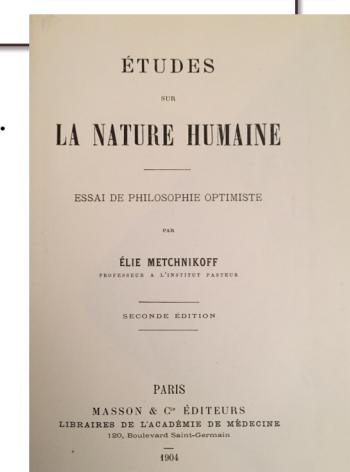


The Journal of Mental Science
July 1910, vol. 234, p.422

***The Treatment of Melancholia by the Lactic Acid Bacillus.*⁽¹⁾ By J. GEORGE PORTER PHILLIPS, M.B., B.S. (Lond.), M.R.C.S., L.R.C.P., Assistant Physician, Bethlem Royal Hospital.**

Sur les 18 cas, 11 se sont remis de leur dépression et des délires qui l'accompagnent.



PROBIOTICS

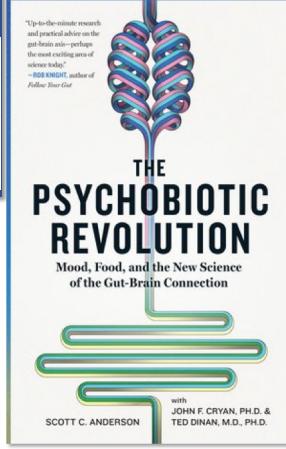


16050–16055 | PNAS | September 20, 2011 | vol. 108 | no. 38

Ingestion of *Lactobacillus* strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve

Javier A. Bravo^{a,1}, Paul Forsythe^{b,c,1}, Marianne V. Chew^b, Emily Escaravage^b, Hélène M. Savignac^{a,d}, Timothy G. Dinan^{a,e}, John Bienenstock^{b,f,2}, and John F. Cryan^{a,d,g,2}

CONCLUSIONS : L'ensemble de ces résultats mettent en évidence le rôle important des bactéries dans la communication bidirectionnelle de l'axe intestin-cerveau et suggèrent que certains organismes pourraient s'avérer être des compléments thérapeutiques utiles dans les troubles liés au stress tels que l'anxiété et la dépression.



frontiers | Frontiers in Microbiology 2023 ; 14:1211447

Deciphering psychobiotics' mechanism of action: bacterial extracellular vesicles in the spotlight

Layla Bleibel, Szymon Dziomba, Krzysztof Franciszek Waleron, Edward Kowalczyk and Michał Seweryn Karbownik

Explore 19 (2023) 669–680

Psychobiotics: Are they the future intervention for managing depression and anxiety? A literature review

Kim Ross

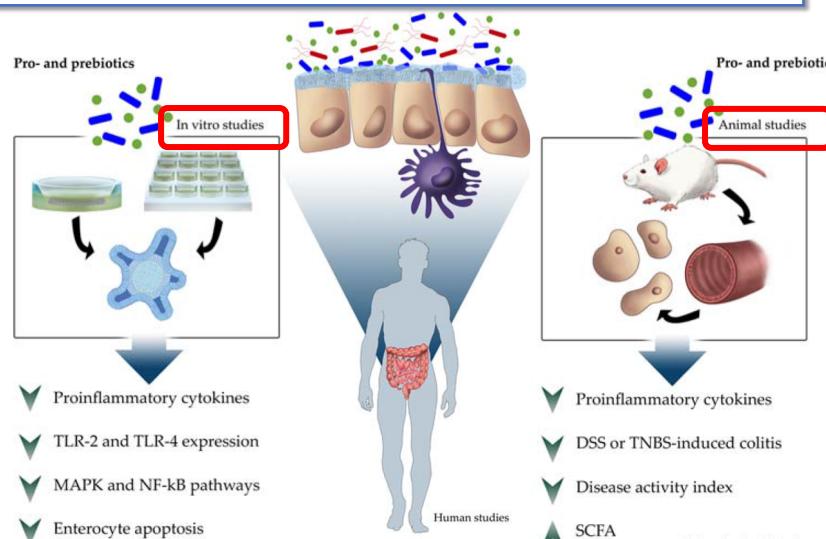
PROBIOTICS



nutrients 2017, 9, 555

Evidence of the Anti-Inflammatory Effects of Probiotics and Synbiotics in Intestinal Chronic Diseases

Julio Plaza-Díaz, Francisco Javier Ruiz-Ojeda, Laura María Vilchez-Padial, Angel Gil,



In vitro studies

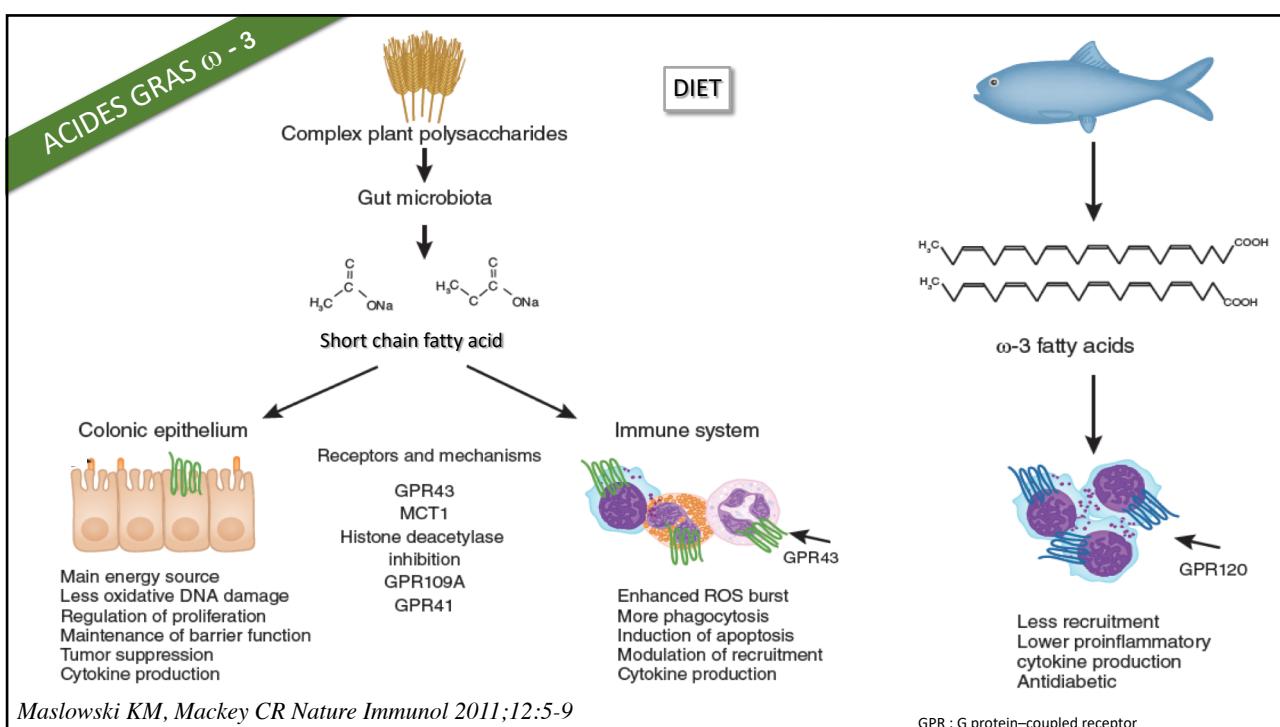
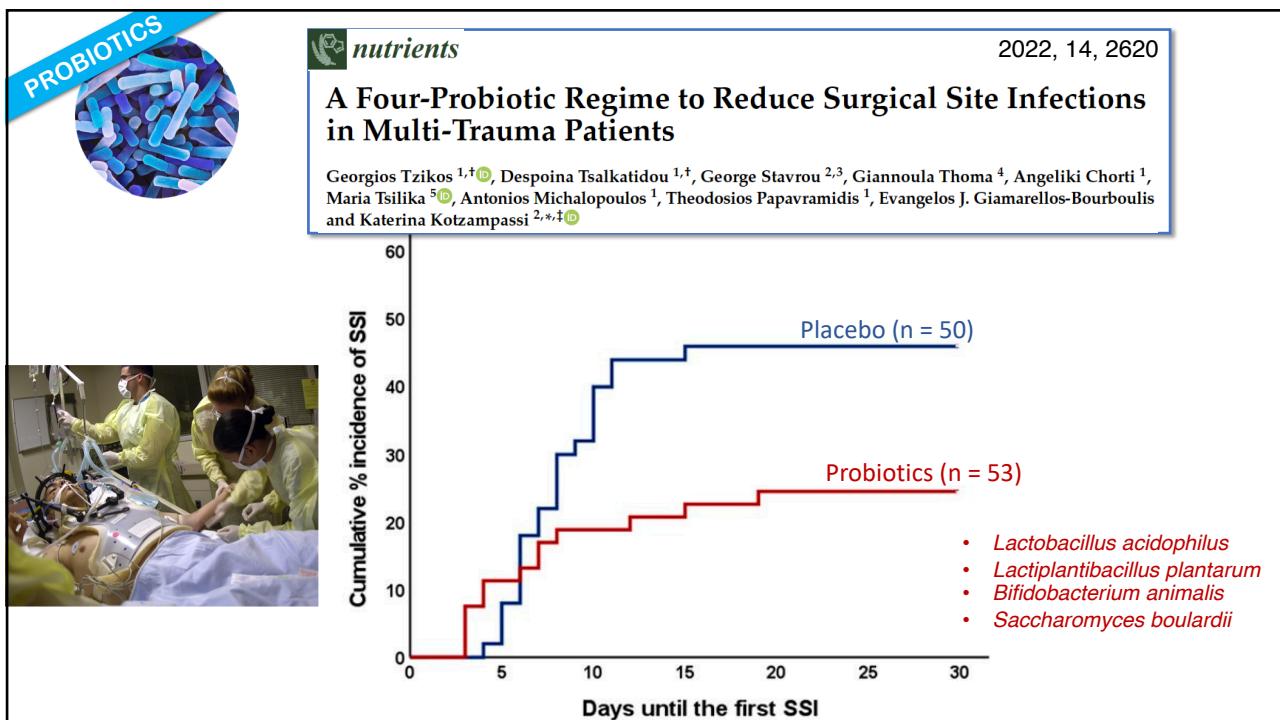
- Pro- and prebiotics
- Inflammation markers: Proinflammatory cytokines, TLR-2 and TLR-4 expression, MAPK and NF-κB pathways, Enterocyte apoptosis

Human studies

- Clinical symptoms, especially in UC
- Proinflammatory cytokines, DSS or TNBS-induced colitis, Disease activity index, SCFA

Animal studies

- Pro- and prebiotics
- * Caution in IBD relapse



ACIDES GRAS ω - 3

Propriétés anti-inflammatoires de la prise par voie orale acides gras polyinsaturés n-3

Composition en acides gras des phospholipides membranaires des neutrophiles

Des volontaires masculins en bonne santé ont consommé différentes quantités d'huile de thon en capsules pendant 12 semaines.

Healy et al. *Lipids* 2000, 35, 763

Diminution de la production d'eicosanoïdes dérivés de l'acide arachidonique

ACIDES GRAS ω - 3

The NEW ENGLAND JOURNAL OF MEDICINE 1989; 320:265-271

The Effect of Dietary Supplementation with n—3 Polyunsaturated Fatty Acids on the Synthesis of Interleukin-1 and Tumor Necrosis Factor by Mononuclear Cells

Stefan Endres, M.D., Reza Ghorbani, B.S., Vicki E. Kelley, Ph.D., Kostis Georgilis, M.D., Gerhard Lonnemann, M.D., Jos W. M. van der Meer, M.D., Joseph G. Cannon, Ph.D., Tina S. Rogers, Ph.D., Mark S. Klempner, M.D., Peter C. Weber, M.D., Ernst J. Schaefer, M.D., Sheldon M. Wolff, M.D., et al.

Neuf volontaires en bonne santé ont ajouté 18 g de concentré d'huile de poisson par jour à leur alimentation occidentale normale pendant six semaines.

→ L'apport en acides gras insaturés est passé de 28 à 34 g.

In vitro production [LPS]	before	10 weeks after the end of suppl.	↓
IL-1 β (ng/ml)	7.4	4.2	43%
IL-1 α (ng/ml)	16.0	9.7	39%
TNF α (ng/ml)	8.5	5.1	40%
PGE2 prod. <i>S. epidermidis</i> (pg/ml)		612	302
			51%
		6 weeks after the end of suppl.	

ACIDES GRAS ω - 3

Clinical Nutrition

Volume 12, Issue 6, December 1993, Pages 321-328

Effect of dietary fish oil supplementation on fever and cytokine production in human volunteers

Cooper AL, Gibbons L, Horan MA, Little RA, Rothwell NJ.



La moitié des sujets ont complété leur alimentation normale avec 4,5 g/jour d'huile de poisson pendant 6 à 8 semaines.

	Δ heart rate (7h)	Δ oral T°C (12h)	Δ VO2 (4h)
Control	+ 16%	+ 1.2°C	+ 28%
Fish oil suppl. 6-8 weeks	+ 7%	+ 0.7°C	+ 3%

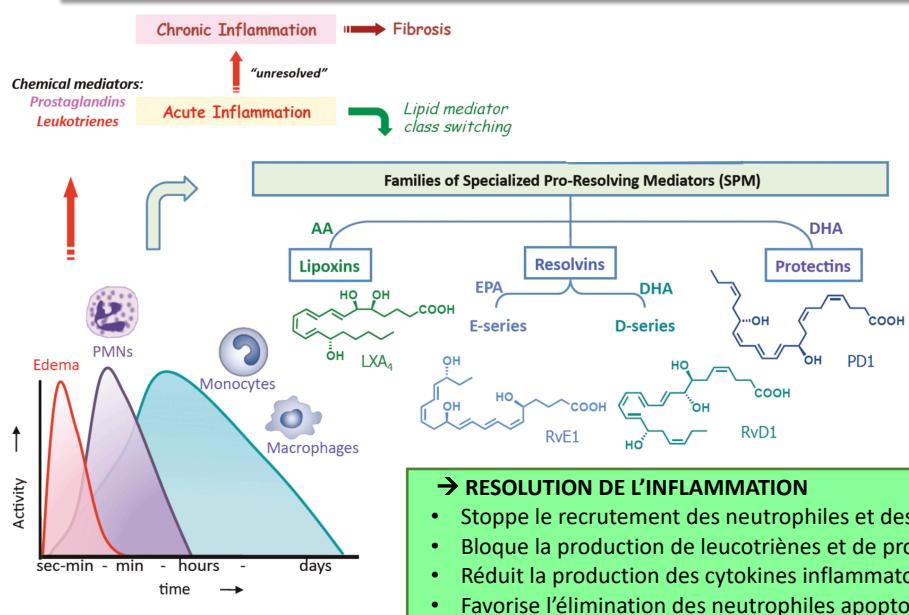
ACIDES GRAS ω - 3

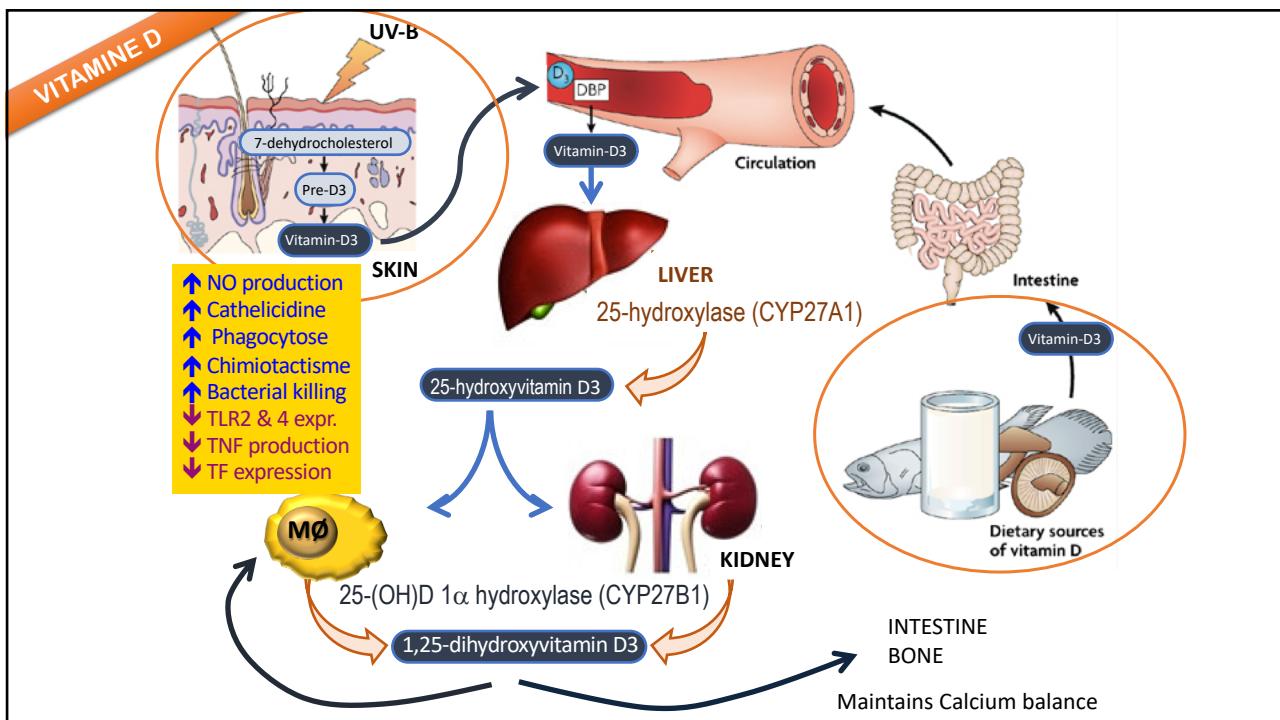
CHEMICAL REVIEWS

2011

Resolvins and Protectins in Inflammation Resolution

Charles N. Serhan*,† and Nicos A. Petasis*,‡





VITAMINE D

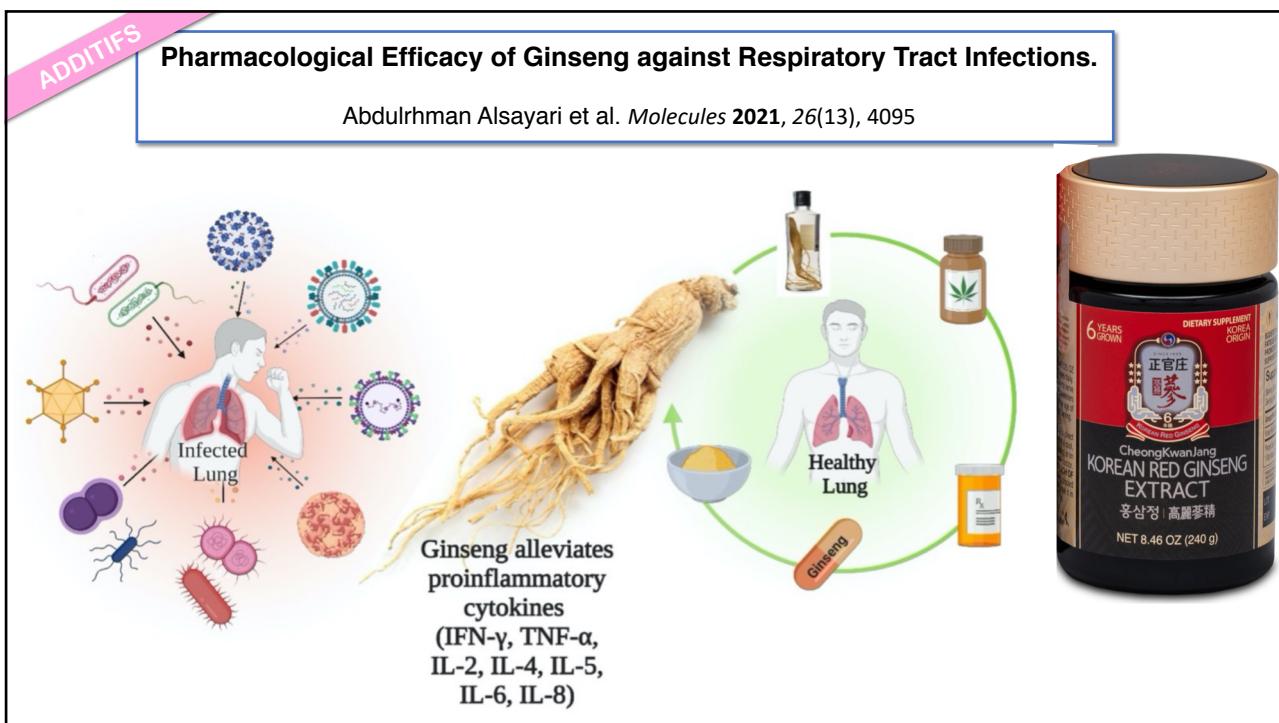
Crit Care Med 2011; 39:671–677

Association of low serum 25-hydroxyvitamin D levels and mortality in the critically ill*

Andrea Braun, MD; Domingo Chang, MD; Karthik Mahadevappa, MBBS; Fiona K. Gibbons, MD; Yan Liu, MS; Edward Giovannucci, MD, ScD; Kenneth B. Christopher, MD, FASN, FCCP

Adjusted	OR	95% CI	P
In-hospital mortality			
25(OH)D ≤ 15 ng/mL	1.72	1.27–2.33	<.0001
25(OH)D 15–30 ng/mL	1.34	1.01–1.79	0.04
25(OH)D ≥ 30 ng/mL	1.00		

Characteristic	Preadmission 25(OH)D Level			p
	≤15 ng/mL	15–30 ng/mL	≥30 ng/mL	
Total number of patients	637	918	844	<.0001
Age (yrs), mean (SD)	61.9 (16.9)	65.1 (16.5)	67.0 (16.2)	.07
Gender, number (%)				
Female	352 (55.3)	511 (55.7)	509 (60.3)	
Male	285 (44.7)	407 (44.3)	335 (39.7)	
Sepsis, number (%)	193 (30.3)	220 (24.0)	164 (19.4)	<.0001



ADDITIFS

Molecular Cell, Vol. 10, 417–426, August, 2002

The Inflammasome: A Molecular Platform Triggering Activation of Inflammatory Caspases and Processing of proIL-1 β

Fabio Martinon, Kimberly Burns, and Jürg Tschopp

Jürg Tschopp (1950 – 2011)
(Lausanne)

Extracellular space

Pannexin

P2X7

ATP

PAMPs

IL18

Pro-IL1 β

Pro-IL18

NO

ROS

Inflammasome activation

NF κ B

Activation of proinflammatory cytokines

Kim et al. Immunol Lett. 2014; 158: 143-50
Han et al. J Ginseng Res. 2017; 41: 513-523
Jiang et al. J Ethnopharmacol. 2020; 251: 112564
Chei S et al. Foods 2020; 9: 526.
Hu et al. Phytomedicine 2020; 76: 153251
Wang et al. Nutrients 2021; 13: 856
Ahn et al. J Ginseng Res. 2021; 45: 456-463
Min J et al. J Ginseng Res. 2022; 46: 675-682
Zhao et al. Front Pharmacol. 2022; 13: 980449.
Cho et al. Int J Mol Sci. 2023; 24: 1077

CHEONG KWAN JANG KOREAN RED GINSENG EXTRACT
NET 8.46 OZ (240 g)

ADDITIFS

Innate Immunity

2014, Vol. 20(7) 735–750

cis-Resveratrol produces anti-inflammatory effects by inhibiting canonical and non-canonical inflammasomes in macrophages

Huang TT, Lai HC, Chen YB, Chen LG, Wu YH, Ko YF, Lu CC, Chang CJ, Wu CY, Martel J, Ojcius DM, Chong KY, Young JD.

Effets du cis-resvératrol sur la sécrétion d'IL-1 β par des macrophages THP-1 humains

Resveratrol (μ M)	LPS (0.5 μ g/ml)	ATP (5 mM)	IL-1 β (pg/ml)
—	—	—	~100
0	+	+	~2200
10	+	+	~1500
100	+	+	~900

Le cis-resvératrol inhibe l'expression des gènes de la caspase-1 et de la caspase-4

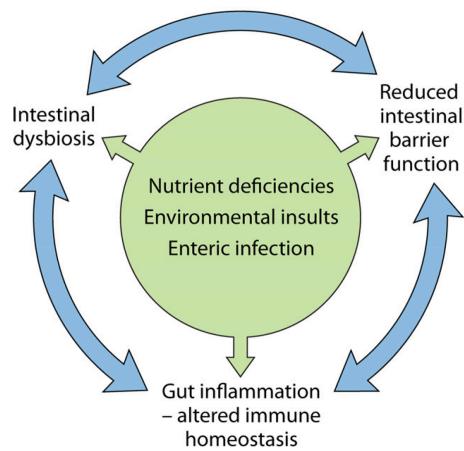
(a)

Resveratrol (μ M)	LPS (0.5 μ g/ml)	ATP (5 mM)	Caspase-1 mRNA	Caspase-4 mRNA
—	—	—	1.0	1.0
0	+	+	~2.7	~2.2
100	+	+	~1.2	~1.3

Clinical Microbiology Reviews October 2017 Volume 30 Issue 4

Impact of Childhood Malnutrition on Host Defense and Infection

Marwa K. Ibrahim,^a Mara Zambruni,^{b,c} Christopher L. Melby,
Peter C. Melby^{b,c,e,f,g,h}



- GALT**
- Small Peyer's patches and germinal centers
 - Fewer intraepithelial lymphocytes, B cells and T cells
 - Fewer antibody-forming cells and less secretory IgA



Thymus

- Reduced thymic epithelium
- Expanded extracellular matrix
- Thymocyte depletion (increased apoptosis, decreased proliferation)
- Reduced thymic hormone

Spleen

- Reduced cellularity
- Disorganized white pulp
- Splenocyte depletion (increased apoptosis, decreased proliferation)
- Altered inflammatory environment

Lymph nodes

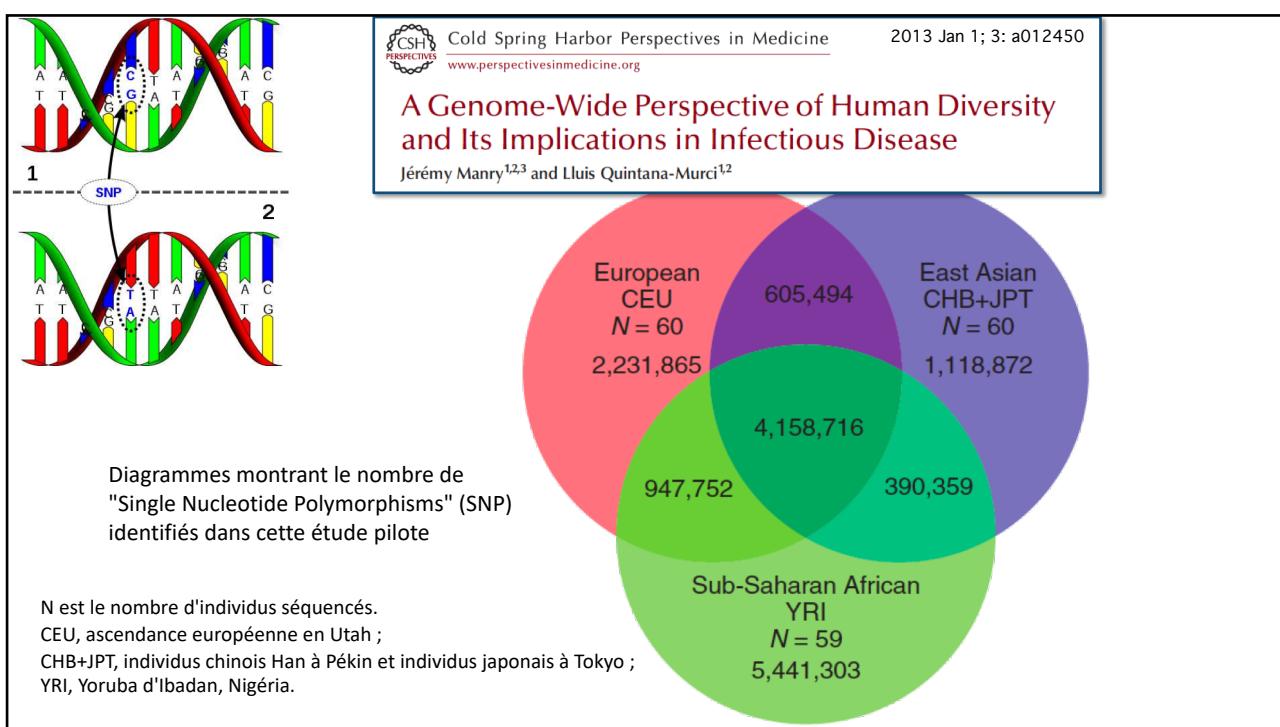
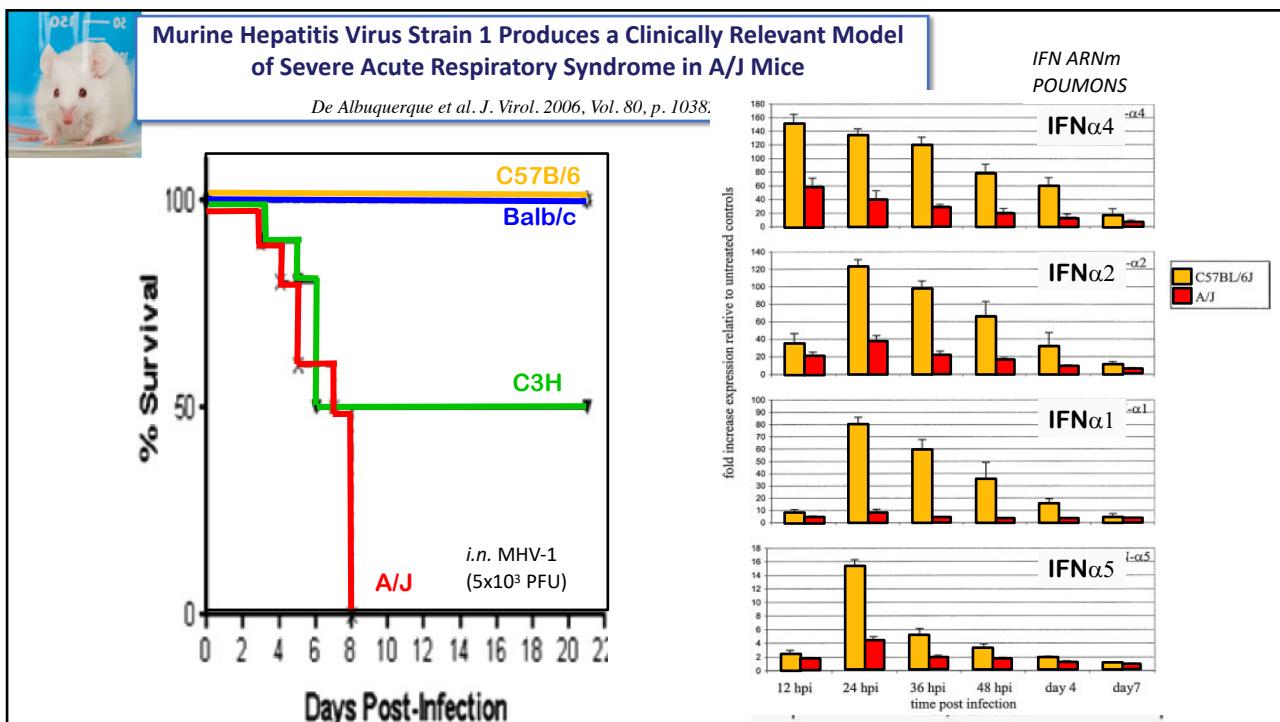
- Reduced cellularity
- Altered leukocyte trafficking
- Altered antigen trafficking through conduit
- Impaired barrier function
- Fewer antibody-forming cells

Bone marrow

- Reduced cellularity
- Expanded extracellular matrix
- Altered stroma
- Erythroid hypoplasia/dysplasia
- Reduced hematopoietic progenitor cells (cell cycle arrest; reduced proliferation)
- Impaired myeloid cell maturation and mobilization

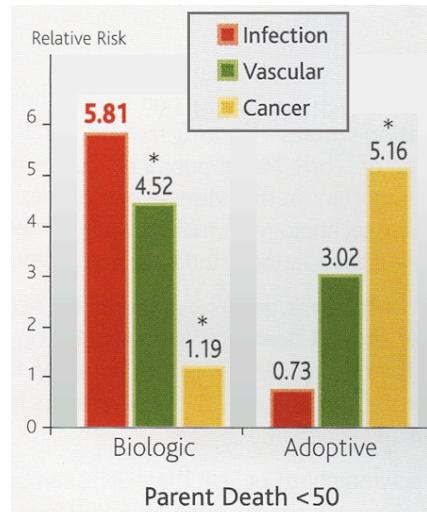
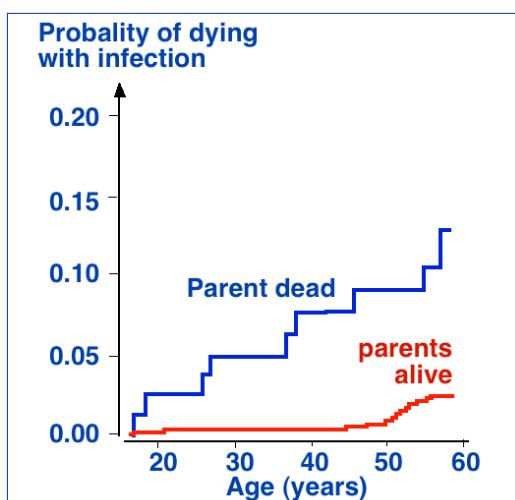
POLYMORPHISME GÉNÉTIQUE



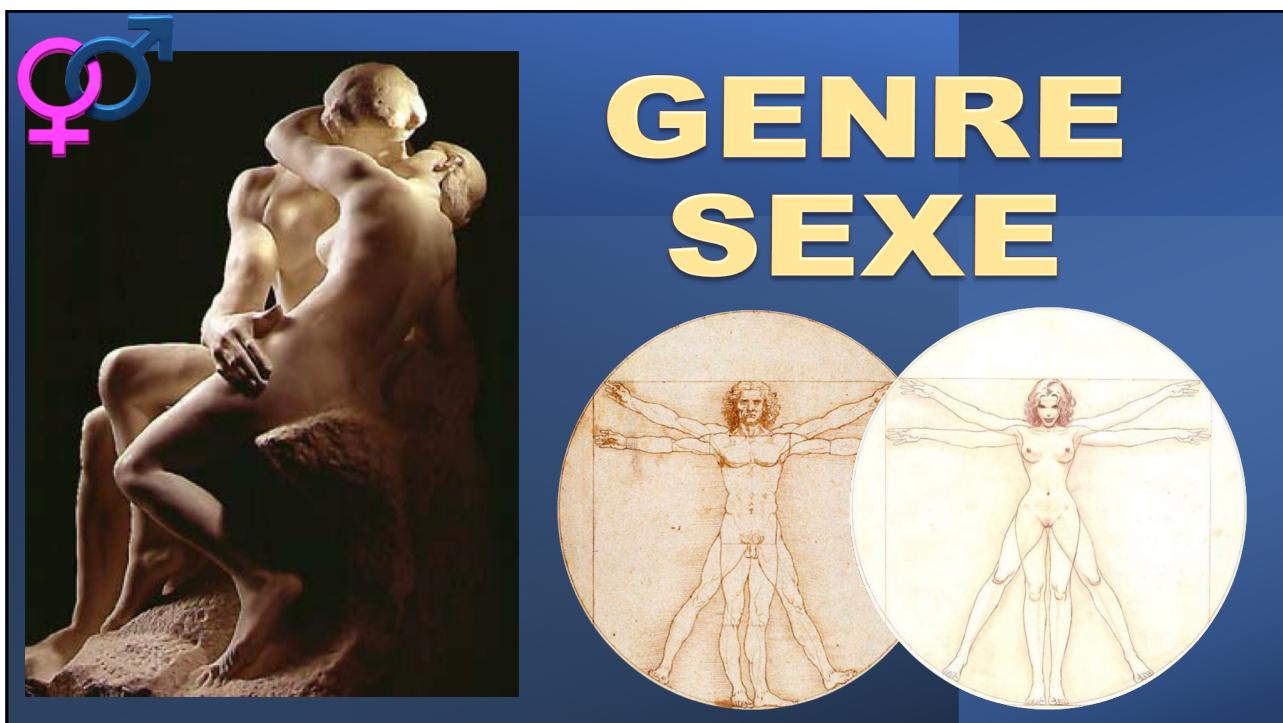


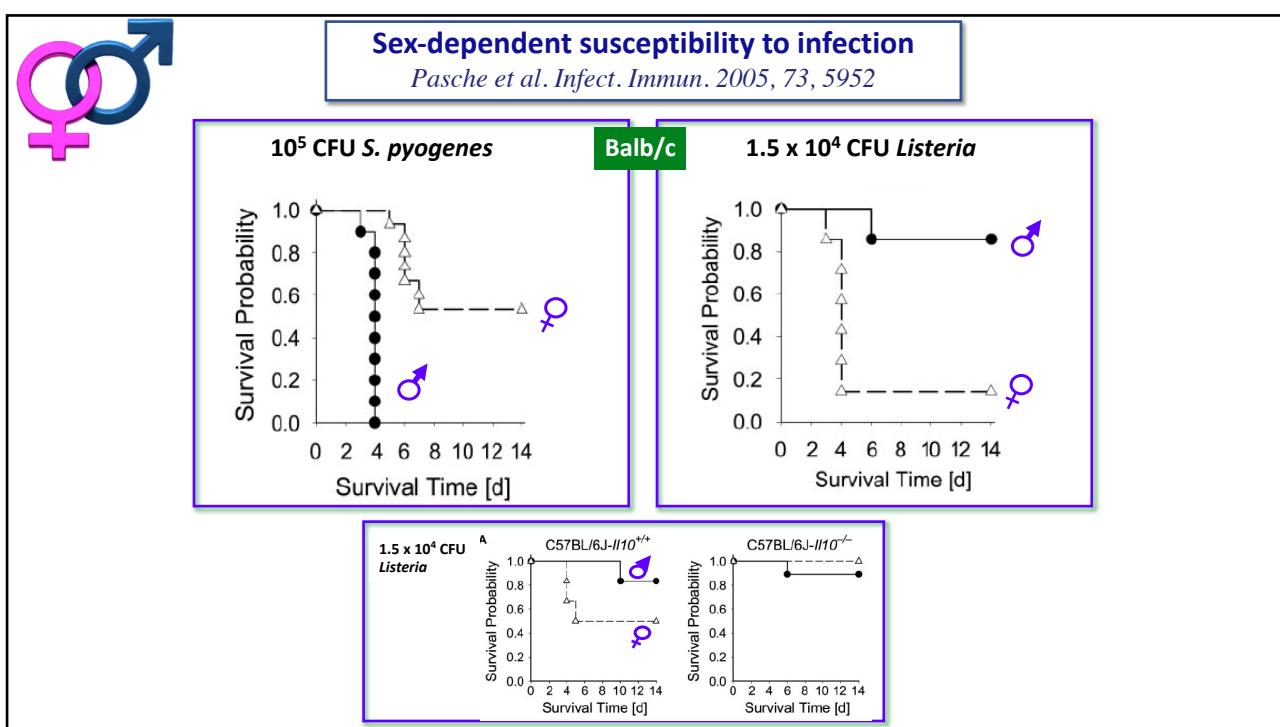
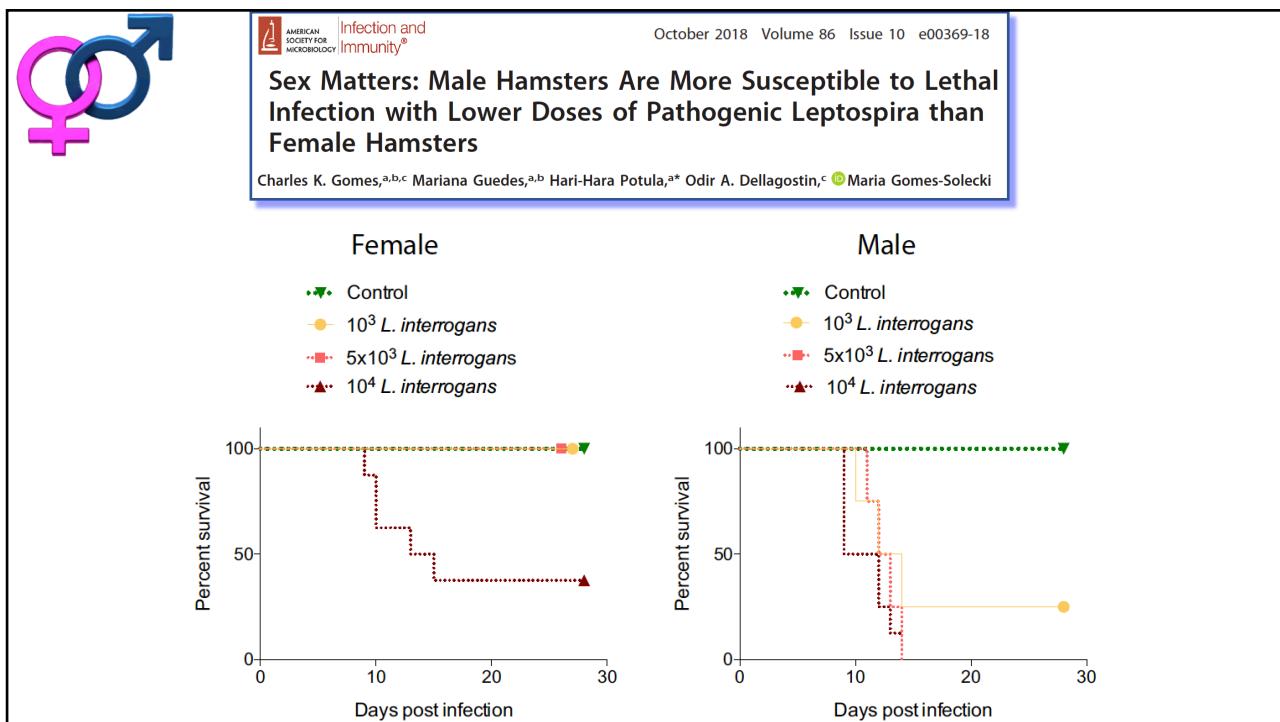
Influences génétiques et environnementales sur la mort prématûrée chez les adoptés adultes

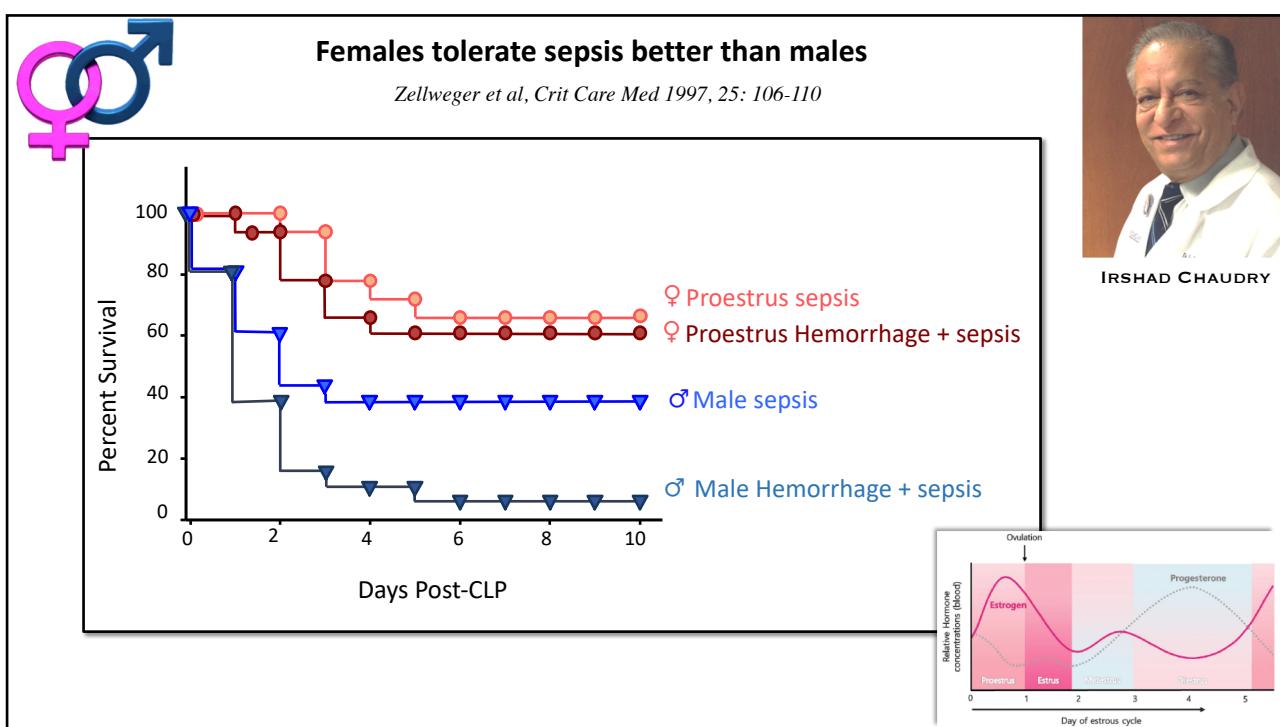
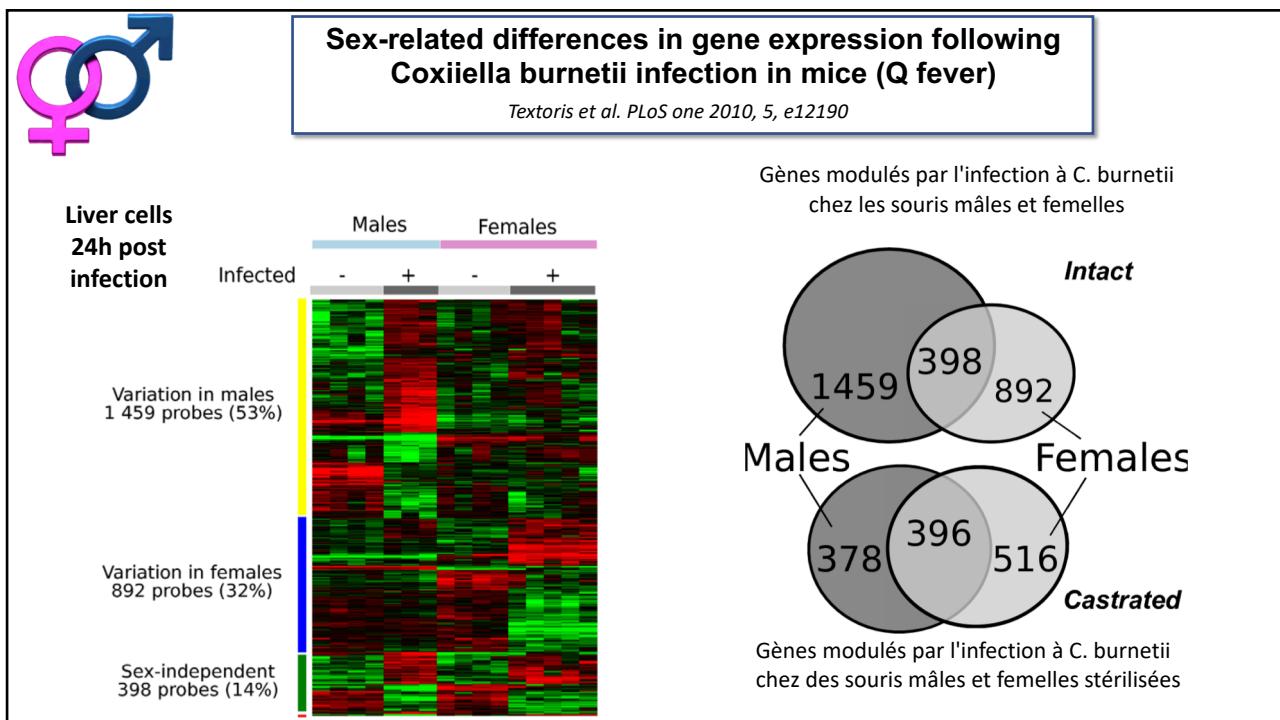
Sorensen et al. N. Engl. J. Med. 1988, 318, 727

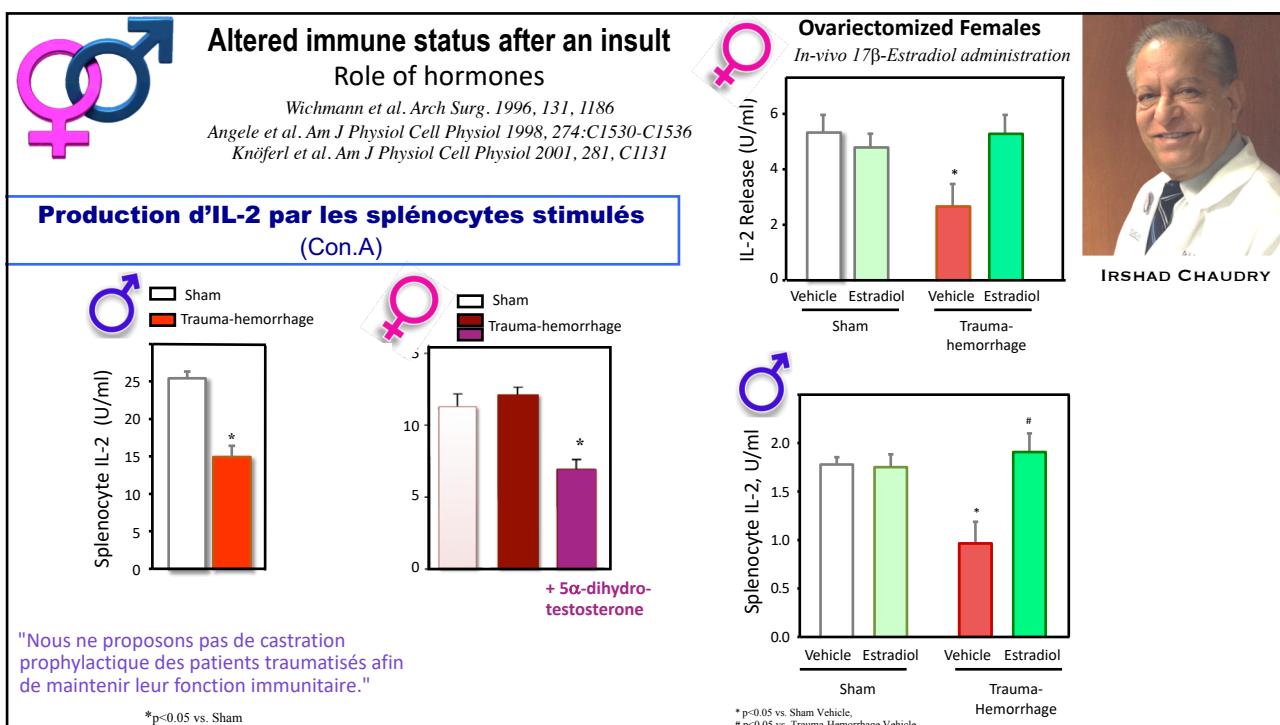
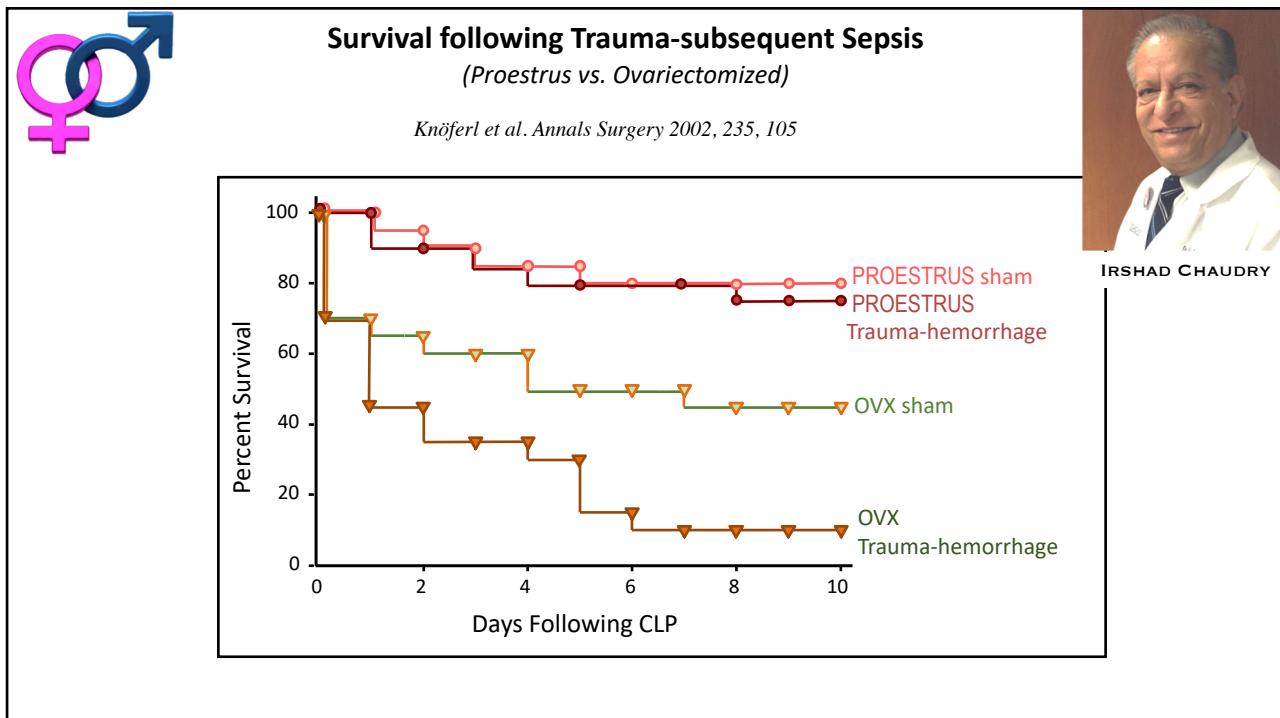


L'héritabilité des décès prématûrés dus à une infection (risque relatif = 5,8) est supérieure à celle des décès dus à des causes cardio- et cérébro-vasculaires (4,5) ou au cancer (1,2)









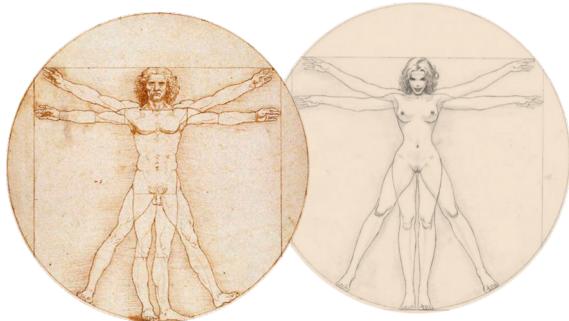
NATURE REVIEWS | IMMUNOLOGY

636 | OCTOBER 2016 | VOLUME 16

Sex differences in immune responses

Sabra L. Klein¹ and Katie L. Flanagan²

chez l'homme/femme
la réponses aux
vaccins diffère selon
les sexes



Target group	Vaccine	Sex difference in Immune response
Children	Hepatitis B	Greater in females
	Diphtheria	Greater in females
	Pertussis	Greater in females
	Pneumococcal	Greater in females
	Rabies	Greater in females
	Measles	Greater in females or equivalent in both sexes
	RTS,S vaccine against malaria	Greater in females
	Human papillomavirus	Greater in females
	Influenza	Greater in females
Adults	Hepatitis B	Greater in females
	Herpes virus	Greater in females
	Yellow fever	Greater in females
	Rabies	Greater in females
	Smallpox	Greater in females
	Influenza	Greater in females
Aged adults	Td/Tdap	Greater in males
	Pneumococcal	Greater in males

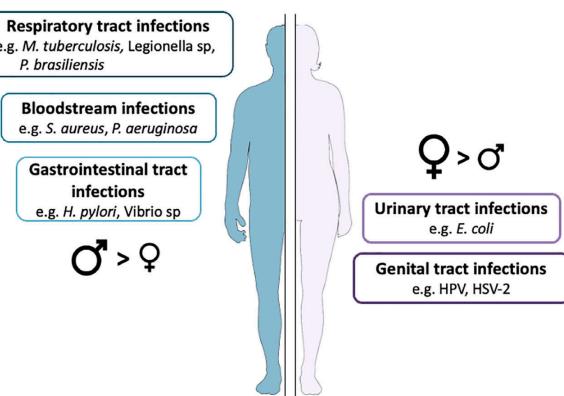


July 2021 | Volume 12 | Article 698121

Sexual Dimorphism and Gender in Infectious Diseases

Laetitia Gay, Cléa Melenotte, Ines Lakbar, Soraya Mezouar, Christian Devaux, Didier Raoult, Marc-Karim Bendiane, Marc Leone and Jean-Louis Mége

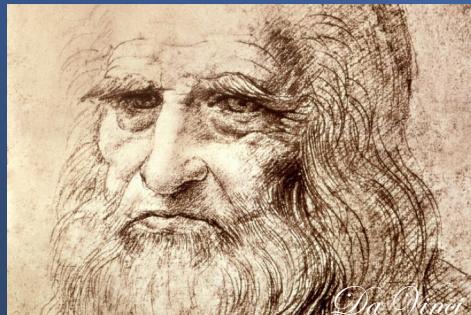
Infection prevalence according to anatomical characteristics.



Effects of sex hormones on the immune system

	Estrogens	Androgens	Progesterone
T cells	↑ Th1 differentiation ↑ TNF, IL-1β, IFN-γ, IL-4 ↑ Treg and activation ↑ T-cell apoptosis	↓ Th1 responses ↓ T-cell proliferation ↓ IL-4 production ↓ Treg cells	↓ Response
B cells	↑ Activity ↑ Antibody production	↓ Antibody production	↓ CD80 and CD86
Macrophages	↑ Phagocytosis ↑ TNF, IFN-γ, IL-6, IL-10 ↑ TLR-4 expression ↓ Nitrite	↓ Phagocytosis ↓ TNF, iNOS and NO ↓ TLR-4 expression ↑ IL-10, TGFβ	↓ iNOS and NO ↓ TNF, IL-1β
NK cells	↑ IFNγ ↑ Granzyme B ↓ FASL	ND	↑ Apoptosis (caspase dependent)
DCs	↑ Maturation ↑ Activation ↑ TLR-7and TLR-9 ↑ CCL2, IL-6, IL-10, CXCL8	↓ IL-1β, IL-6 and TNF	↓ CD40, CD80, CD86 ↑ IL-18 and IL-10 ↓ TNF, IL-1β
Neutrophils	↑ Numbers ↑ Degranulation ↑ Elastase release	↑ Numbers ↓ Kinases ↓ Leukotriene formation	ND
Eosinophils	↓ Numbers ↓ Mobilization ↑ Degranulation	↓ Degranulation	↑ Numbers ↑ Degranulation

ÂGE

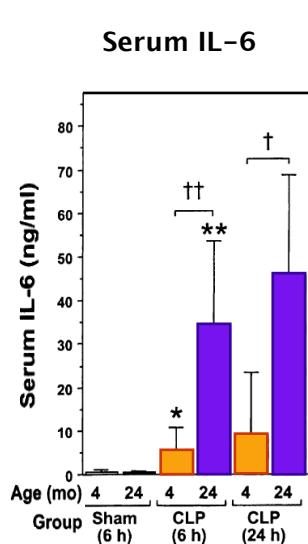
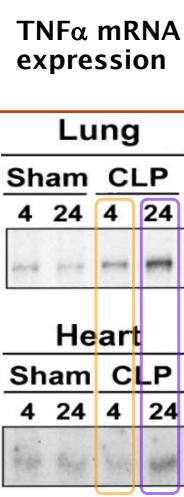
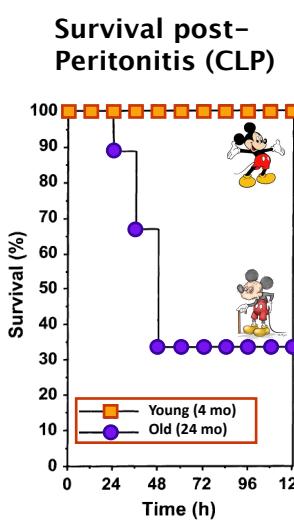


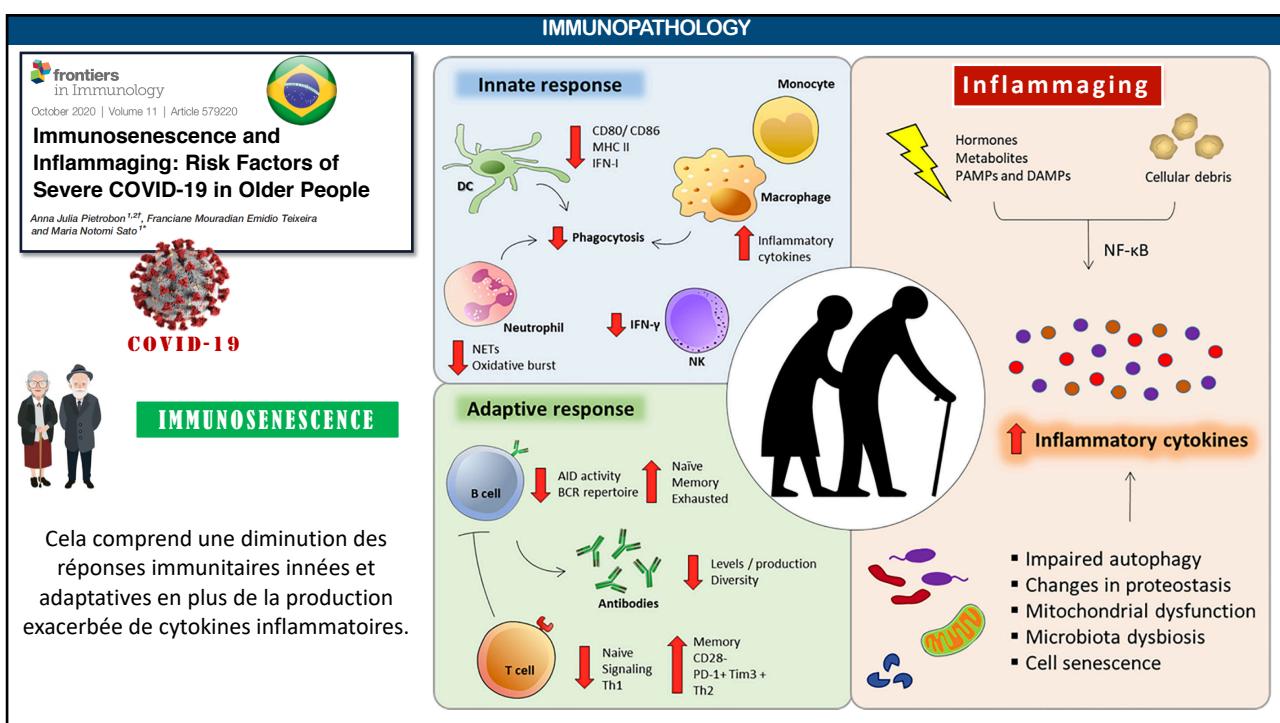
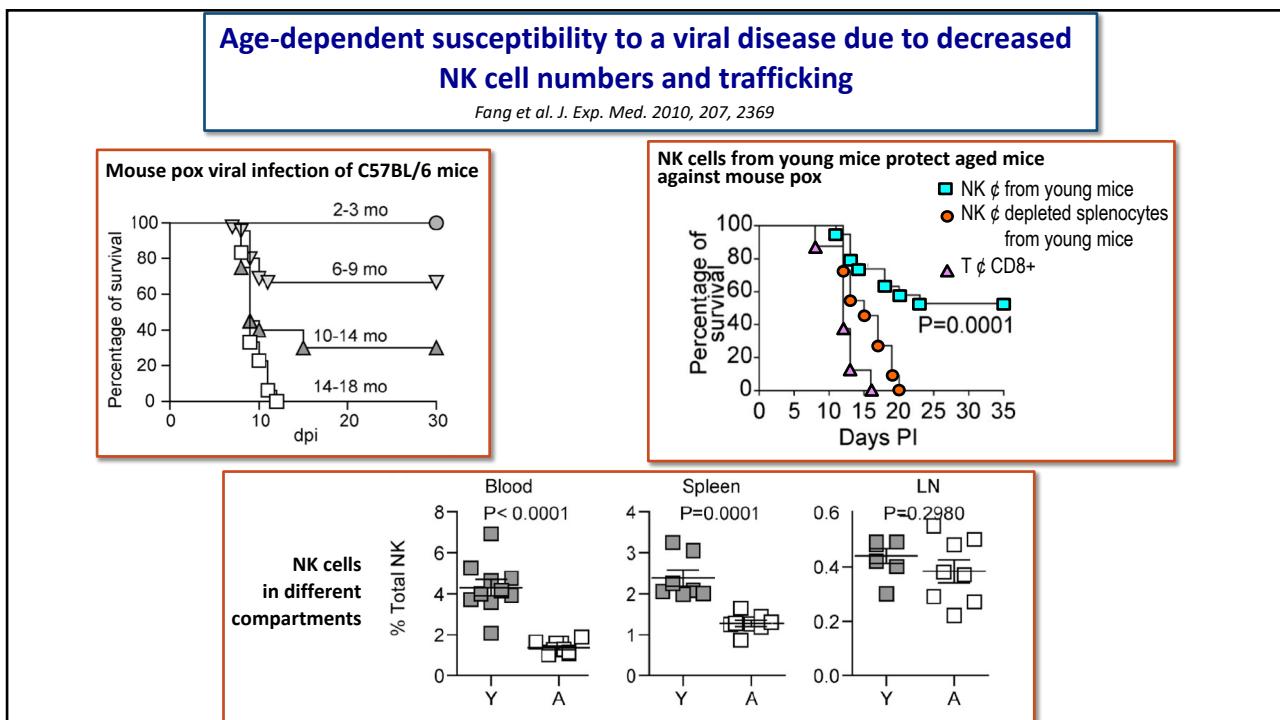
Avec l'âge, notre système immunitaire décline, entraînant une augmentation de l'incidence et de la gravité des infections et du cancer, et la vaccination devient moins efficace → **IMMUNOSENESCENCE**



Effect of ageing on mortality and cytokine production

Saito et al. *Mechan. Ageing Develop.* 2003, 124, 1047







HANS SELYE
(1907-1982)

1936

NATURE	JULY 4, 1936
A syndrome produced by diverse noxious agents	
HANS SELYE. McGill University, Montreal, Canada.	

STRESS IN HEALTH AND DISEASE
HANS SELYE

THE STRESS OF LIFE
Hans Selye, M.D.

The famous classic—
Completely revised,
expanded, and
updated with new
research findings

To fight or flight

HANS SELYE
STRESS WITHOUT DISTRESS

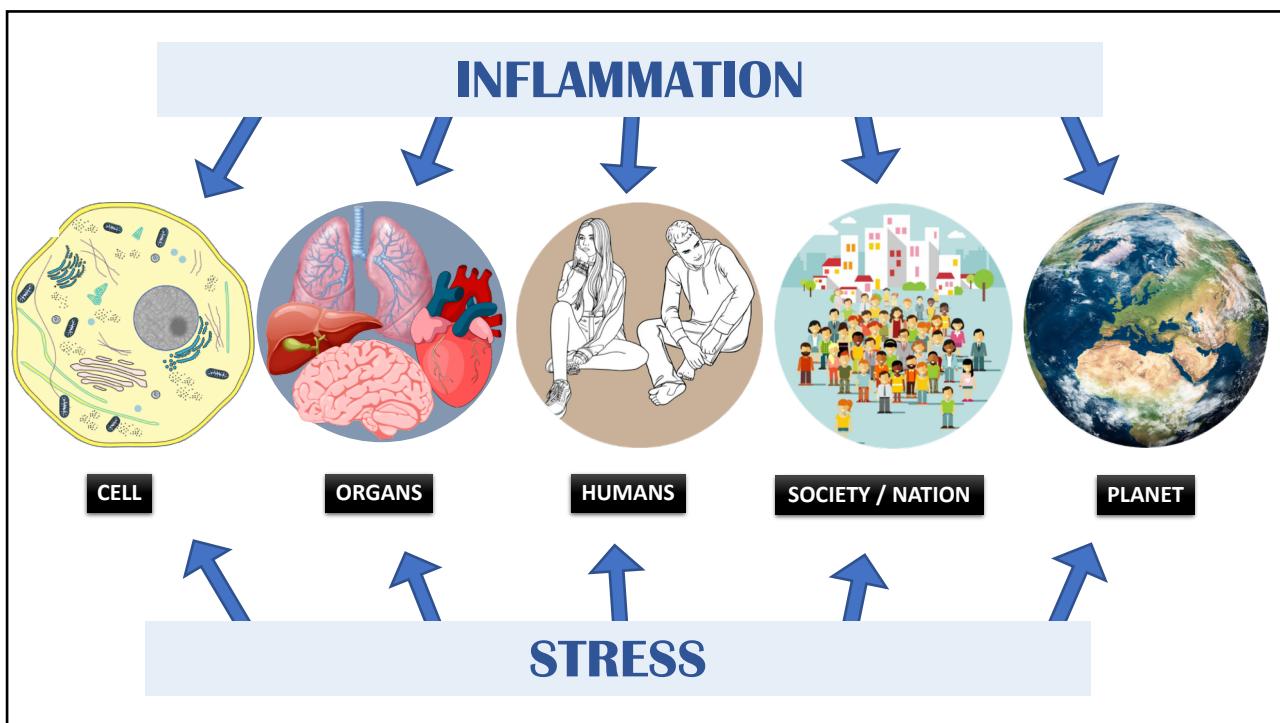
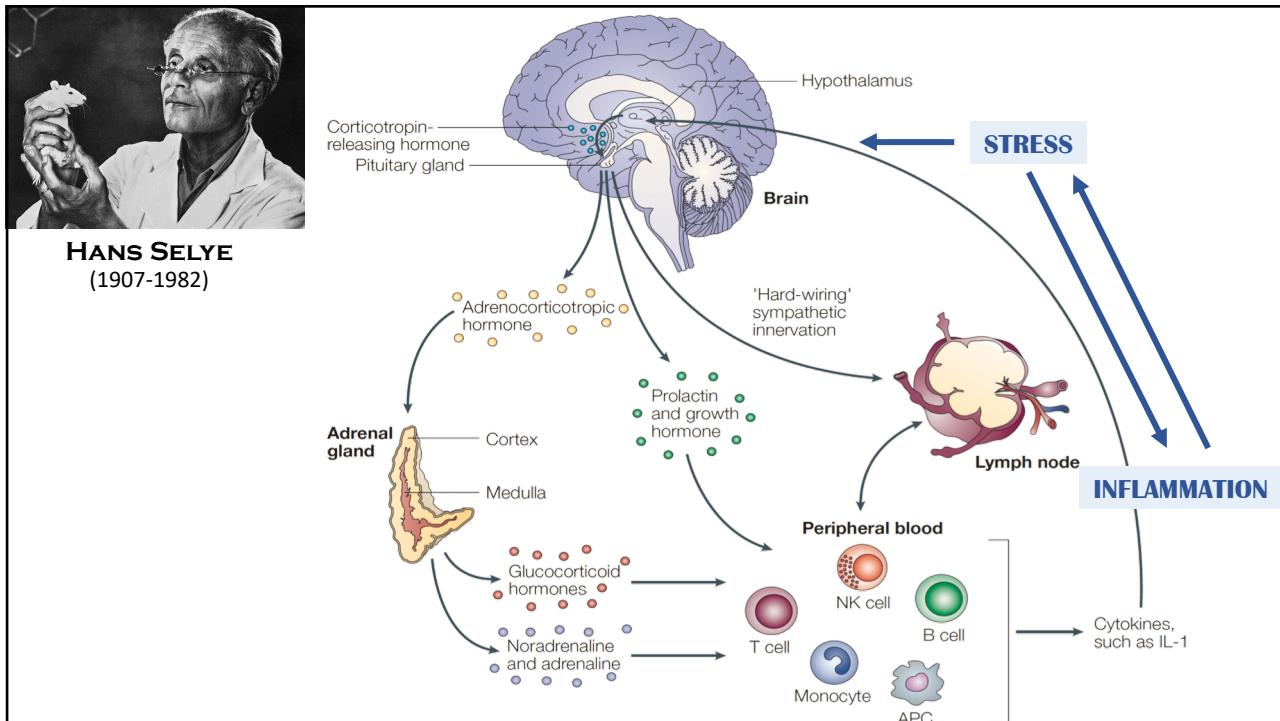
HOW TO USE STRESS AS
A POSITIVE FORCE TO ACHIEVE
A REWARDING LIFE STYLE.
“DR. HANS SELYE KNOWS MORE
ABOUT STRESS THAN ANY
OTHER SCIENTIST ALIVE.”
—Alan Weiss, author of Future Shock

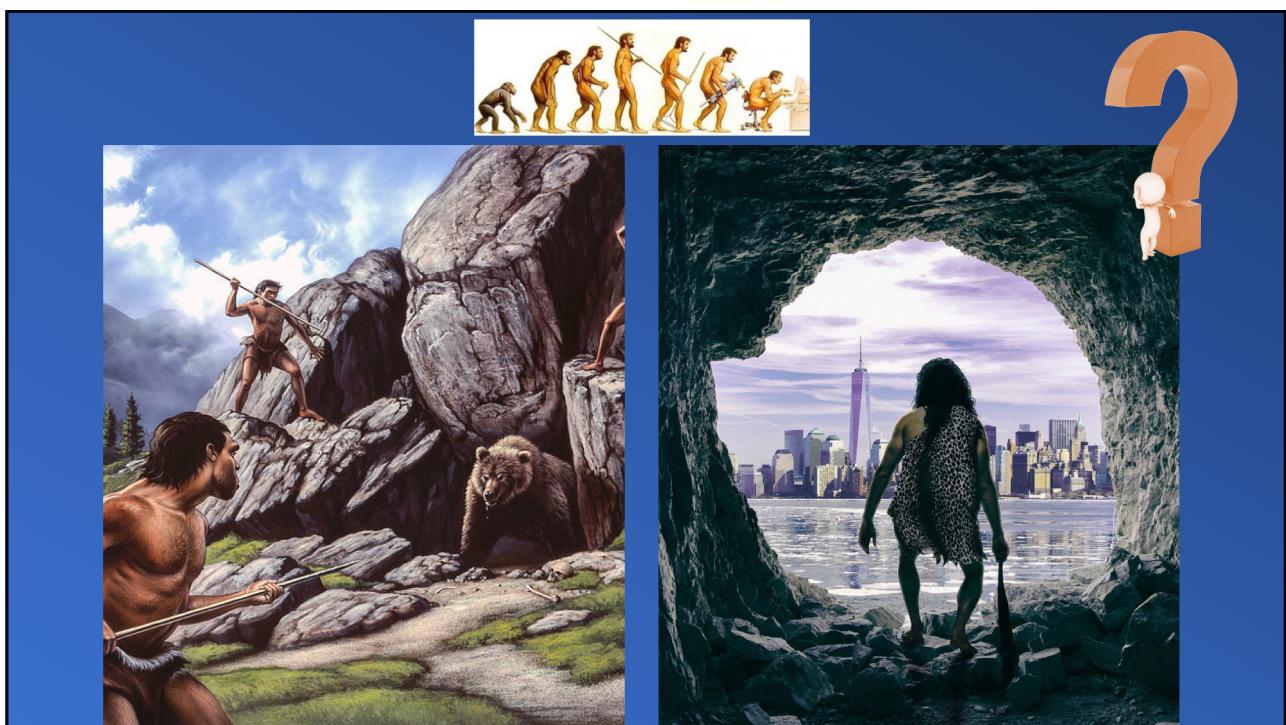
Distress vs Eustress

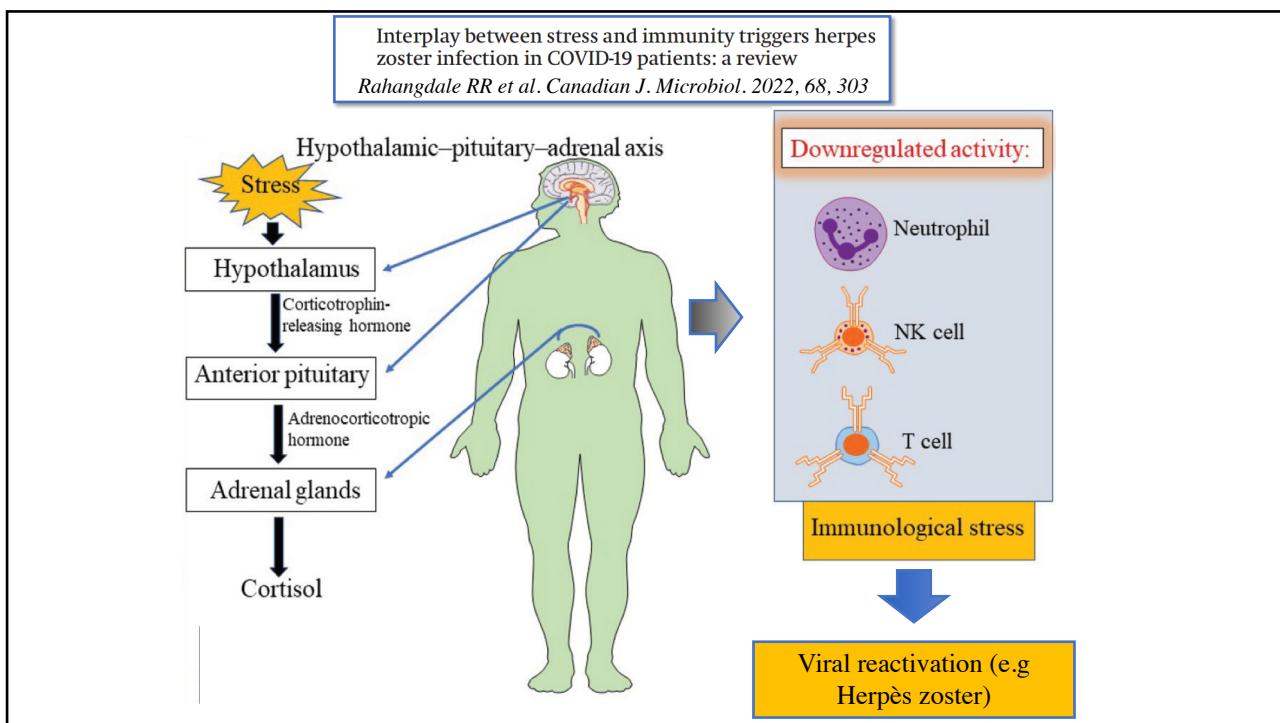
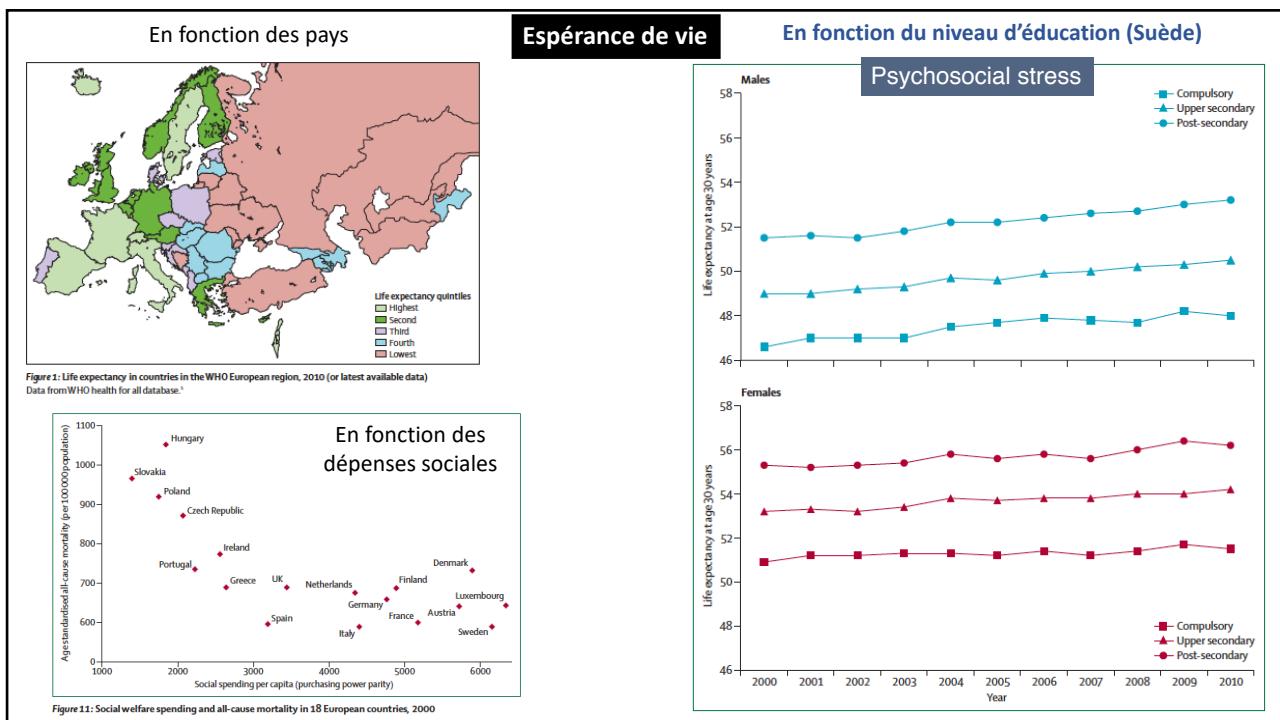
SELYE

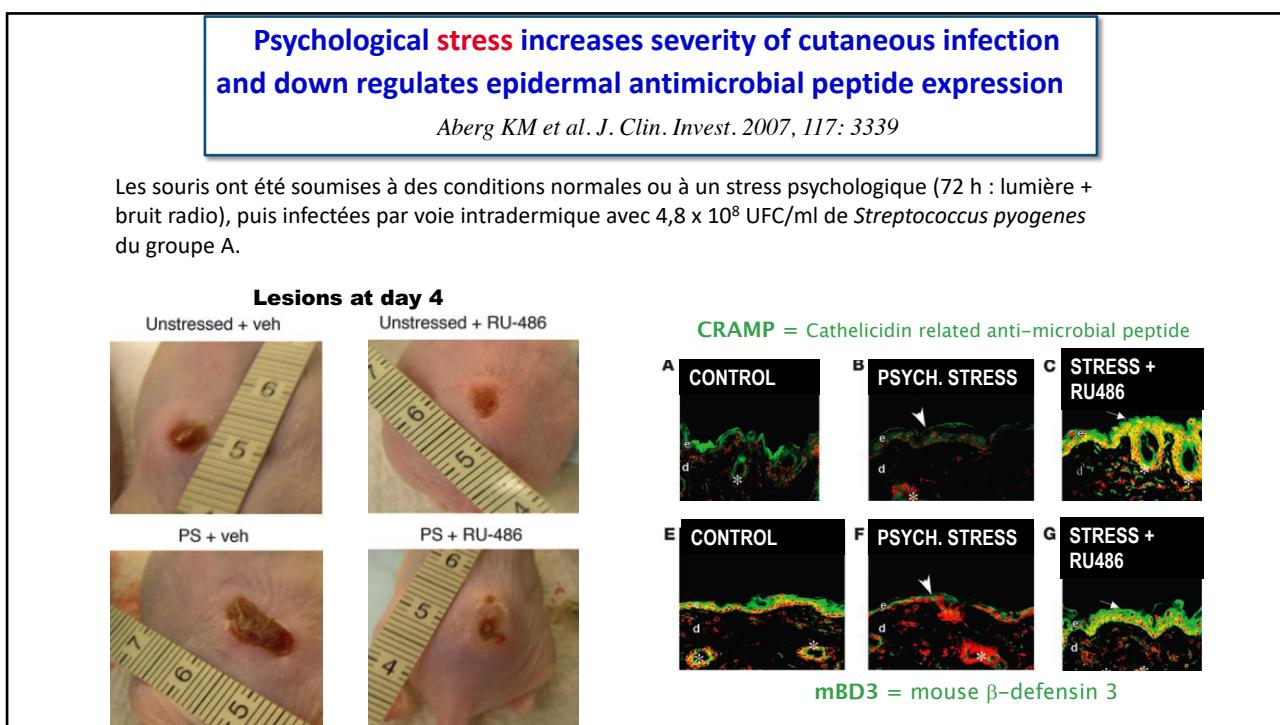
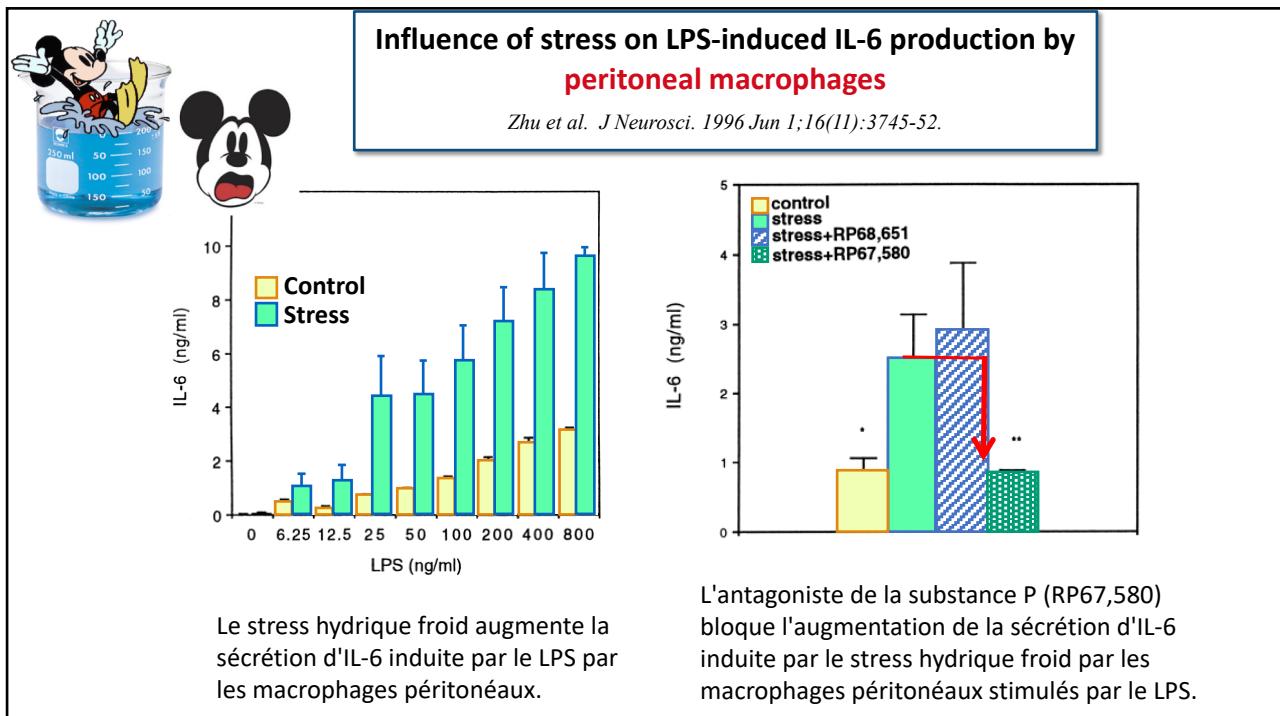
90 Ft MAGYARORSZAG 46

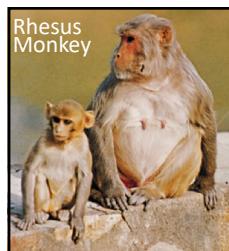
Canada 46











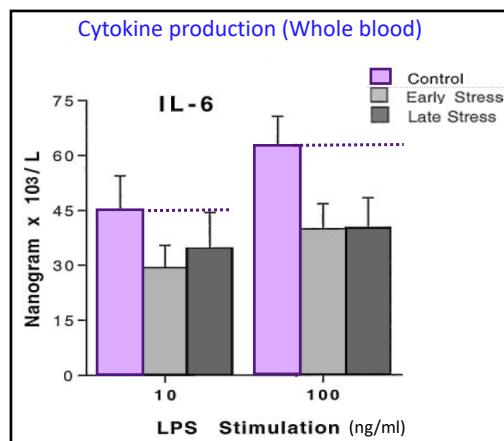
Stress during pregnancy (*in utero*)

Coe et al.
Pediatric Res. 2007, 61, 520
J. Clin. Endocrin. Metab. 2002, 87, 675



Early : 50 – 92 days pregnancy ; Late : 105 – 147 days pregnancy

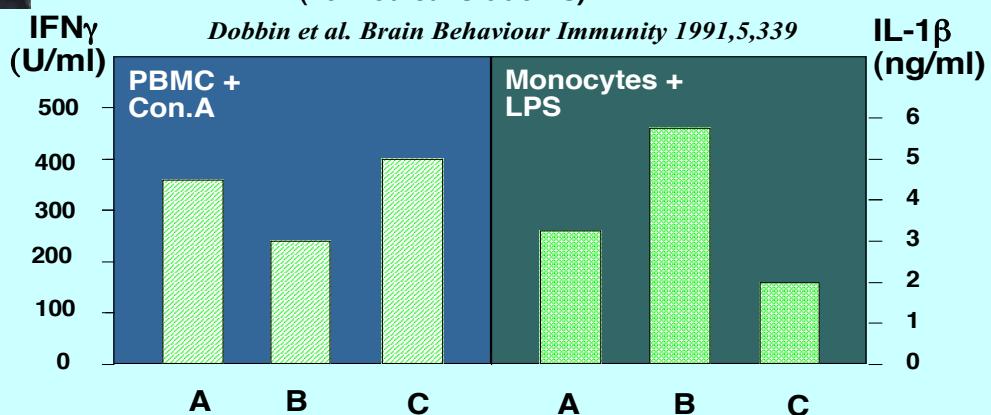
Expérience
pratiquée chez les jeunes
primates agés de 2 ans



Effect of stress on cytokine production

(29 Medical students)

Dobbin et al. Brain Behaviour Immunity 1991, 5, 339



A : No exam (4 week before / 4 week after)

B : just after a major written exam

C : 10 days after, and back from 7 days vacation

Am J Respir Crit Care Med Vol 178, pp 453–459, 2008

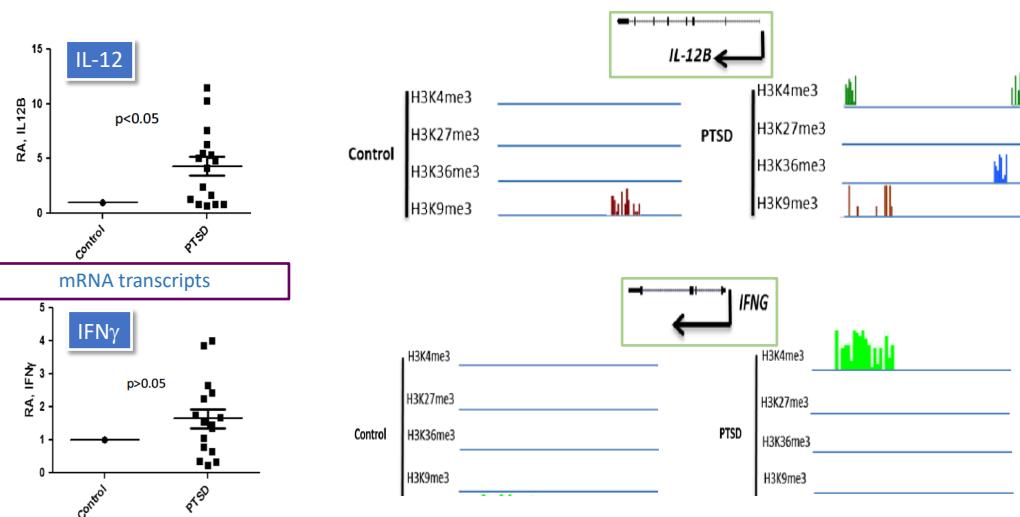
Violence, Abuse, and Asthma in Puerto Rican ChildrenRobyn T. Cohen^{1,2}, Glorisa J. Canino³, Hector R. Bird⁴, and Juan C. Celedón^{1,2,5}

PREDICTORS OF ASTHMA AND ALLERGY OUTCOMES	CURRENT ASTHMA	
	odds ratios (confidence intervals)	P values
Maternal history of asthma	2.98 (1.81–4.93)	<i>P</i> < 0.0001
Paternal history of asthma	2.28 (1.30–3.99)	<i>P</i> = 0.0045
Two or more stressful life events in past year	0.91 (0.61–1.35)	<i>P</i> = 0.6921
Witnessed neighborhood violence	1.16 (0.66–2.06)	<i>P</i> = 0.5988
Physical or sexual abuse	2.15 (1.07–4.36)	<i>P</i> = 0.0329

Evidence for epigenetic regulation of IL-12 and IFN γ in PBMC from post-traumatic stress disorder patients

Bam et al. J Neuroimmune Pharmacol. 2016 Mar;11(1):168–81.

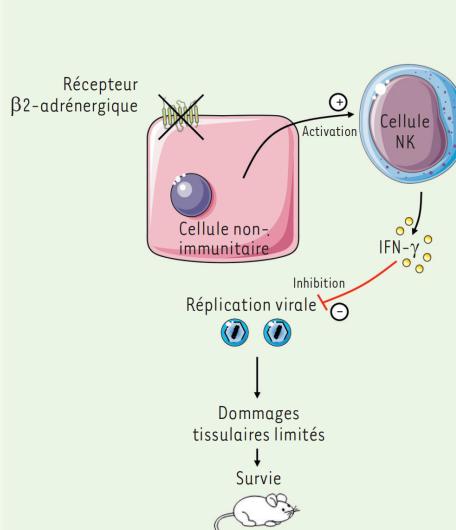
Persian Gulf war, or of the recent Iraq or Afghanistan wars, recruited from the local VA hospital (n=16) vs 17 controls



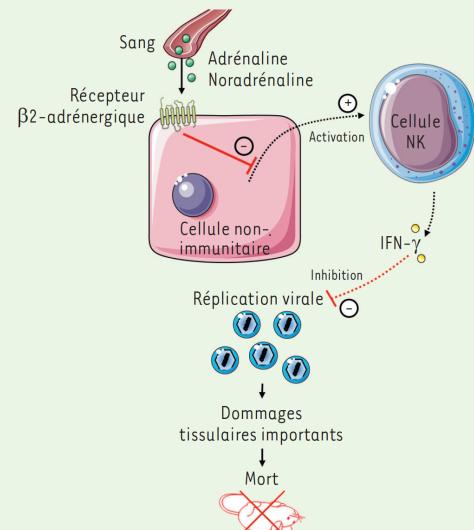
Des signaux adrénériques liés au stress affaiblissent les défenses immunitaires antivirales

Elisabeth Wieduwild, Clara Daher, Sophie Ugolini - Médecine / science novembre 2020, vol. 36, 993,

A Absence de signaux $\beta 2$ -adrénériques

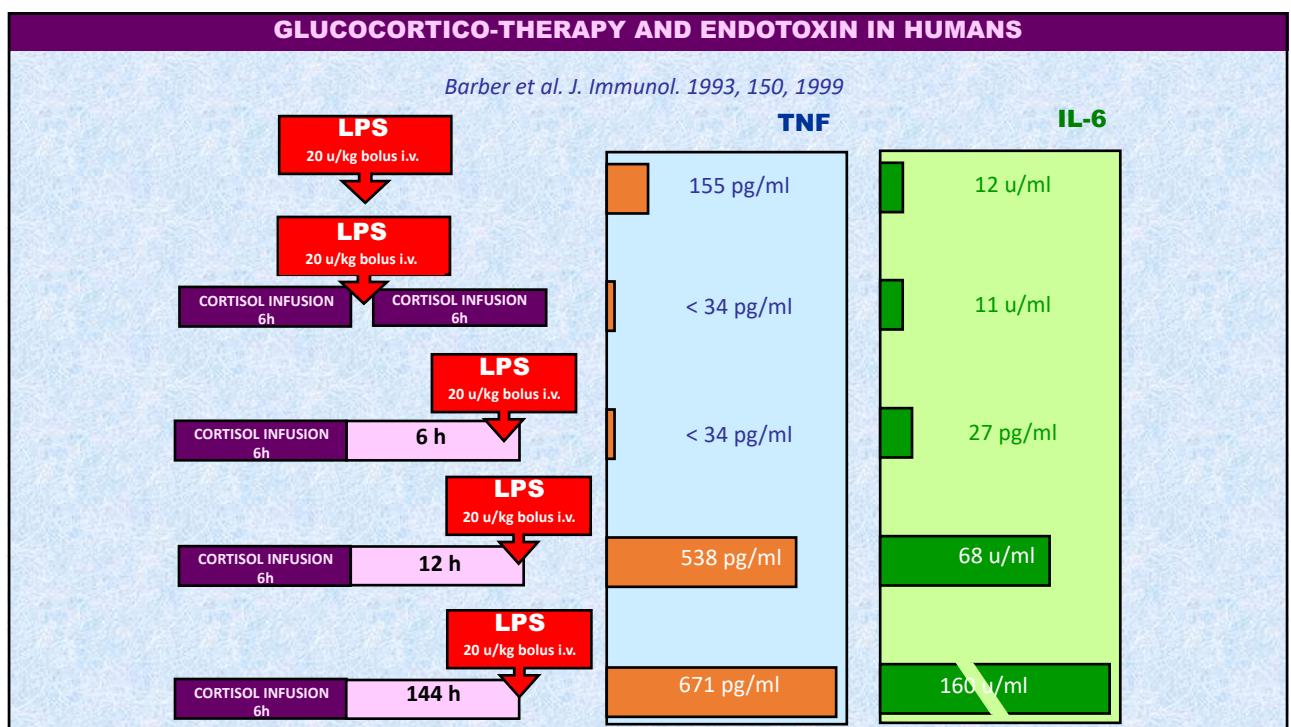
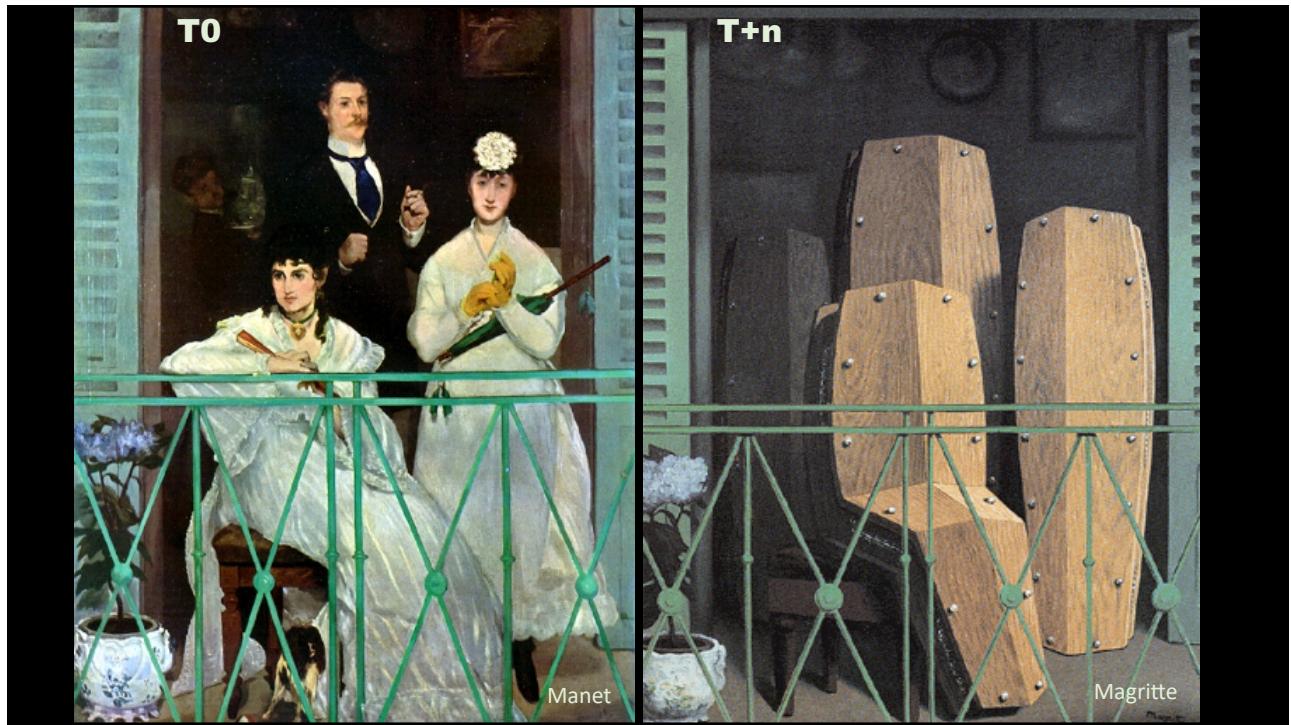


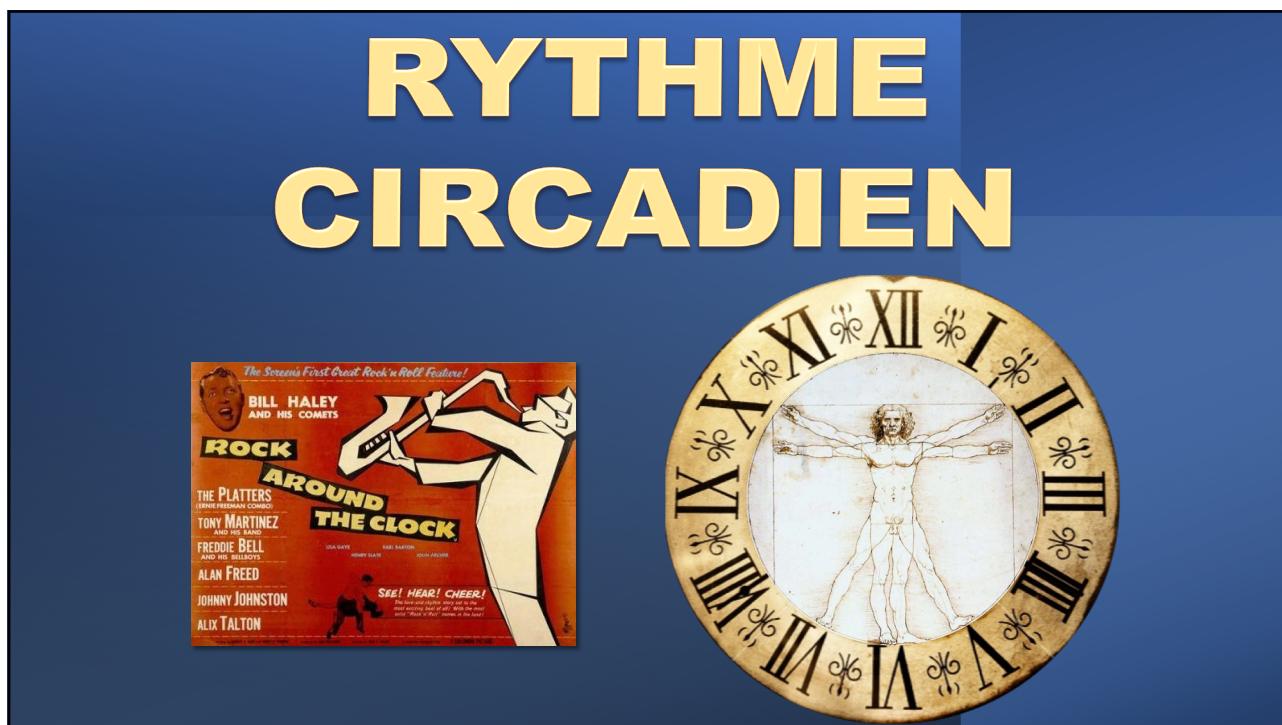
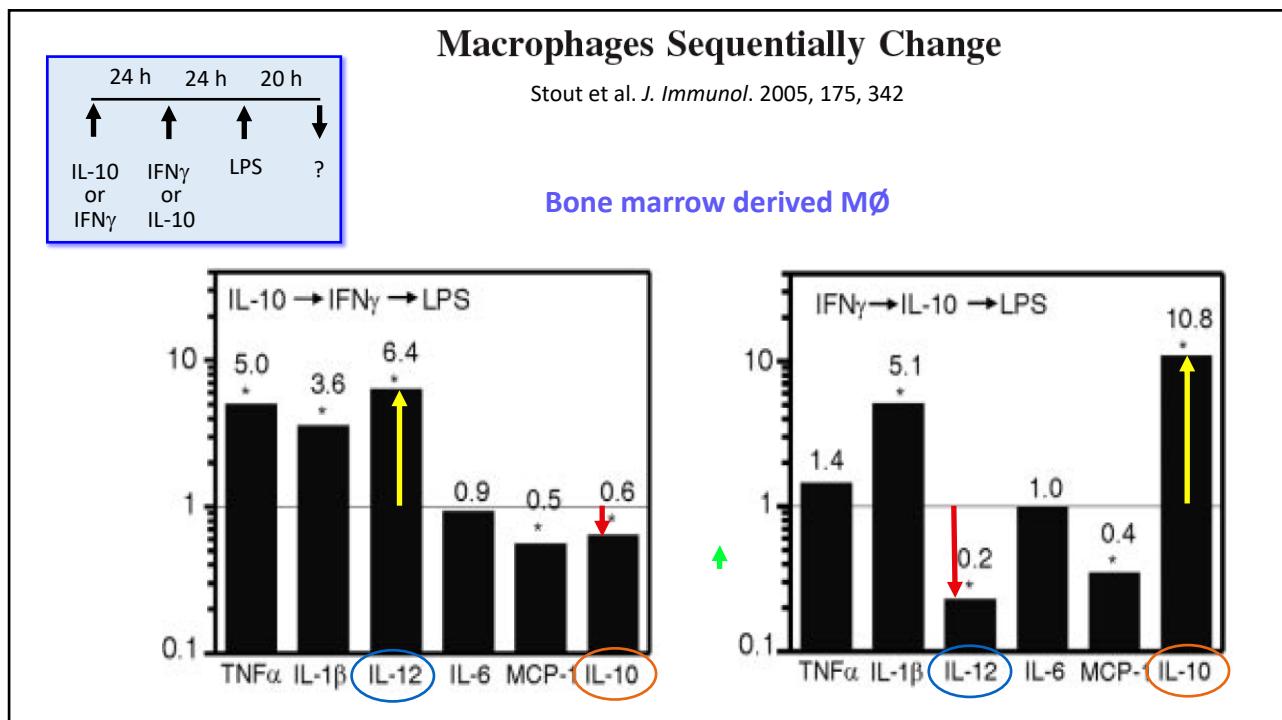
B Signaux $\beta 2$ -adrénériques – Stress

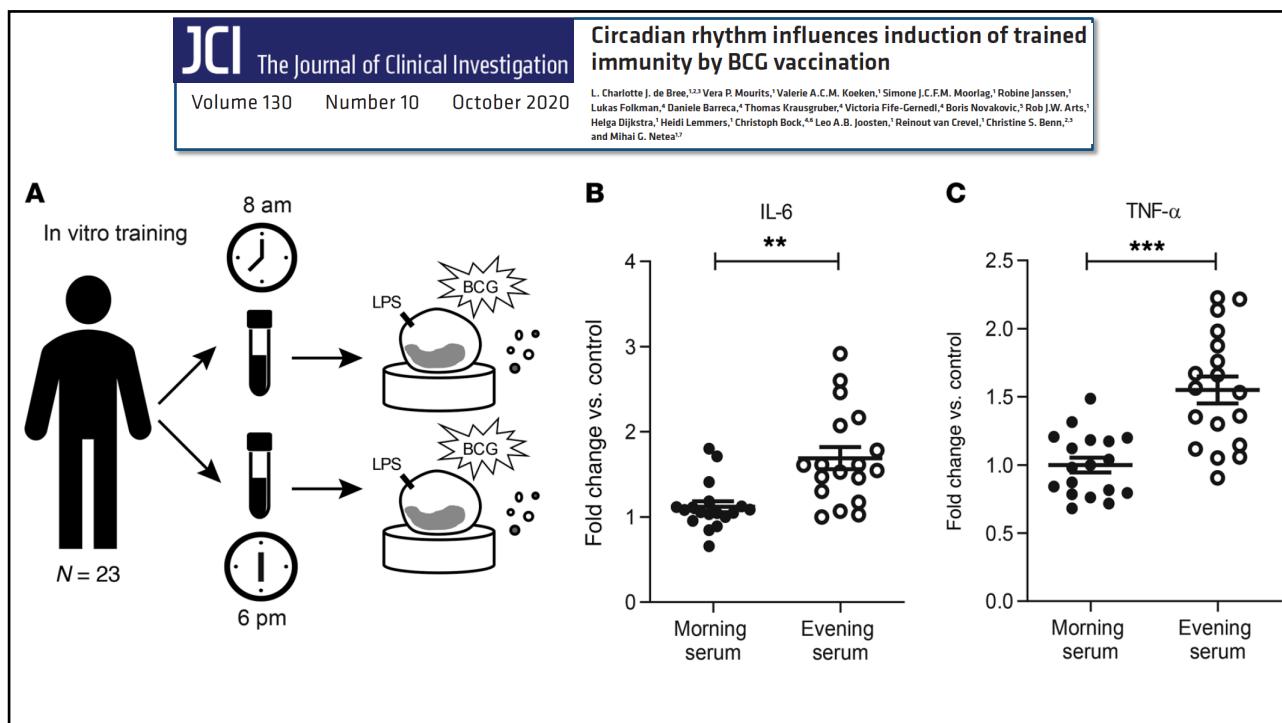
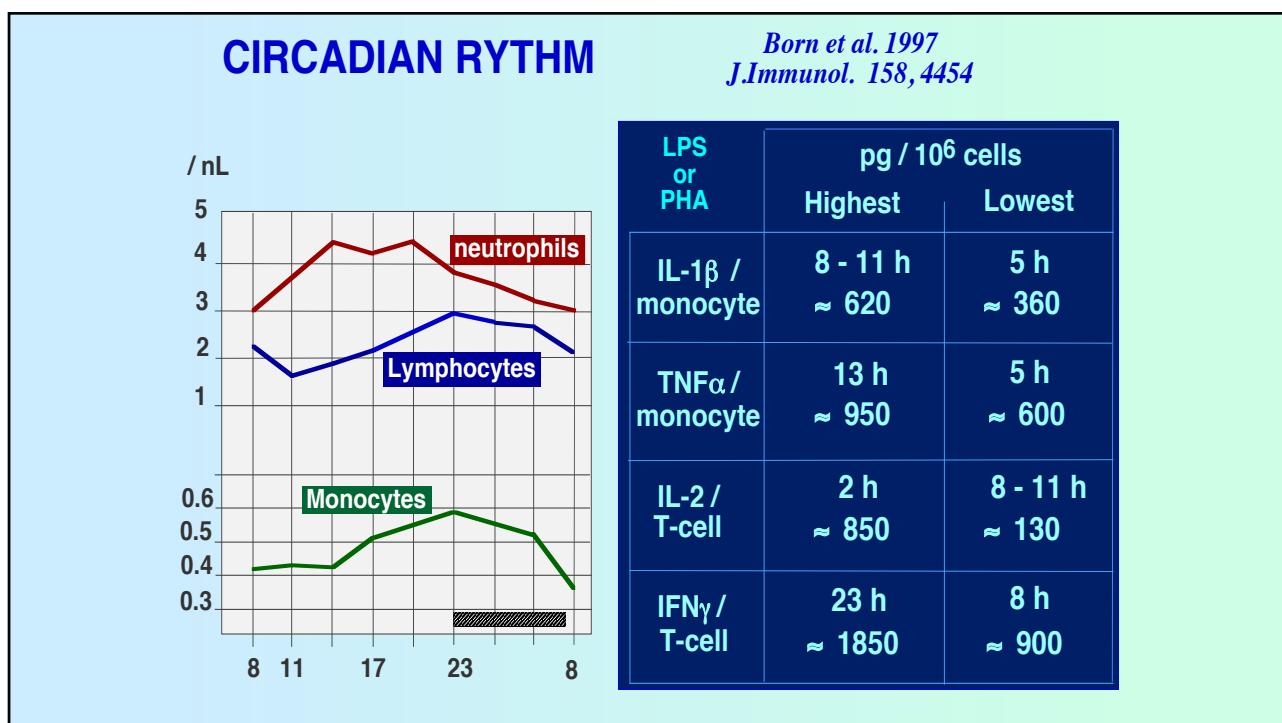


TIMING





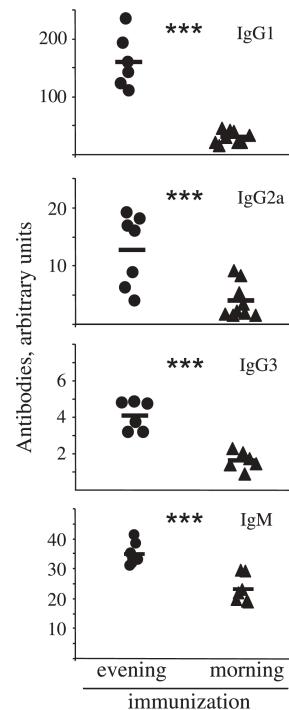
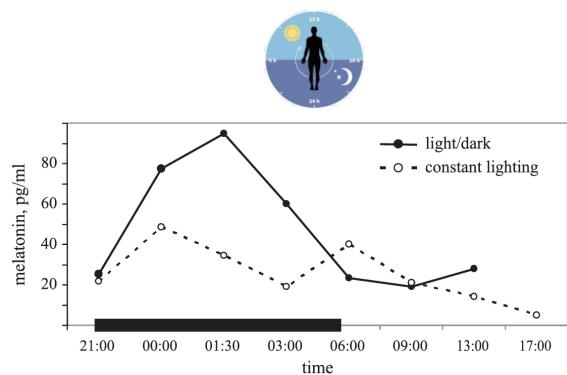




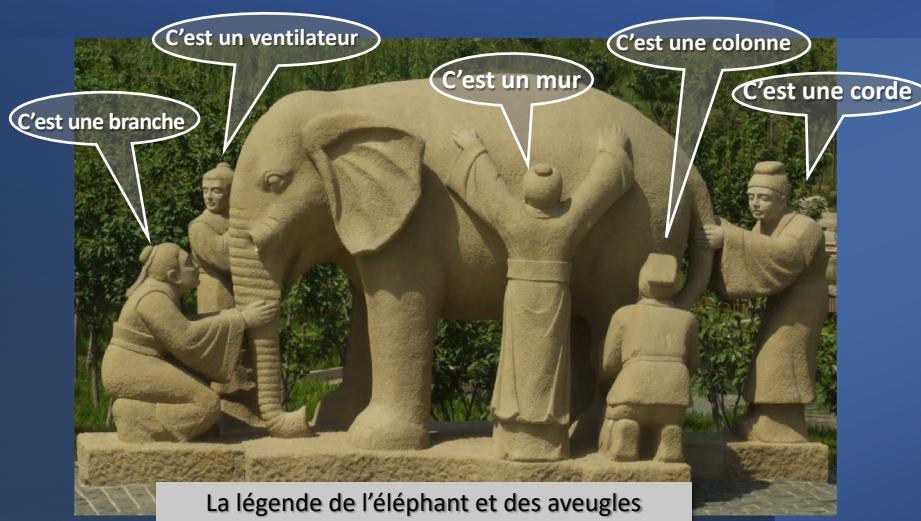
International Immunology, Vol. 22, No. 1, pp. 25–34 November 2009

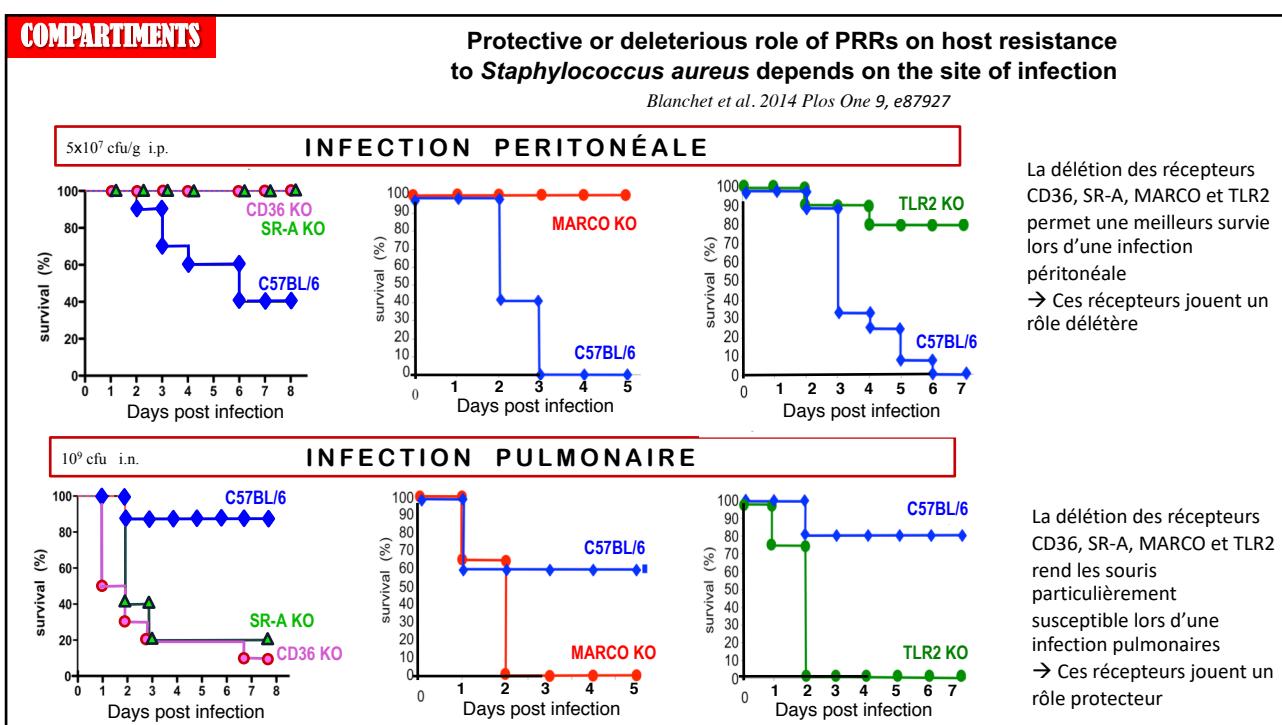
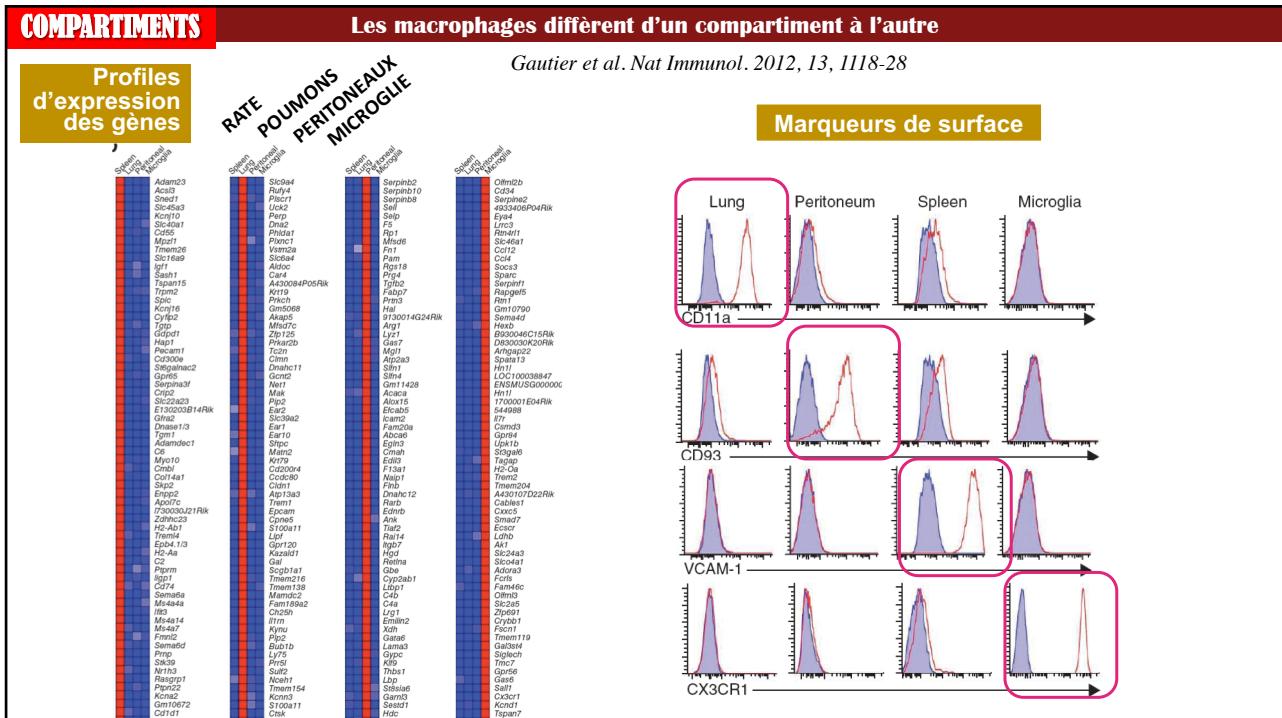
Regulation of T-cell-independent and T-cell-dependent antibody production by circadian rhythm and melatonin

Vitalij Černyšiov, Natalija Gerasimčik, Mykolas Mauricas and Irutė Girkontaitė



COMPARTIMENTS







Université Libre de Saint-Germain-en-Laye

Séminaires de Biologie 2023 -2024

Infection et Immunité



(2)

Les paramètres qui influencent l'étude du système immunitaire

MODÈLES *IN VITRO*



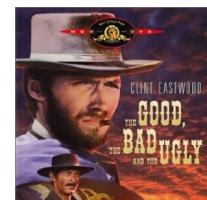
MODÈLES ANIMAUX



DOGMES



LES SCIENTIFIQUES



MODÈLES *IN VITRO* EXPERIMENTAUX

CULTURE MEDIUM



SERUM
(FETAL CALF, OTHERS...)

CULTURE ON PLASTIC





INFLUENCE DU SÉRUM

15 SEPTEMBER 2016 | VOL 537 | NATURE | 433



Les composés bioactifs présents dans le sérum fœtal bovin varient considérablement d'un lot à l'autre..

Components	Average (range)
Endotoxin	0.356 ng ml ⁻¹ (0.008–10.0)
Total protein	3.8 g dl ⁻¹ (3.2–7.0) 2 x
Alkaline phosphatase	255 mU ml ⁻¹ (111–352) 3 x
Lactic dehydrogenase	864 mU ml ⁻¹ (260–1,215) 5 x
Cortisol	0.5 µg dl ⁻¹ (<0.1–2.3) 23 x
Insulin	10 µU ml ⁻¹ (6–14) 2.3 x
Parathyroid hormone	1,718 pg ml ⁻¹ (85–6,180) 73 x
Progesterone	8 ng dl ⁻¹ (<0.3–36) 120 x
Testosterone	40 ng dl ⁻¹ (21–99) 5 x
Prostaglandin E	5.91 ng ml ⁻¹ (0.5–30.5) 61 x
TSH	1.22 ng ml ⁻¹ (<0.2–4.5) 23 x
FSH	9.5 ng ml ⁻¹ (<2–33.8) 17 x
Growth hormone	39.0 ng ml ⁻¹ (18.7–51.6) 3 x
Prolactin	17.6 ng ml ⁻¹ (2.00–49.55) 25 x

TSH, thyroid stimulating hormone; FSH, follicle stimulating hormone

INFLUENCE DU SÉRUM ... SUR LA MORPHOLOGIE DES MACROPHAGES

Azeredo Miranda Mota et al Mem Inst Oswaldo Cruz, Rio de Janeiro: 1-8, 2014

Les macrophages péritonéaux cultivés avec 2 % de sérum de souris (MS) ont une apparence morphologique différente, un nombre plus élevé d'organites ressemblant à des vésicules et des surfaces plus grandes par rapport aux MØ cultivés dans 2 % de sérum de veau fétal (SVF).

INFLUENCE DU SÉRUM ... SUR LA PRODUCTION DE CYTOKINES PAR LES MACROPHAGES

Warren et al. J. Infect. Dis. 2010, 201, 223

Effet de 10% de sérum sur la production de cytokines par des macrophages de souris en réponse au LPS (20 ng/puits)

Sérum de veau foetal Sérum de souris

Cytokine	MØ dérivés de la moelle osseuse (Sérum de veau foetal)	MØ péritonéaux (Sérum de veau foetal)	MØ dérivés de la moelle osseuse (Sérum de souris)	MØ péritonéaux (Sérum de souris)
TNF	~3300 pg/ml	~5700 pg/ml	~800 pg/ml	~1100 pg/ml
IL-6	~4400 pg/ml	~2200 pg/ml	~600 pg/ml	~1000 pg/ml
IL-10	~1800 pg/ml	~2200 pg/ml	~600 pg/ml	~1200 pg/ml

MONOCYTES HUMAINS

TNF (pg/ml)

LPS (ng/ml)

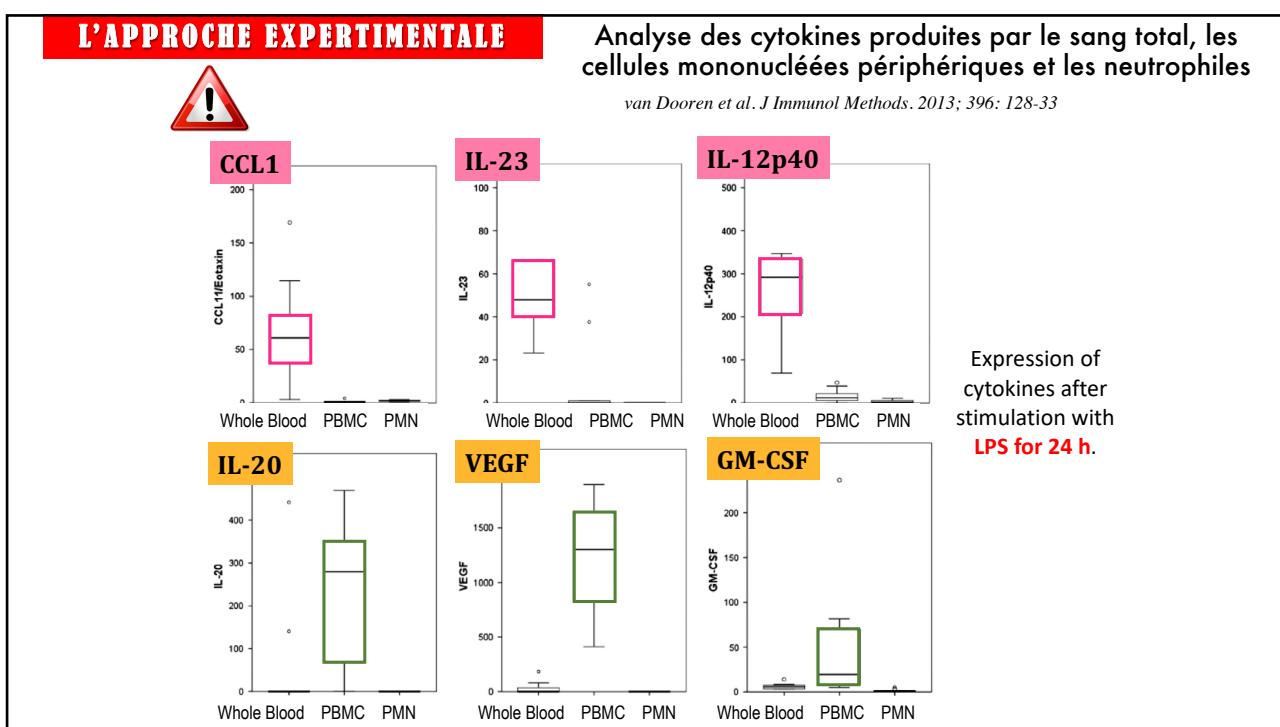
INFLUENCE DU MILIEU DE CULTURE

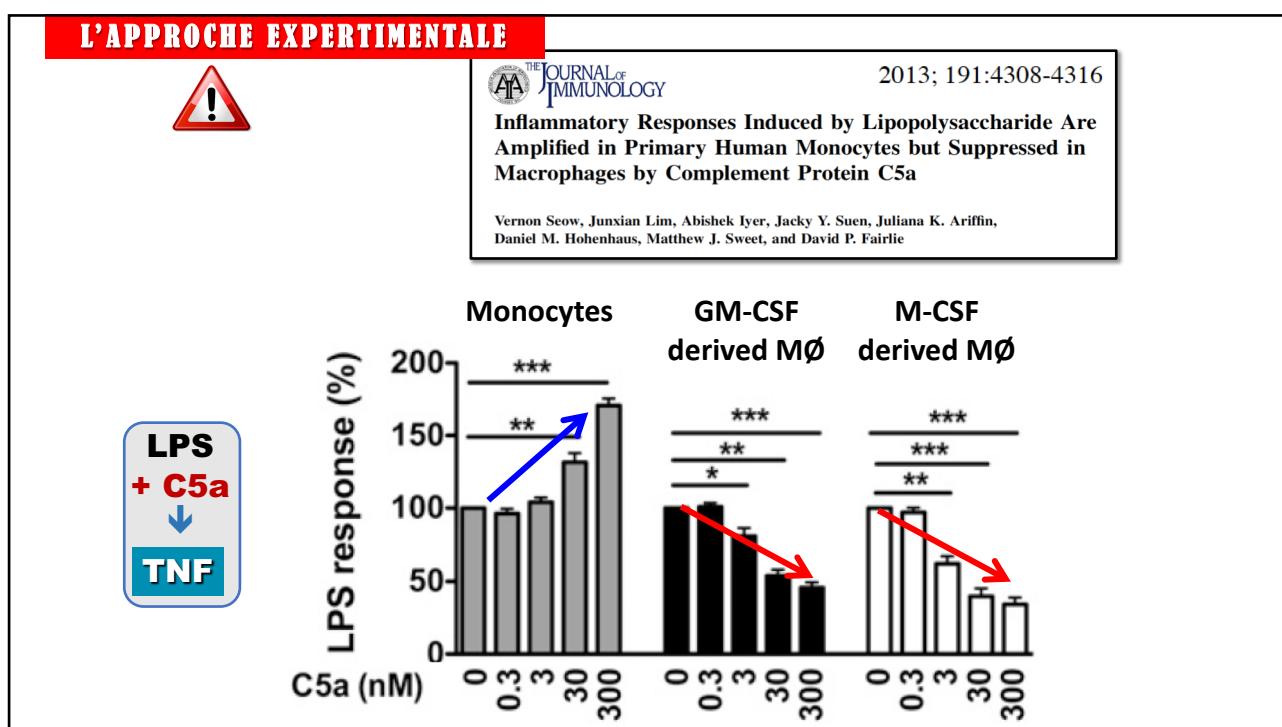
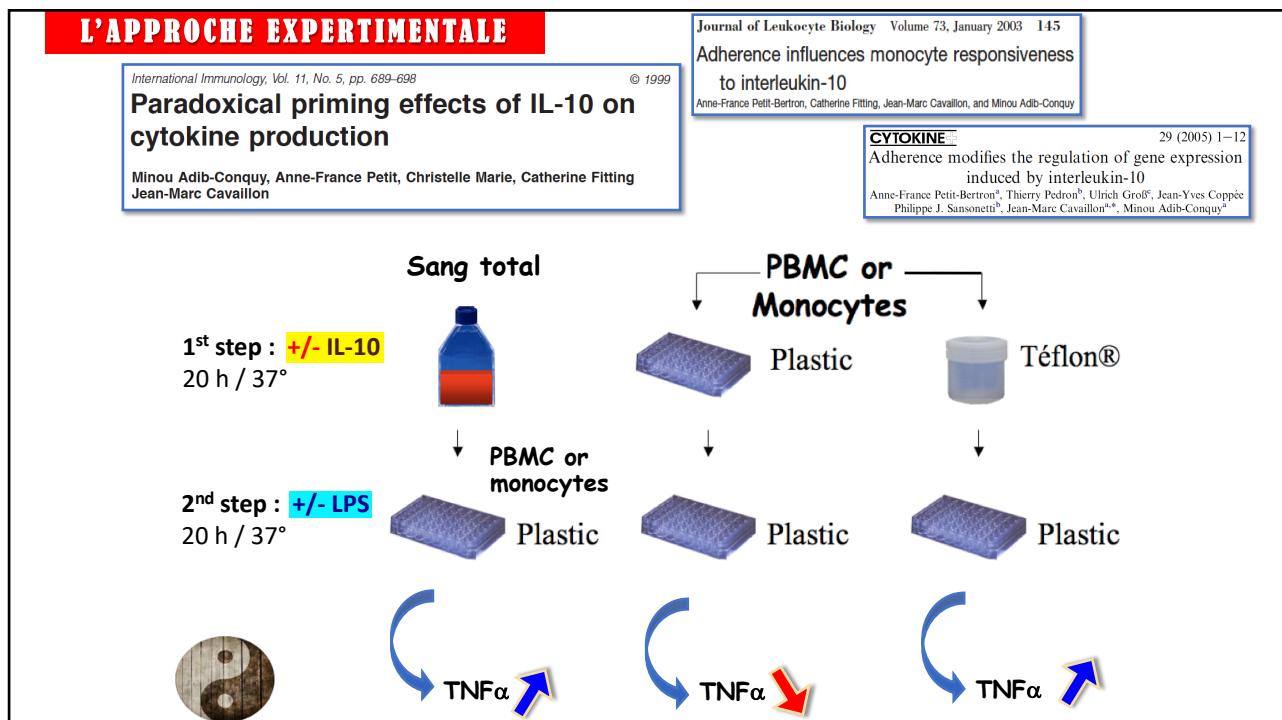
Le milieu de culture reflète-t-il l'environnement local des cellules étudiées ?

Le foie exprime une activité arginase élevée
→ La concentration en arginine est négligeable

	ARGININE	1200 µmol/L	10 µmol/L
Kupffer cells + LPS	TNF	+++	±
	PGE ₂	±	+++

Callery et al. *Surgery* 1991, 110, 221





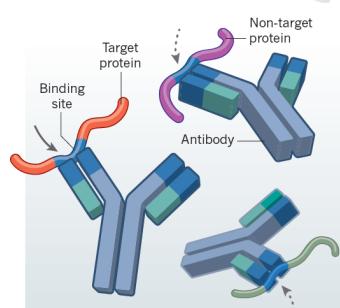
MAUVAIS ANTICORPS

274 | NATURE | VOL 521 | 21 MAY 2015

BLAME IT ON THE ANTIBODIES

Antibodies are the workhorses of biological experiments, but they are littering the field with false findings. A few evangelists are pushing for change.

BY NICK DAVIS

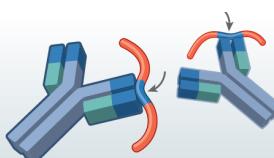


CROSS-REACTIVITY

Problem: An antibody is supposed to recognize only its target protein, but sometimes binds to others, depending on the proteins present in a sample.

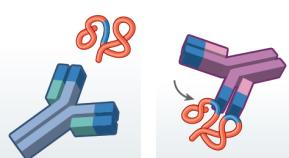
BAD ANTIBODIES

The most common problems with antibodies and how to avoid them.



VARIABILITY

Problem: Separate batches of antibody can perform differently. This happens most often when the antibody is produced from a new set of animals.



WRONG APPLICATION

Problem: Different experiments and experimental conditions can change a protein's folding and therefore its binding ability.

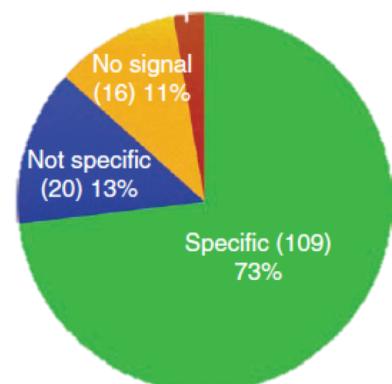
MAUVAIS ANTICORPS

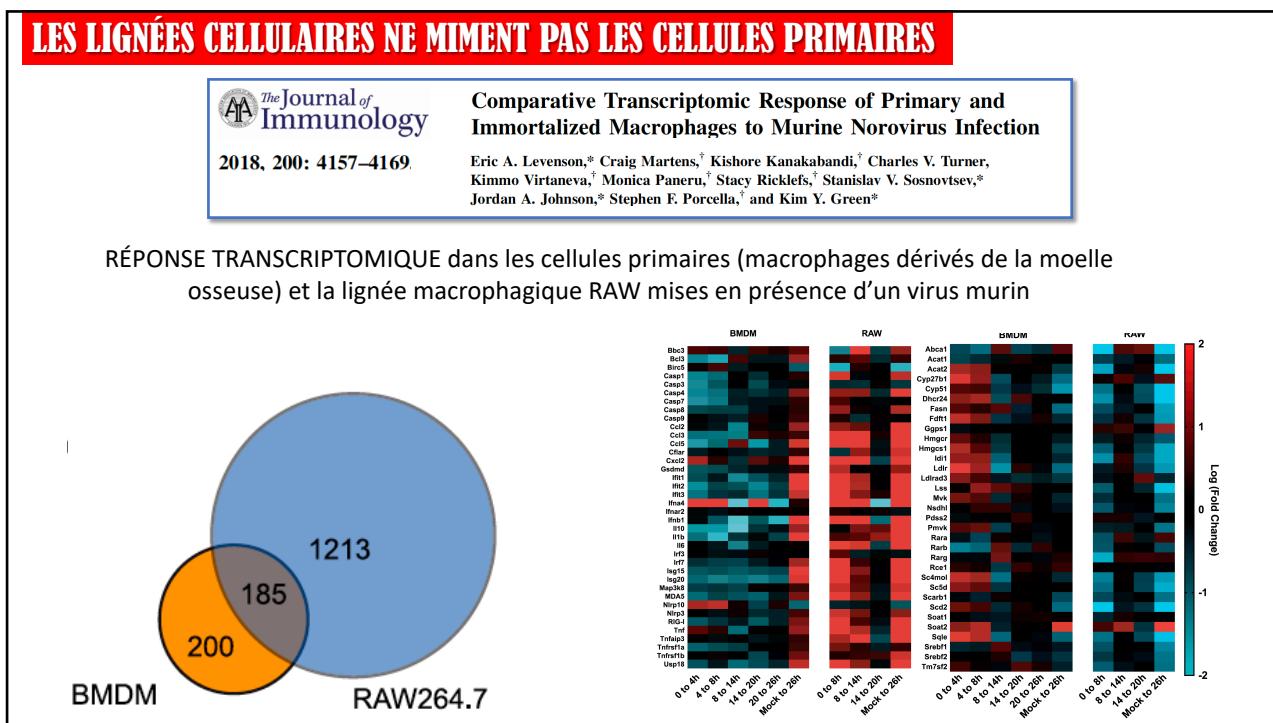
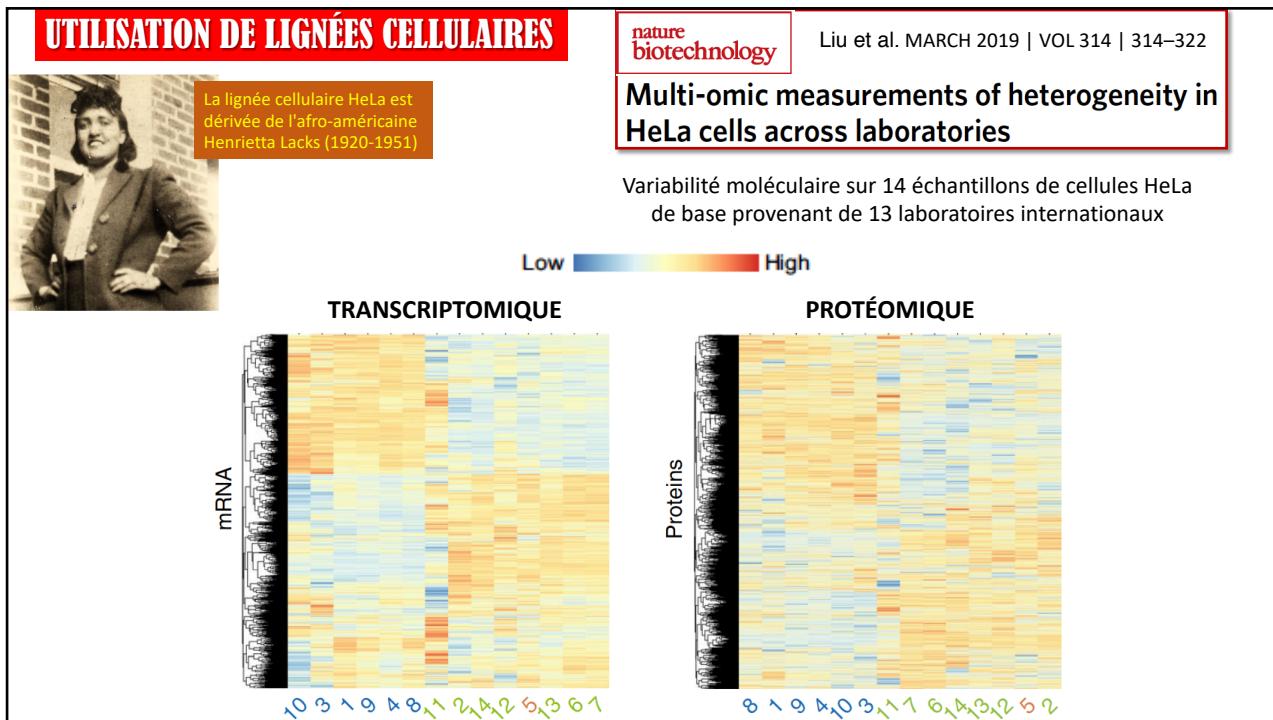
NATURE STRUCTURAL & MOLECULAR BIOLOGY VOLUME 18 NUMBER 1 JANUARY 2011
An assessment of histone-modification antibody quality

Thea A Egelhofer^{1,16}, Aki Minoda^{2,3,16}, Sarit Klugman^{4,5,16}, Kyungjoon Lee⁶, Paulina Kolasinska-Zwierz^{7,8}, Artyom A Alekseyenko^{9,10}, Ming-Sin Cheung^{7,8}, Daniel S Day⁶, Sarah Gadel¹¹, Andrey A Gorchakov^{9,10}, Tingting Gu¹¹, Peter V Kharchenko⁶, Samantha Kuan^{4,5}, Isabel Latorre^{7,8}, Daniela Linder-Basso¹², Ying Luu^{4,5}, Queminh Ngo^{4,5}, Marc Perry¹³, Andreas Rechtsteiner¹, Nicole C Riddle¹¹, Yuri B Schwartz¹², Gregory A Shanower¹², Anne Vielle^{7,8}, Julie Ahringer^{7,8}, Sarah C R Elgin¹¹, Mitzi I Kuroda^{9,10}, Vincenzo Pirrotta¹, Bing Ren^{4,5}, Susan Strome¹, Peter J Park⁶, Gary H Karpen^{2,3}, R David Hawkins^{4,5} & Jason D Lieb^{14,15}

Low

Une évaluation de 246 anticorps utilisés dans des études épigénétiques a révélé qu'un quart d'entre eux échouaient aux tests de spécificité, ce qui signifie qu'ils se liaient souvent à plus d'une cible. Quatre anticorps étaient parfaitement spécifiques – mais contre la mauvaise cible !!!







Des endotoxines sont présentes dans l'environnement, les produits naturels et utilisés *in vivo*

Air and environment	Natural products	Drugs
Poultry housing dust PMID: 22029777 Swine confinements PMID: 23293050 Cotton industry PMID: 17341727 Rice production PMID: 6492187 Agricultural industries PMID: 16395461 Livestock farming PMID: 24280684 Cheese factories PMID: 24812257 Home and offices PMID: 34738178 Cockroach feces PMID: 28106812 Sewage treatment plants PMID: 34678984 Waste water treatment plants PMID: 7992797 Hay dust PMID: 1925440 Humidifiers PMID: 33251102	Allergens PMID: 1702943 Medicinal herbs PMID: 33132322 Raw or farm milk PMID: 2745822 Infant formula milk powder PMID: 33922125	Antibiotics PMID: 7380997 Bacteriophage therapy PMID: 15213806 Radiopharmaceutical preparations PMID: 23696179
	Medical devices	Vaccines
	Surgical gloves PMID: 1976681 Surgical instrument PMID: 16928962 Microelectrode PMID: 24778808 Wound dressings PMID: 12808594 Titanium implant PMID: 12500875 Prosthetic material PMID: 11922375 Sterile catheters PMID: 7380997 Intravenous solution PMID: 16807850	BCG PMID: 13641561 Influenza virus PMID: 893659 Mumps vaccine PMID: 321714 Tetanus toxoid PMID: 321714 Veterinary vaccines PMID: 29935930
Water	Other media	Others
Drinking water PMID: 12224557 Hemodialysis fluid PMID: 25641063 Marine bath water PMID: 24642437	Contact lenses and solutions PMID: 1463420 Radiographic contrast media PMID: 552831	Feed additives for livestock PMID: 26768246 Animal diet PMID: 28052076 Electronic cigarette PMID: 31017484 Cigarette smoke PMID: 17852769

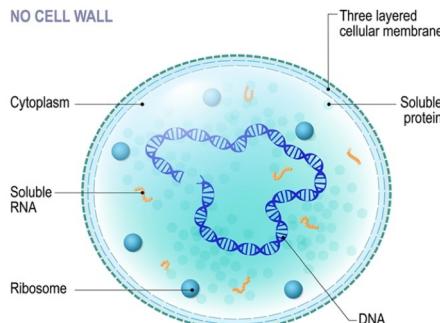
Bonhomme D, Cavaillon J-M, Werts C. *J.Biol.Chem.* 2024

Des molécules utilisées dans des études *in vitro* sont contaminés par des endotoxines

Purified proteins	Culture medium	Mitogens
Ovalbumin PMID: 7039979 Allergens PMID: 18771487 Bovine serum albumin PMID: 5924502 Human albumin PMID: 4584590 Hemoglobin PMID: 8041288 β -lactoglobulin PMID: 14657886 Human gamma globulin PMID: 4100051 Antibodies PMID: 9407503 Human placental G-CSF PMID: 6985122 Apolipoproteins A-I PMID: 25778625 Alpha-lactalbumin PMID: 20600530 Monoclonal antibodies PMID: 3112017 Tetanus toxoid PMID: 321714	Culture media PMID: 699956 Fetal calf serum PMID: 9439764 Collagen PMID: 969286 Gelatin PMID: 36476713 Ficoll PMID: 9930943 Medium for cell isolation PMID: 10458490 Culture medium for human <i>in vitro</i> fertilization PMID: 3732534	Pokeweed mitogen PMID: 16522770 Concanavalin A PMID: 1151067 Lipoteichoic acid PMID: 11159964 Phytohemagglutinin PMID: 321714 PPD of the tubercle bacillus PMID: 321714
Recombinant proteins	Water	Nucleic acids
Heat shock proteins PMID: 12516564 Erythropoietin PMID: 444662 Plasminogen kringle 5 PMID: 14579737 SARS-CoV-2 Spike PMID: 35015170 Human growth hormone PMID: 6386853 Adiponectin PMID: 22374965 C-reactive protein (CRP) PMID: 16254214 Cytokines PMID: 827473 Osteopontin PMID: 15871665	Distilled water PMID: 36554408 Osmosis water PMID: 36554408	RNA PMID: 33194561 Poly (I:C) PMID: 31415868 Plasmid PMID: 7779915 DNA PMID: 8717385 Ribosomal preparation PMID: 7325439
Natural products	Sugars	Enzymes
	Natural plant products PMID: 33132322 Glutathione PMID: 29673413 Alginate PMID: 16265647 Chitosan PMID: 37050208 Cotton PMID: 16722191 Pollen PMID: 23238878	CRISPR-Cas9 PMID: 34744169 Pancreatic elastase PMID: 15879145 Collagenase PMID: 9930943 Enzyme conjugates PMID: 6348074 Trypsin PMID: 17910052 Lysozyme PMID: 10656326 Superoxide dismutase and catalase PMID: 15251190
	3'-Sialyllactose PMID: 29281012 Hyaluronan PMID: 27061945 Cane sugar PMID: 526016 Heparin PMID: 23586950	



Mycoplasma

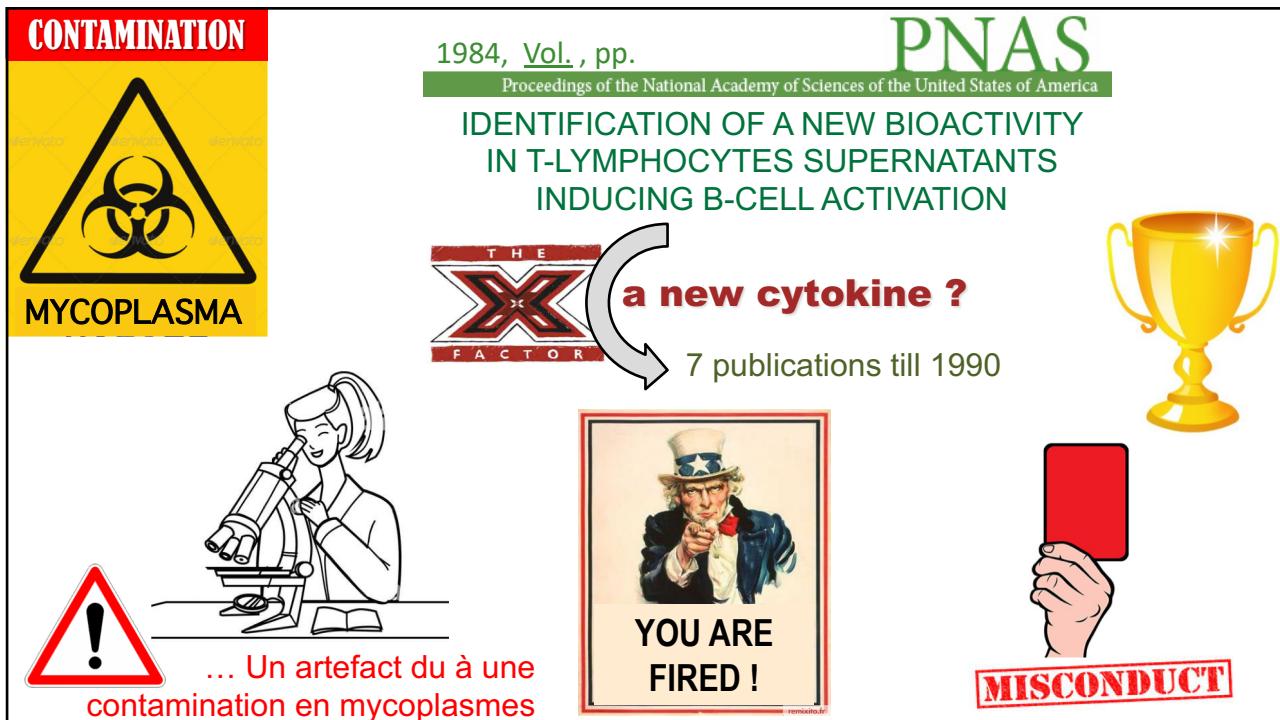


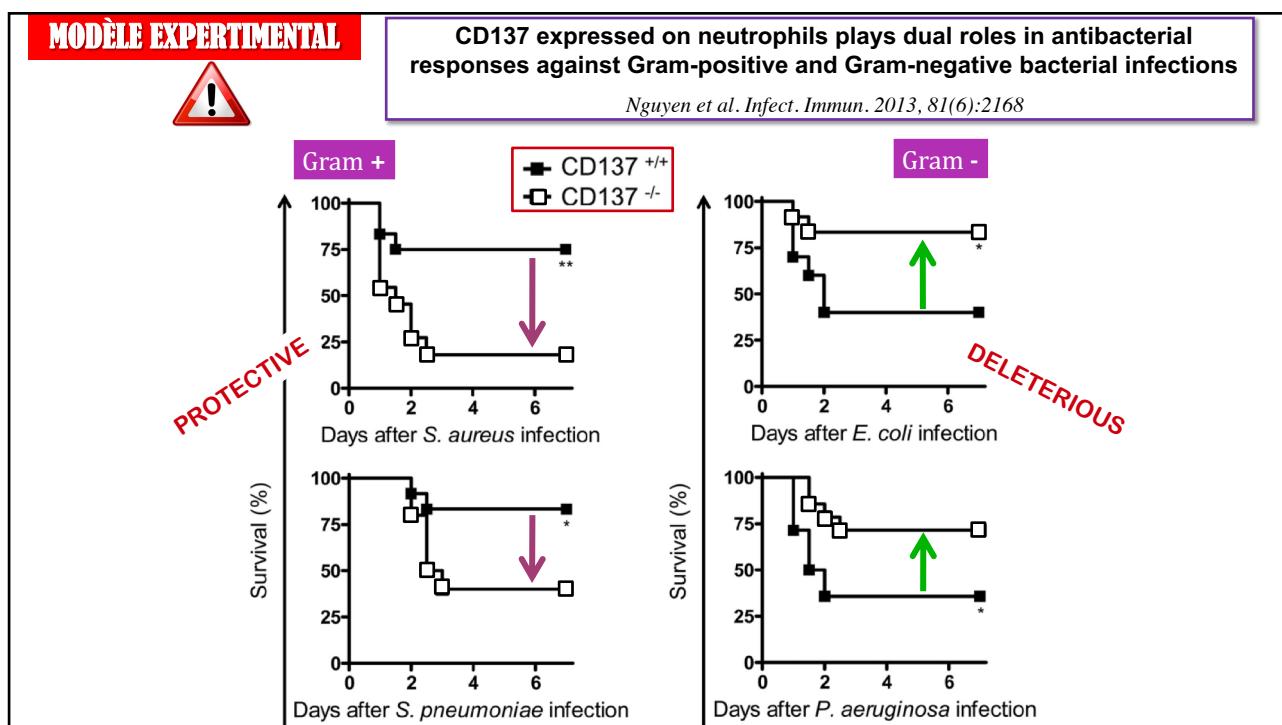
Detection of multiple mycoplasma infection in cell cultures by PCR

Timenetsky et al. Braz J Med Biol Res. 2006, 39, 907-914

301 cell cultures from 15 laboratories

→ 30.9% were contaminated.

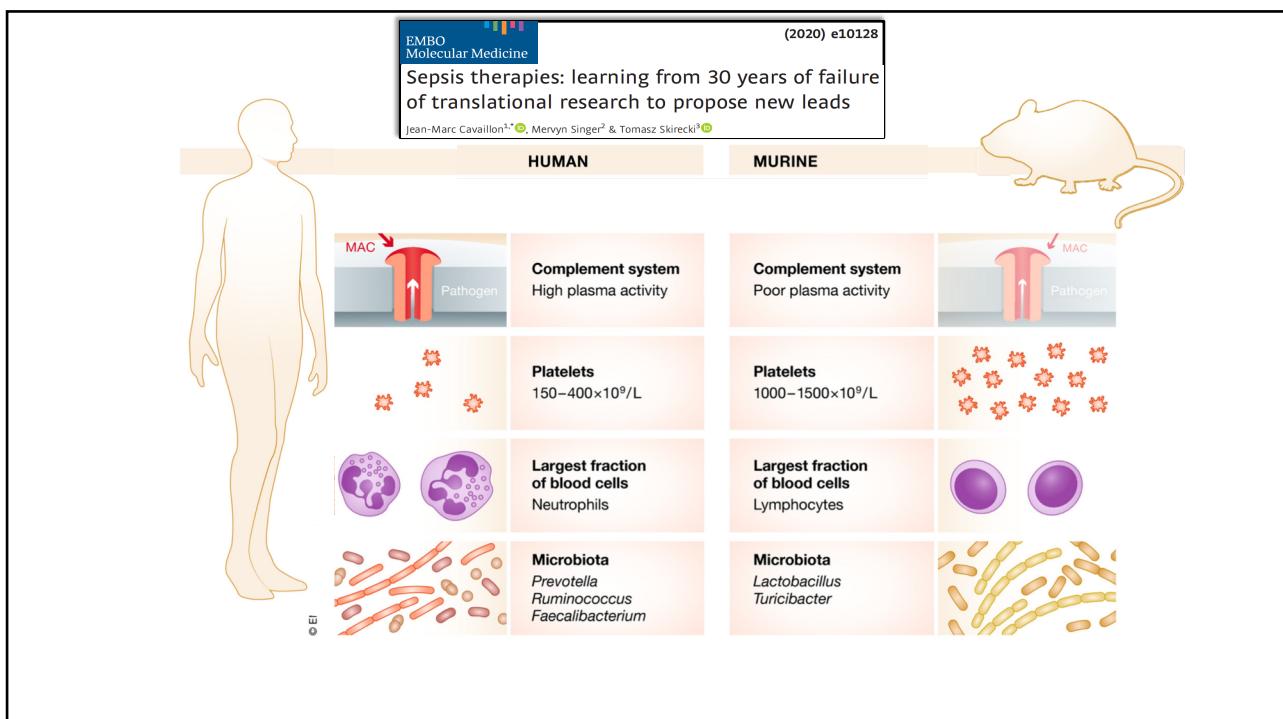
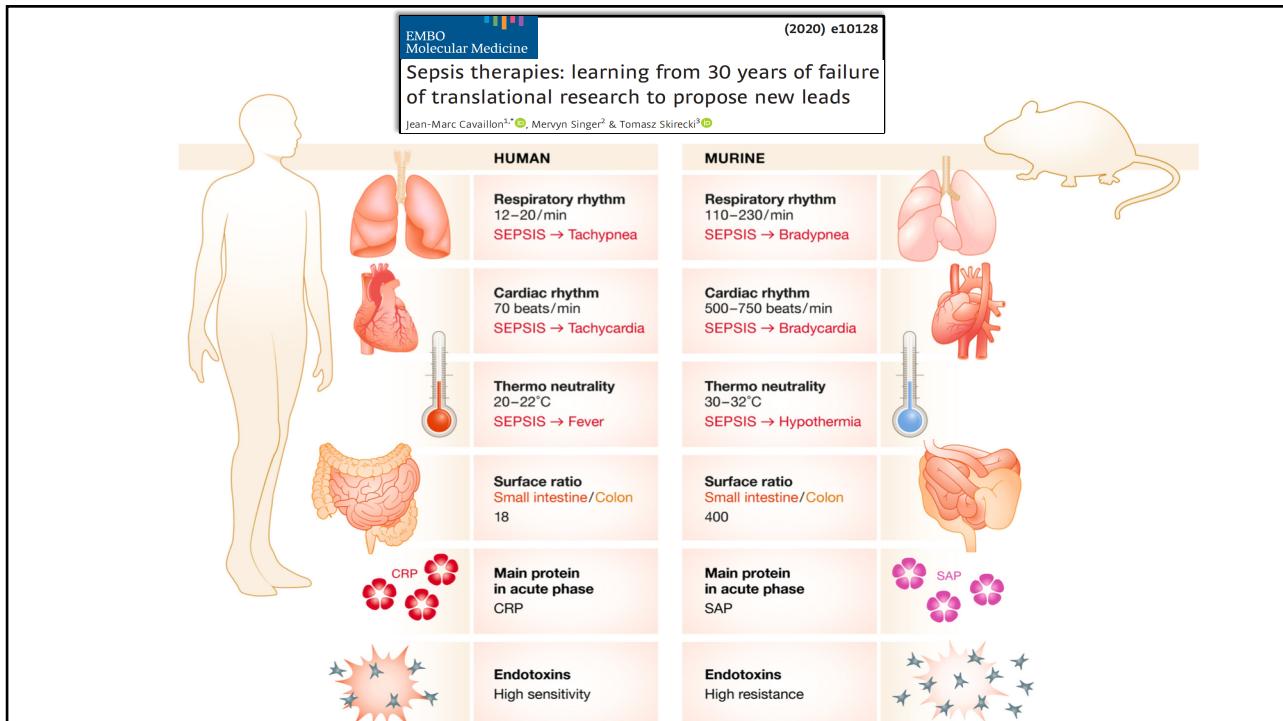


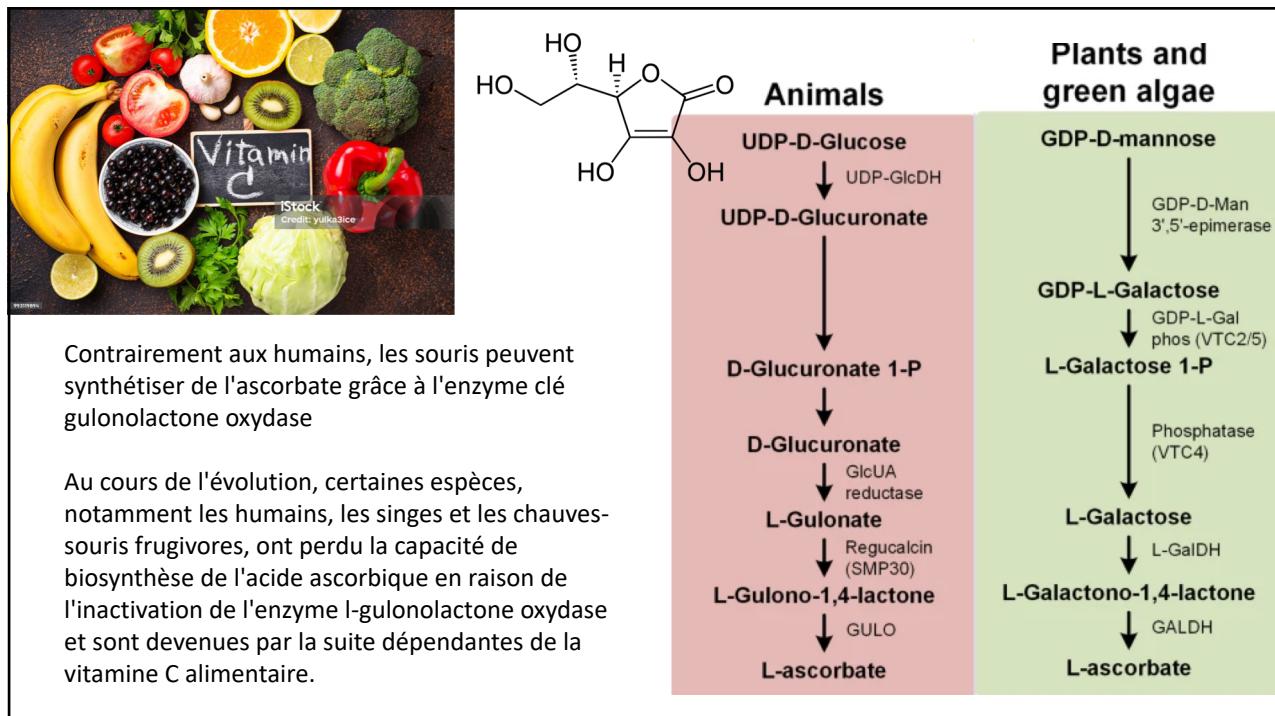


MODÈLES ANIMAUX









Contrairement aux humains, les souris peuvent synthétiser de l'ascorbat grâce à l'enzyme clé gulonolactone oxydase

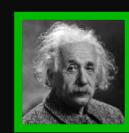
Au cours de l'évolution, certaines espèces, notamment les humains, les singes et les chauves-souris frugivores, ont perdu la capacité de biosynthèse de l'acide ascorbique en raison de l'inactivation de l'enzyme L-gulonolactone oxydase et sont devenues par la suite dépendantes de la vitamine C alimentaire.

IMMUNITÉ INNÉE & INFLAMMATION

SENSITIBITÉ AUX TOXINES BACTÉRIENNES



RESISTANT



SENSIBLE

Les souris sont 100,000 fois plus résistantes aux endotoxines que les humains

The Journal of Infectious Diseases 2010;201:175–7

EDITORIAL COMMENTARY

Murine Responses to Endotoxin: Another Dirty Little Secret?

Robert S. Munford

Laboratory of Clinical Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland



PNAS

PNAS | April 6, 2010 | vol. 107 | no. 14 | 6127–6133

“Control” laboratory rodents are metabolically morbid: Why it matters

Bronwen Martin^a, Sunggoan Ji^a, Stuart Maudsley^b, and Mark P. Mattson^{c,1}

ALIMENTATION AD LIBITUM



PAS D' EXERCICE



→ Expérimentation sur des animaux obèses et sédentaires

Cell Metabolism

23, 554–562, March 8, 2016

Voluntary Running Suppresses Tumor Growth through Epinephrine- and IL-6-Dependent NK Cell Mobilization and Redistribution

Line Pedersen,¹ Manja Idorn,² Gitte H. Olofsson,² Britt Lauenborg,¹ Intawat Nookaew,^{3,4} Rasmus Hvass Hansen,⁵ Helle Hjorth Johannessen,⁵ Jürgen C. Becker,⁶ Katrine S. Pedersen,¹ Christine Dethlefsen,¹ Jens Nielsen,³ Julie Gehl,¹ Bente K. Pedersen,¹ Per Thor Straten,^{2,8} and Pernille Hojman^{1,7,*}

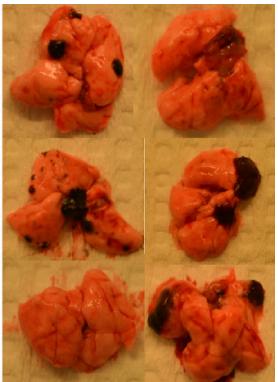


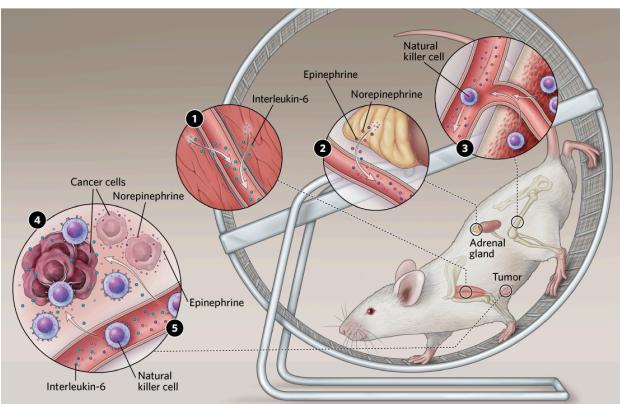
Méタstase dans les poumons de souris ayant reçue une injection de mélanome

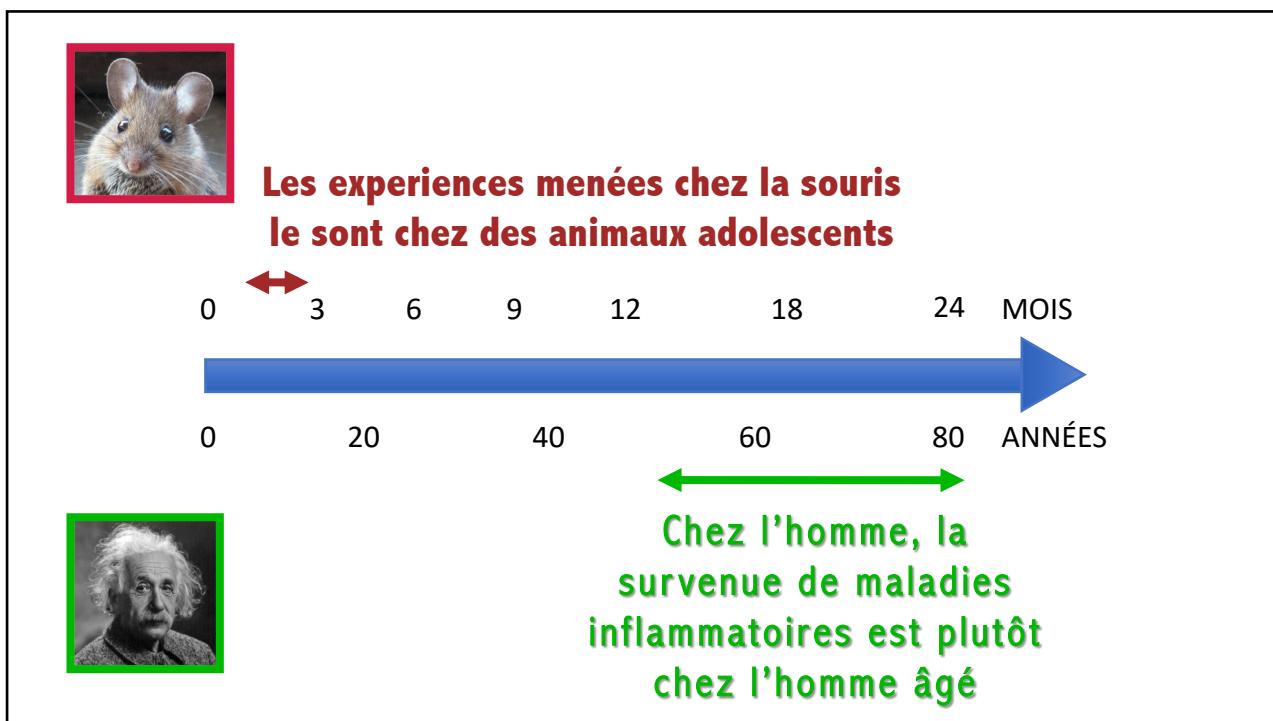
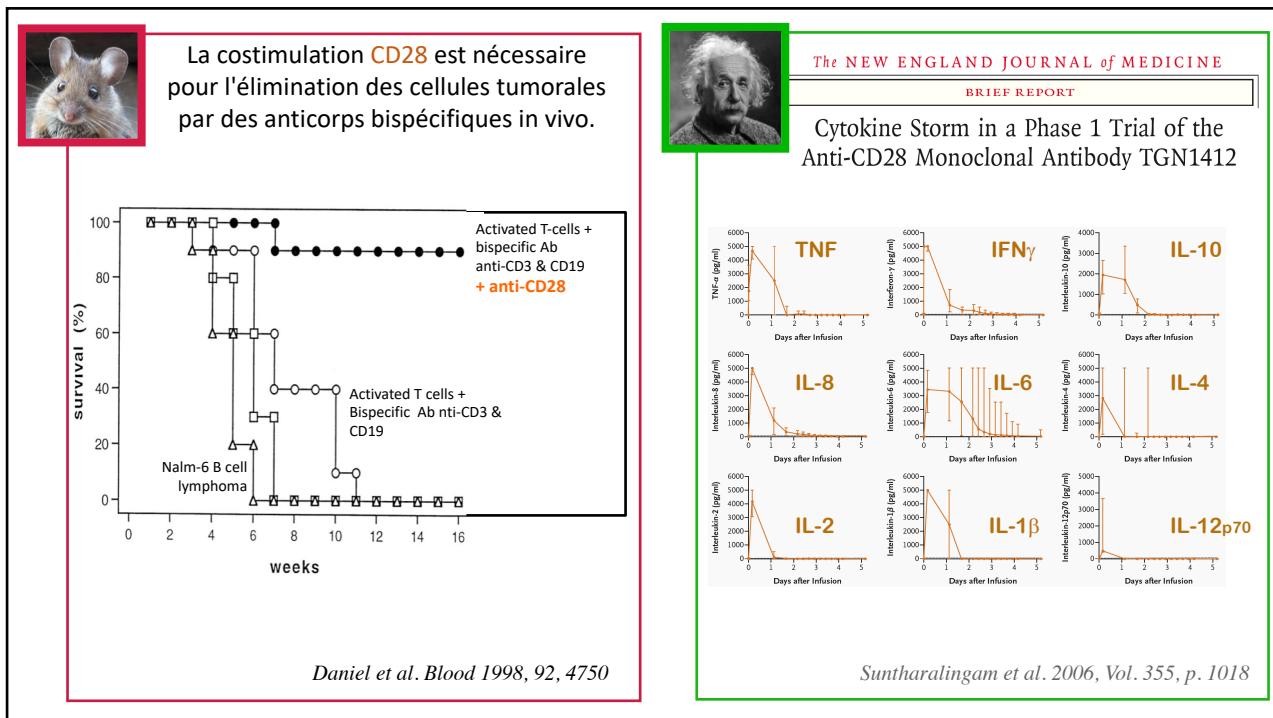
SOURIS SÉDENTAIRES



SOURIS SOUMISES A L'EXERCICE







JEM *J. Exp. Med.* 2012, 209, 1069

Unstressing intemperate models: how cold stress undermines mouse modeling

Christopher L. Karp

EXPÉRIMENTATION SUR DES SOURIS STRESSÉES PAR LE FROID CHEZ LES SOURIS LA THERMO-NEUTRALITÉ EST DE 30 - 32°C

Journal of Thermal Biology 37 (2012) 654–685
Thermal physiology of laboratory mice: Defining thermoneutrality
C.J. Gordon*

Effet de la température ambiante sur la consommation alimentaire

Proportion moyenne du temps passé par les souris sur une période de 3 jours à chaque température.

COMPLIANCE
RULES
REGULATIONS
GUIDELINES

LES SOURIS EN STRESS THERMIQUE NE DÉVELOPPE PAS DE FIÈVRE

INFECTION AND IMMUNITY, Mar. 2000, p. 1265–1270

Febrile Core Temperature Is Essential for Optimal Host Defense in Bacterial Peritonitis

QINQI JIANG,^{1,2} ALAN S. CROSS,³ ISHWAR S. SINGH,¹ T. TIMOTHY CHEN,⁴ ROSE M. VISCARDI,⁵ AND JEFFREY D. HASDAY^{1,2,6,7*}

Housing
23°C → 36.5°C
35.5°C → 39.2°C

Core Temp.

100 CFU *K. pneumoniae*

Survie

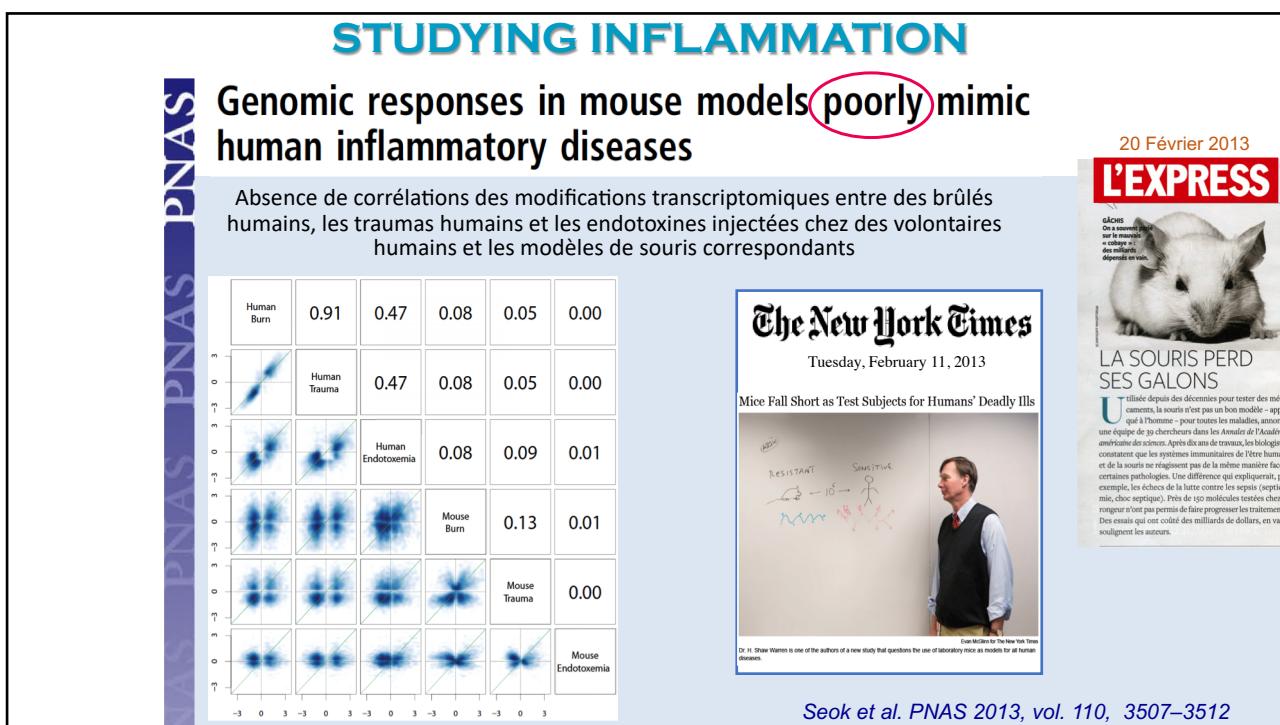
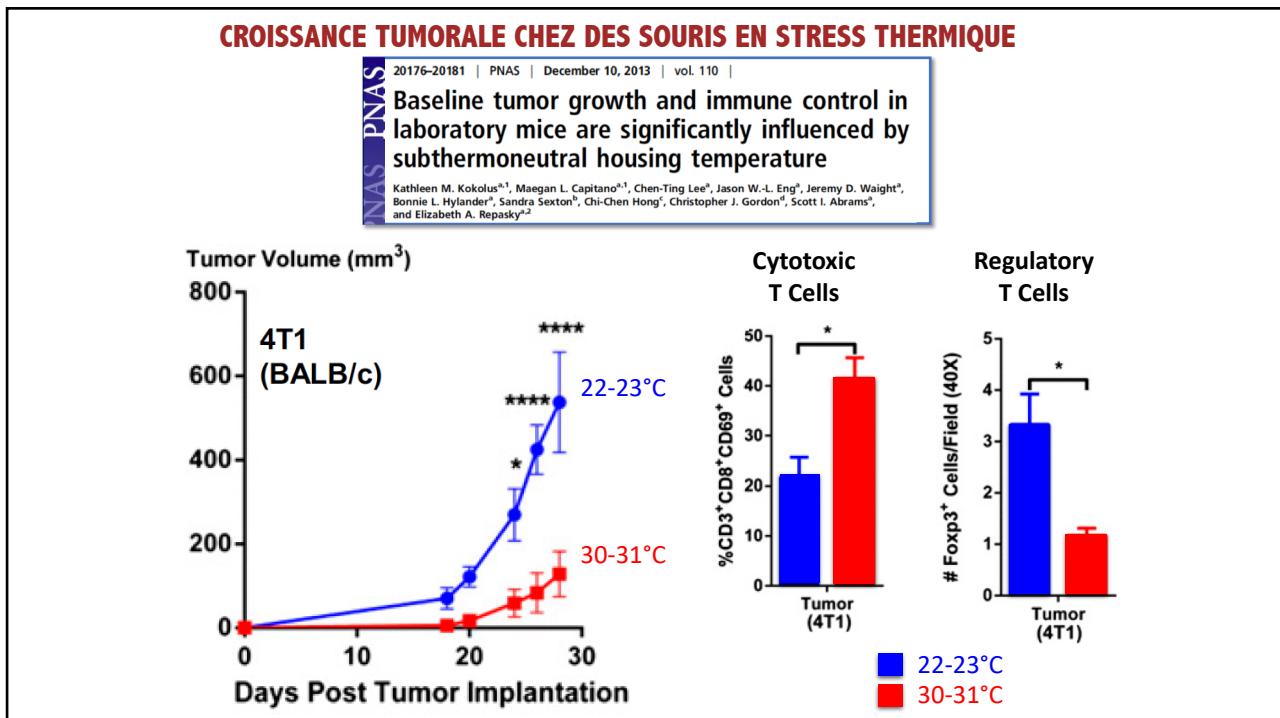
Number surviving
Days after inoculation

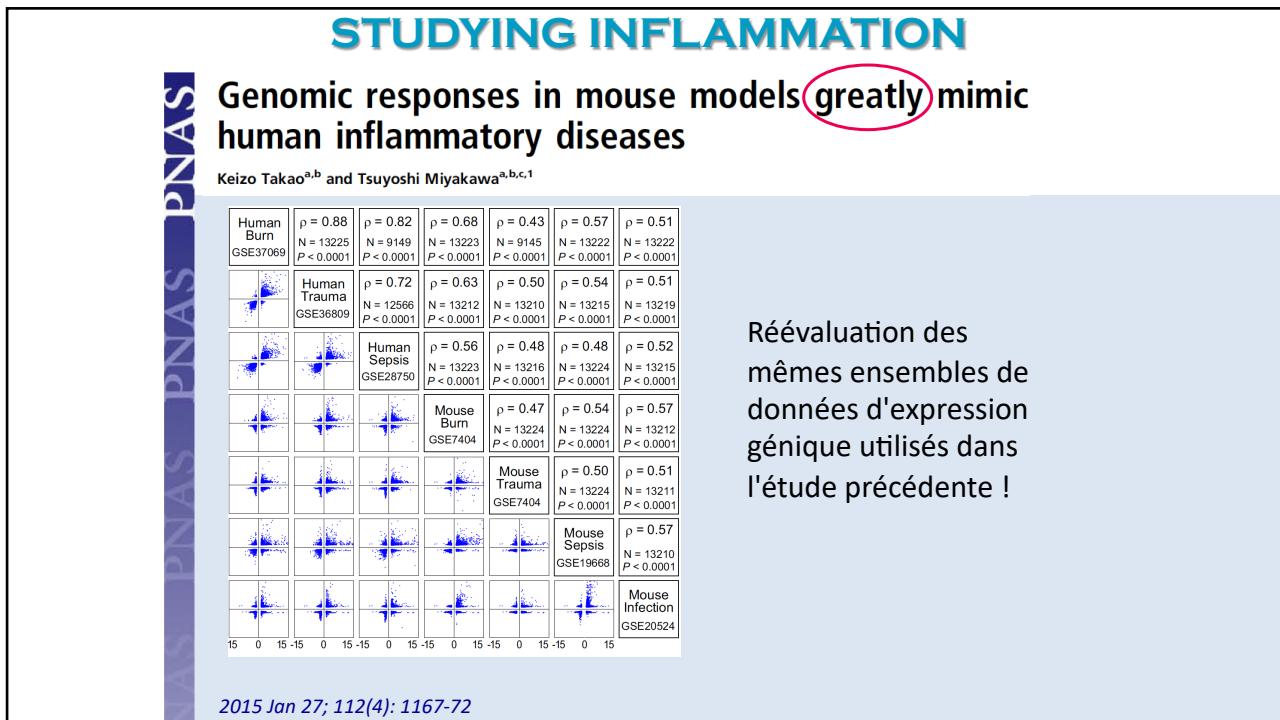
P < 0.00002

Charge bactérienne dans la cavité péritonéale

No Fever (blue squares)
Fever (red circles)

Bacterial load (cfu per ml)
Time after inoculation (h)





The Guardian

Fri 20 Mar 2015 12.14 CET

Mice losing their allure as experimental subjects to study human disease

Recent research has revealed that clinical trials involving the rodents do not automatically produce effective treatments for humans

"Once you start modelling a human disease to find the right treatment, you run up against major differences between us and mice"- Jean-Marc Cavaillon. Photograph: Alamy

<https://www.theguardian.com/science/2015/mar/20/mice-clinical-trials-human-disease>

PERTINENCE DES MODÈLES ANIMAUX

Science AAAS



2014 Sep 19; 345: 1446-7



Outsmarting the placebo effect

Can a genetic test to predict a person's level of placebo response help new drugs win approval?

By Kelly Servick

October 2012 | Volume 7 | Issue 10 | e48135

PLOS ONE

Catechol-O-Methyltransferase val158met Polymorphism Predicts Placebo Effect in Irritable Bowel Syndrome

Kathryn T. Hall^{1,2*}, Anthony J. Lembo^{2,3}, Irving Kirsch^{2,4}, Dimitrios C. Ziosas⁵, Jeffrey Douaiher⁶, Karin B. Jensen^{2,7}, Lisa A. Conboy², John M. Kelley^{2,7,8}, Efi Kokkotou^{2,3}, Ted J. Kaptchuk^{1,2}

PERTINENCE DES MODÈLES ANIMAUX

Progress in Neuro-Psychopharmacology and Biological Psychiatry



Volume 50, 3 April 2014, Pages 27–36

Review article

→ 262 publications

Developing zebrafish models of autism spectrum disorder (ASD)

Adam Michael Stewart^{a, b}, Michael Nguyen^c, Keith Wong^d, Manoj K. Poudel^a, Allan V. Kalueff^a,  

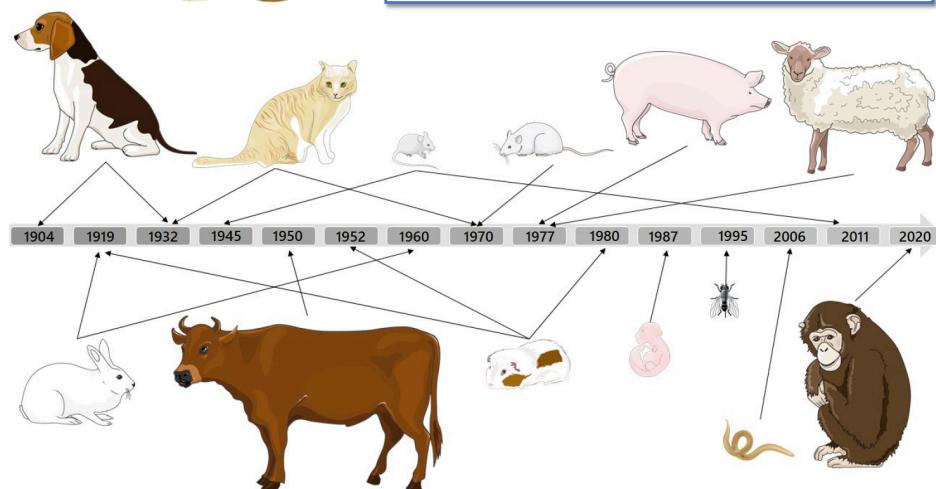



PERTINENCE DES MODÈLES ANIMAUX

Pharmacology 2021;106:356–368

Animal Models in Pharmacology: A Brief History Awarding the Nobel Prizes for Physiology or Medicine

Catarina V. Jota Baptista^a Ana I. Faustino-Rocha^{b,c} Paula A. Oliveira



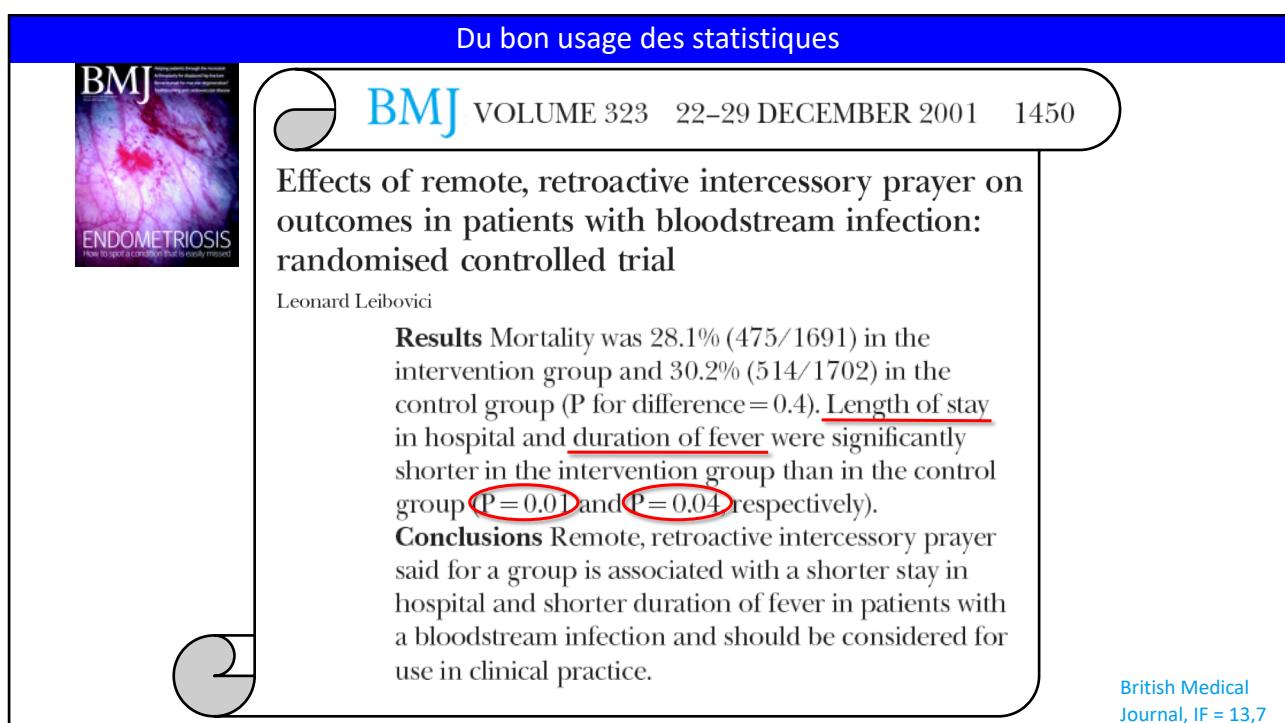
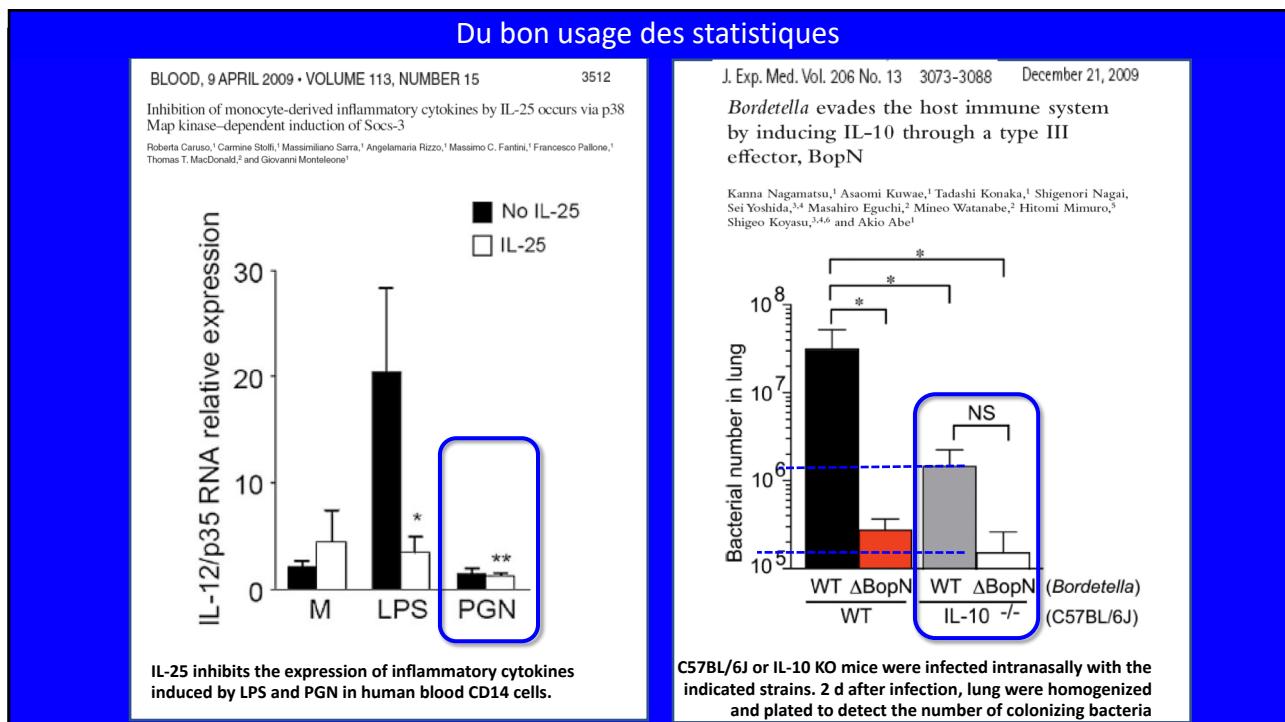
ANALYSES STATISTIQUES

Pour publier un travail scientifique,
il est requis d'avoir atteint une
signification statistique

$$\frac{3a(y+G)^2}{39} + (y+G) \frac{3y}{39}$$

$$\frac{a^2(G^2)}{39} + (y+G) \frac{13}{39} + \frac{2}{3} \frac{y^2}{39}$$





Du bon usage des statistiques

**nature
human behaviour** | VOL 2 | JANUARY 2018 | 6-10 | **comment**

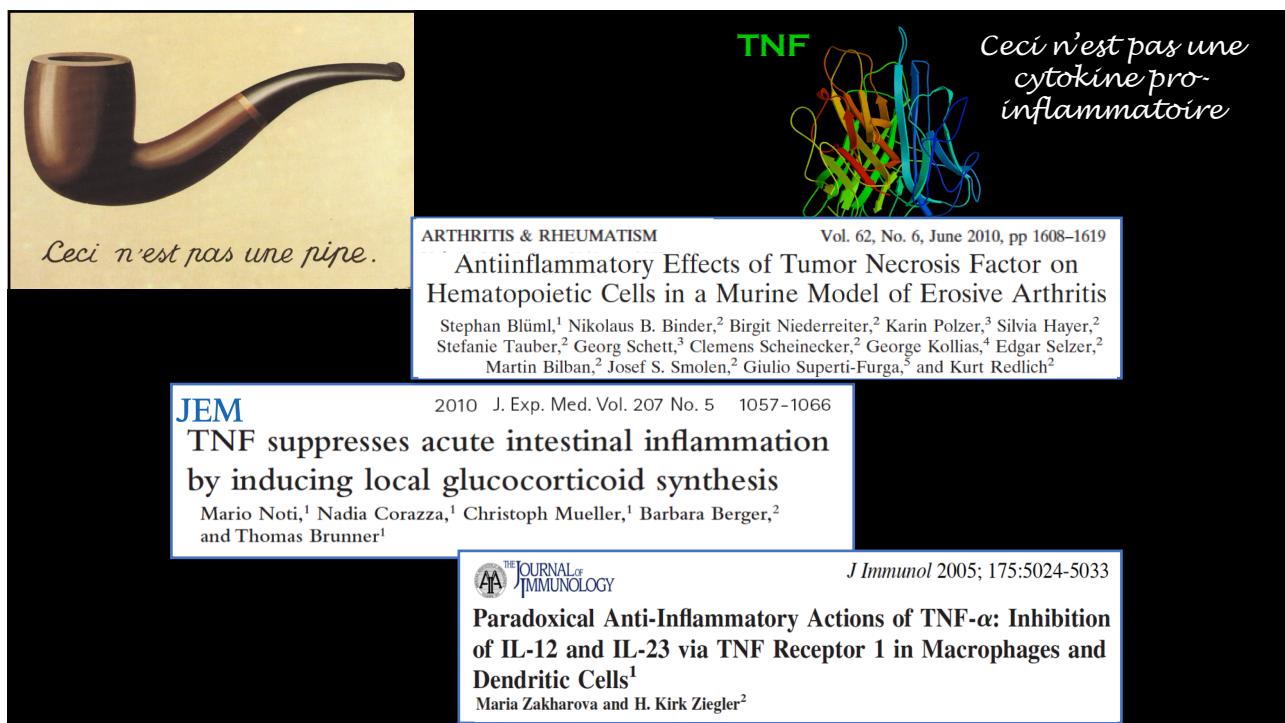
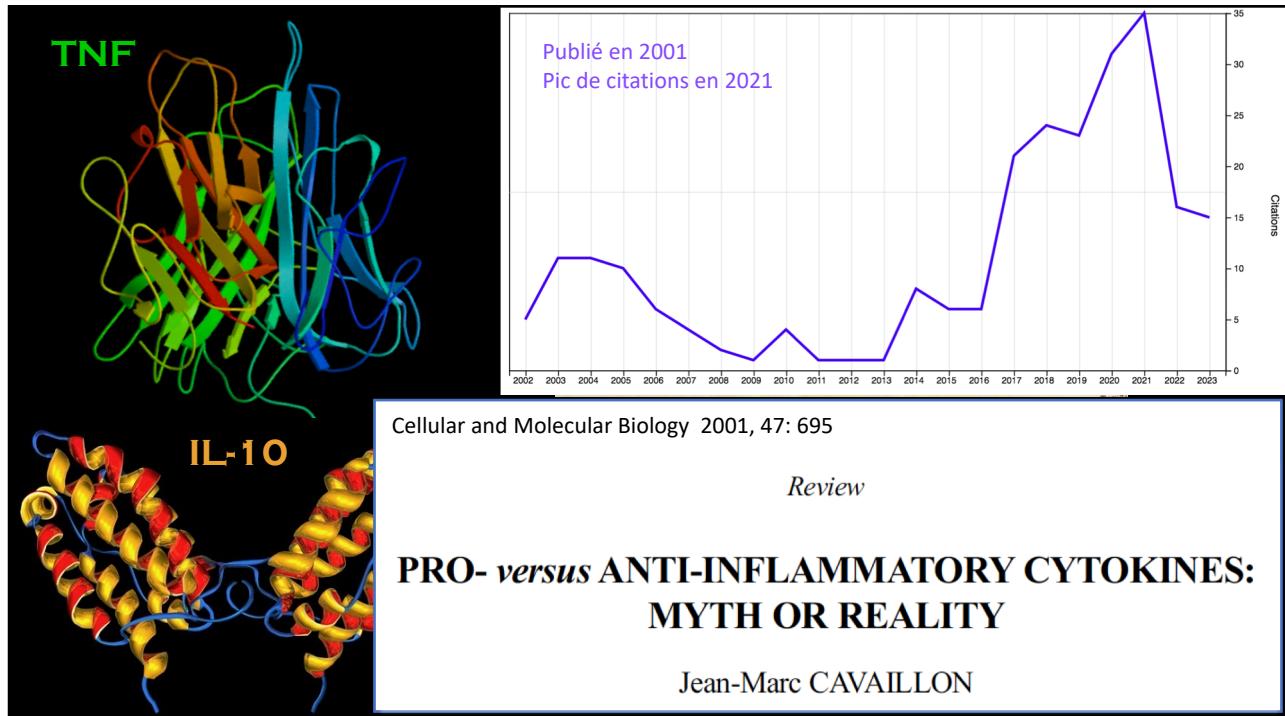
Redefine statistical significance

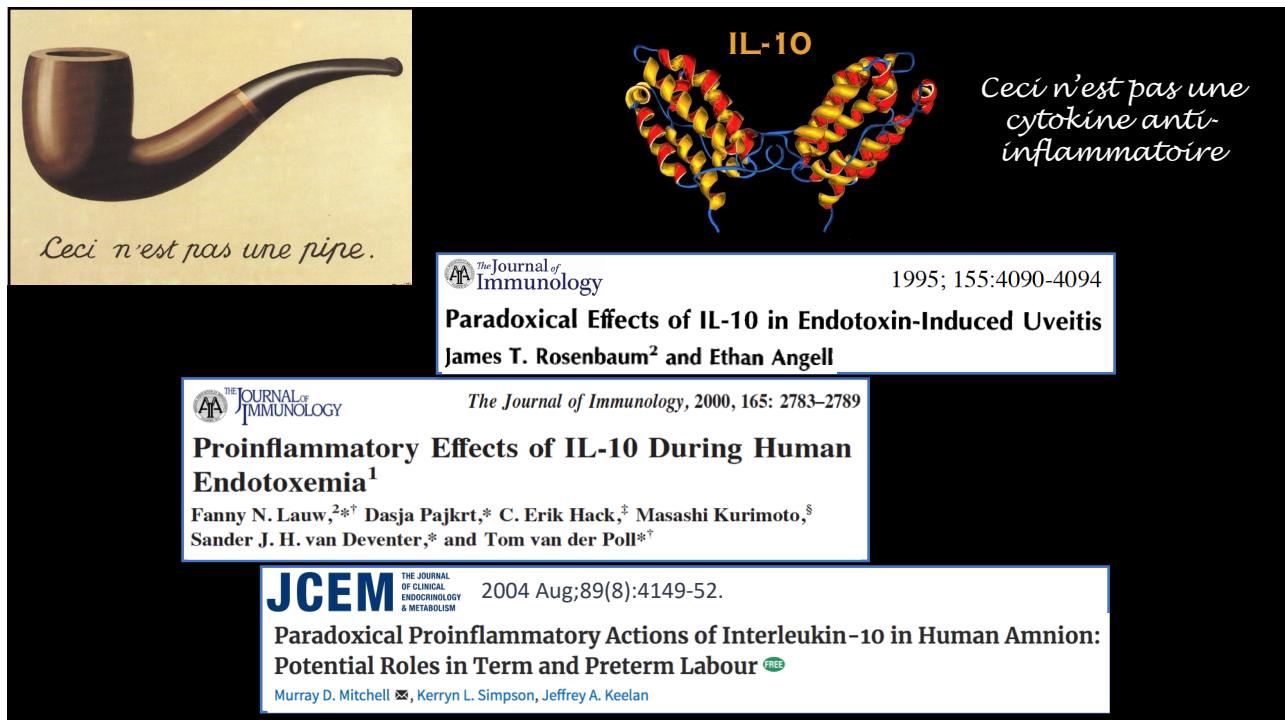
Daniel J. Benjamin, James O. Berger, Magnus Johannesson, Brian A. Nosek, E.-J. Wagenmakers, Richard Berk, Kenneth A. Bollen, Björn Brembs, Lawrence Brown, Colin Camerer, David Cesarini, Christopher D. Chambers, Merlise Clyde, Thomas D. Cook, Paul De Boeck, Zoltan Dienes, Anna Dreber, Kenny Easwaran, Charles Efferson, Ernst Fehr, Fiona Fidler, Andy P. Field, Malcolm Forster, Edward I. George, Richard Gonzalez, Steven Goodman, Edwin Green, Donald P. Green, Anthony Greenwald, Jarrod D. Hadfield, Larry V. Hedges, Leonhard Held, Teck Hua Ho, Herbert Hoijtink, Daniel J. Hruschka, Kosuke Imai, Guido Imbens, John P. A. Ioannidis, Minjeong Jeon, James Holland Jones, Michael Kirchner, David Laibson, John List, Roderick Little, Arthur Lupia, Edouard Machery, Scott E. Maxwell, Michael McCarthy, Don Moore, Stephen L. Morgan, Marcus Munafó, Shinichi Nakagawa, Brendan Nyhan, Timothy H. Parker, Luis Pericchi, Marco Perugini, Jeff Rouder, Judith Rousseau, Victoria Savalei, Felix D. Schönbrodt, Thomas Selke, Betsy Sinclair, Dustin Tingley, Trisha Van Zandt, Simine Vazire, Duncan J. Watts, Christopher Winship, Robert L. Wolpert, Yu Xie, Cristobal Young, Jonathan Zinman and Valen E. Johnson

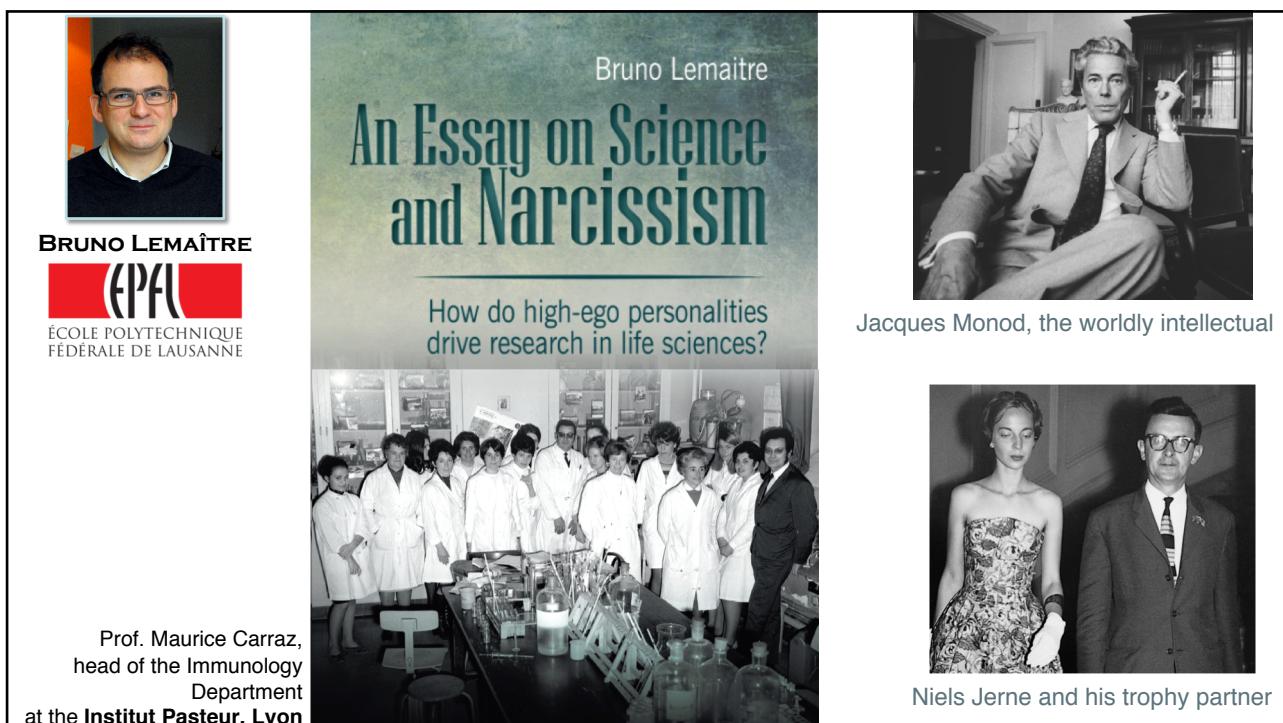
DG

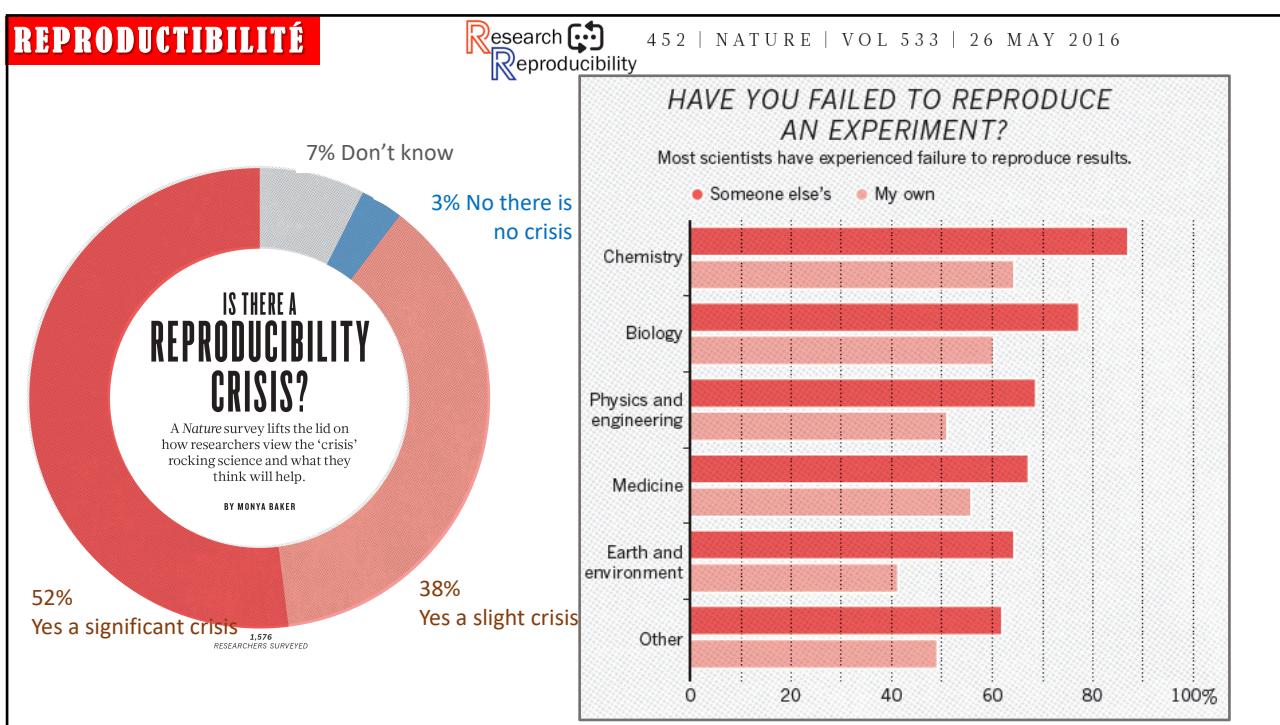
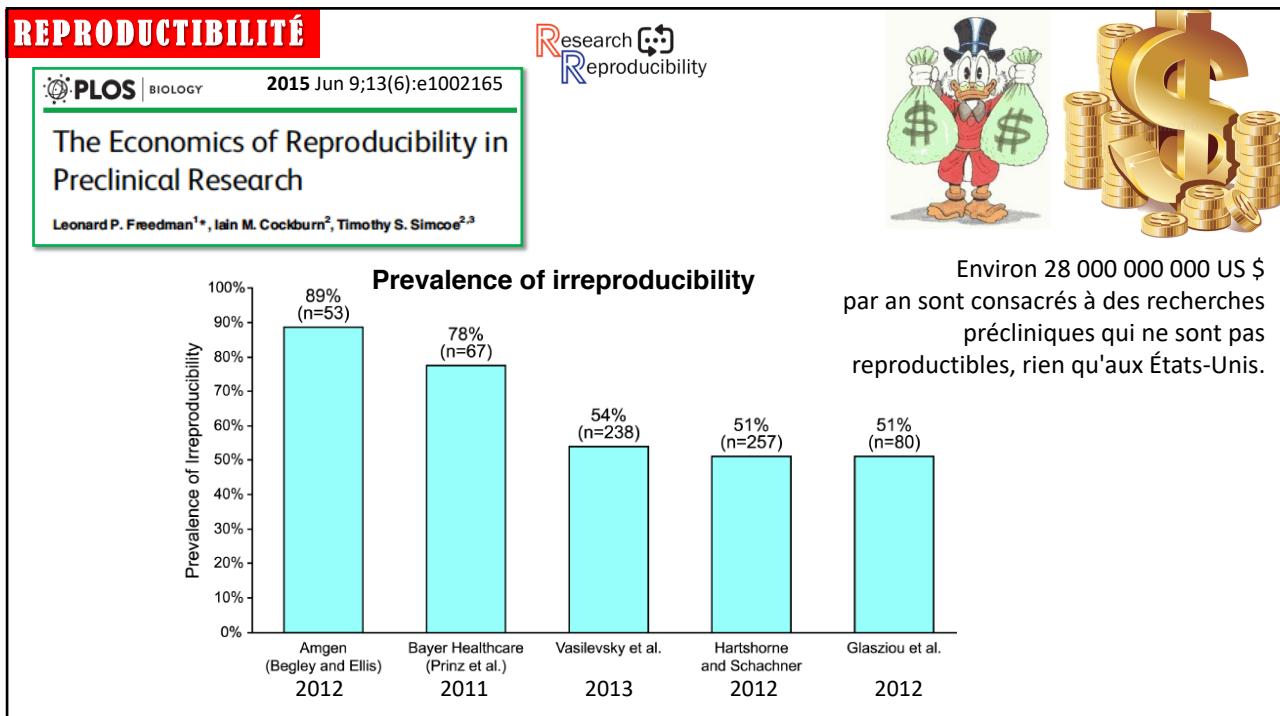
Nous proposons de modifier le seuil de valeur P par défaut pour la signification statistique de 0,05 à 0,005 pour les allégations de nouvelles découvertes.













John P. A. Ioannidis
professeur de médecine
Université de Stanford

Essay PLoS Medicine | August 2005 | Volume 2 | Issue 8 | e124

Why Most Published Research Findings Are False

John P. A. Ioannidis

CITÉ 6248 X

Actuellement, de nombreux résultats de recherche publiés sont faux ou exagérés, et on estime que 85 % des ressources de recherche sont gaspillées.



October 2014 | Volume 11 | Issue 10 | e1001747

PLOS MEDICINE

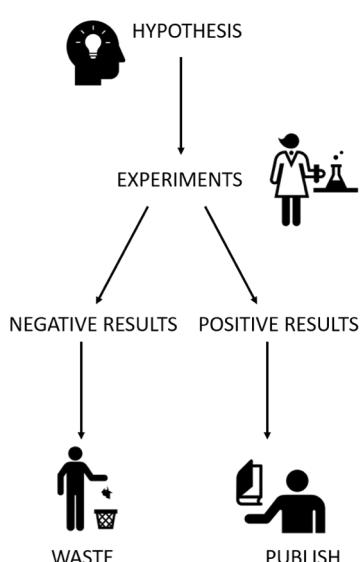
Essay

How to Make More Published Research True

John P. A. Ioannidis^{1,2,3,4*}

¹ Meta-Research Innovation Center at Stanford (METRICS), Stanford University, Stanford, California, United States of America, ² Department of Medicine, Stanford Prevention Research Center, Stanford, California, United States of America, ³ Department of Health Research and Policy, Stanford University School of Medicine, Stanford, California, United States of America, ⁴ Department of Statistics, Stanford University School of Humanities and Sciences, Stanford, California, United States of America

UN DES BIAIS DE LA PUBLICATION SCIENTIFIQUE : LA NON PUBLICATION DE RÉSULTATS NÉGATIFS



HYPOTHESIS

↓

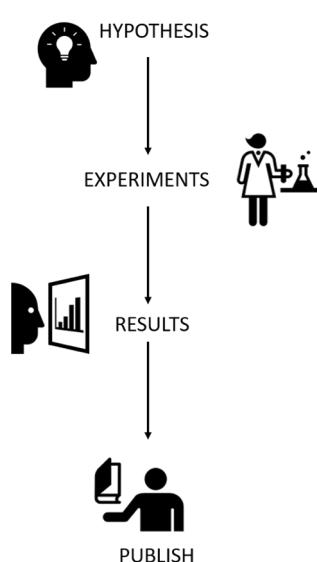
EXPERIMENTS

↓

NEGATIVE RESULTS **POSITIVE RESULTS**

↓

WASTE **PUBLISH**



HYPOTHESIS

↓

EXPERIMENTS

↓

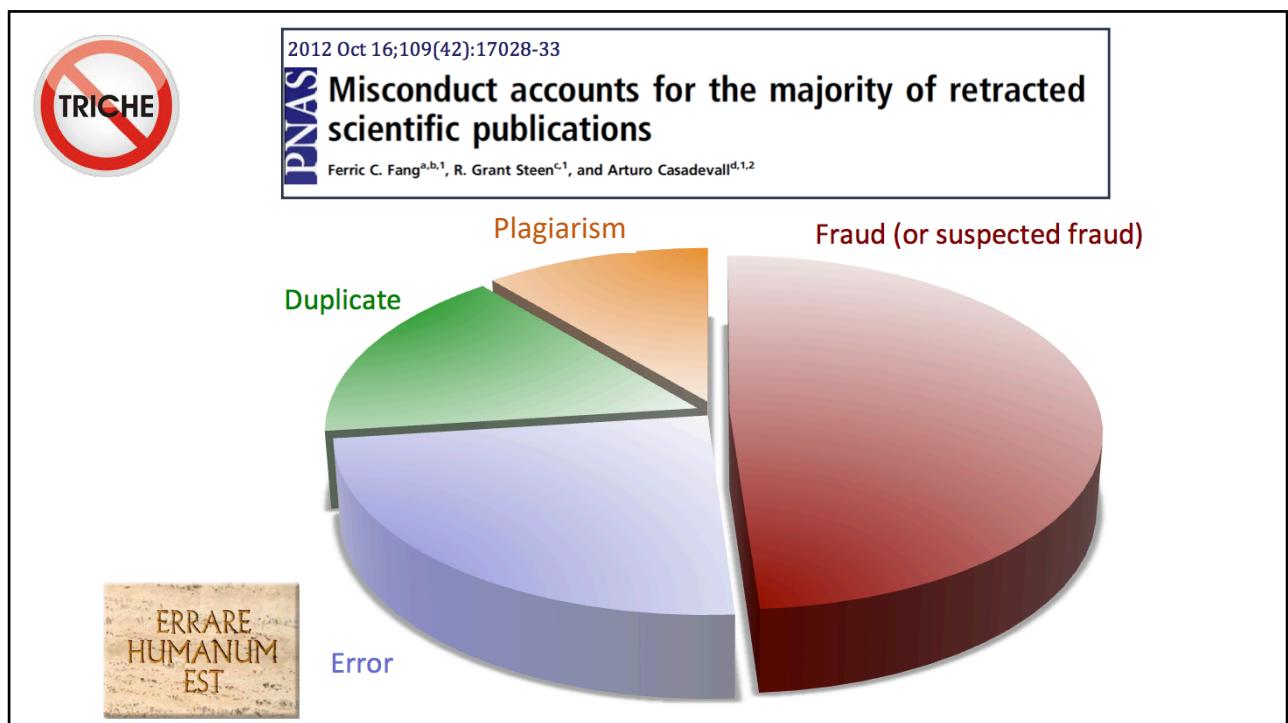
RESULTS

↓

PUBLISH

Figure 1: Common approach taken by publishers in which experiments that deliver positive results are published and those that deliver negative results are discarded.

Figure 2: A more neutral approach in which all results generated from well-thought out and conducted experiments are published.





Plagiarism in Scientific Writing

BMJ 2023;381:p1403

PLAGIARISM RISK WITH ARTIFICIAL INTELLIGENCE

Educators, students, and plagiarism in age of AI
Donovan Simpson clinical teaching fellow

BJS, 2023, 110, 1897
Self-plagiarism
B. M. Nandakumar^{1,*}  and H. K. Ramakrishna²

224 | Nature | Vol 625 | 11 January 2024



Claudine Gay was the first Black president of Harvard University.

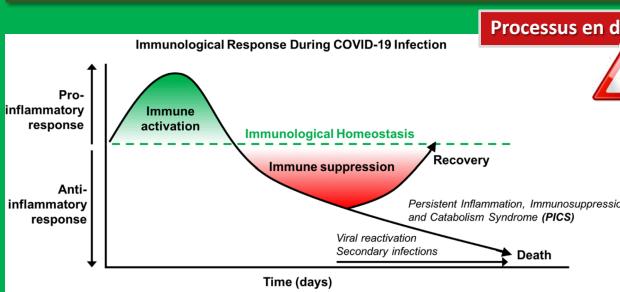
HARVARD PRESIDENT'S RESIGNATION LEAVES ACADEMICS REELING

University head steps down amid plagiarism claims and controversy over congressional testimony.

2023 Clinical Reviews in Allergy & Immunology (2023) 64:66–74

A Review of Persistent Post-COVID Syndrome (PPCS)

Bryan Oronsky¹  · Christopher Larson¹ · Terese C. Hammond² · Arnold Oronsky³ · Santosh Kesari²
Michelle Lybeck¹ · Tony R. Reid¹

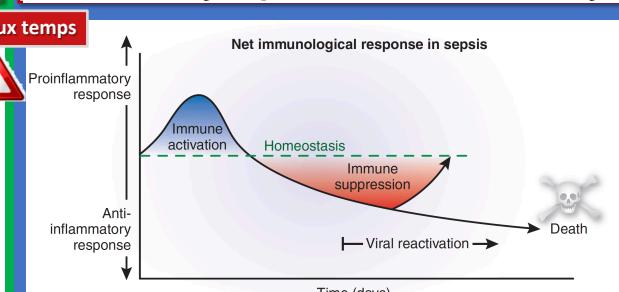


2009 NATURE MEDICINE VOLUME 15 | NUMBER 5 | MAY 2009

BEDSIDE TO BENCH

Tilting toward immunosuppression

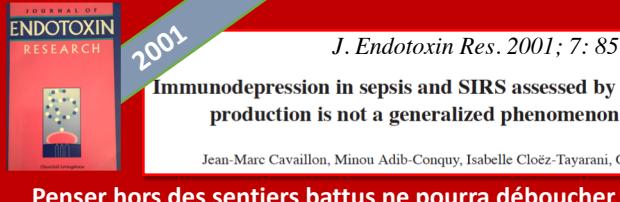
Richard S Hotchkiss, Craig M Coopersmith, Jonathan E McDunn & Thomas A Ferguson



2001 J. Endotoxin Res. 2001; 7: 85

Immunodepression in sepsis and SIRS assessed by ex vivo cytokine production is not a generalized phenomenon: a review

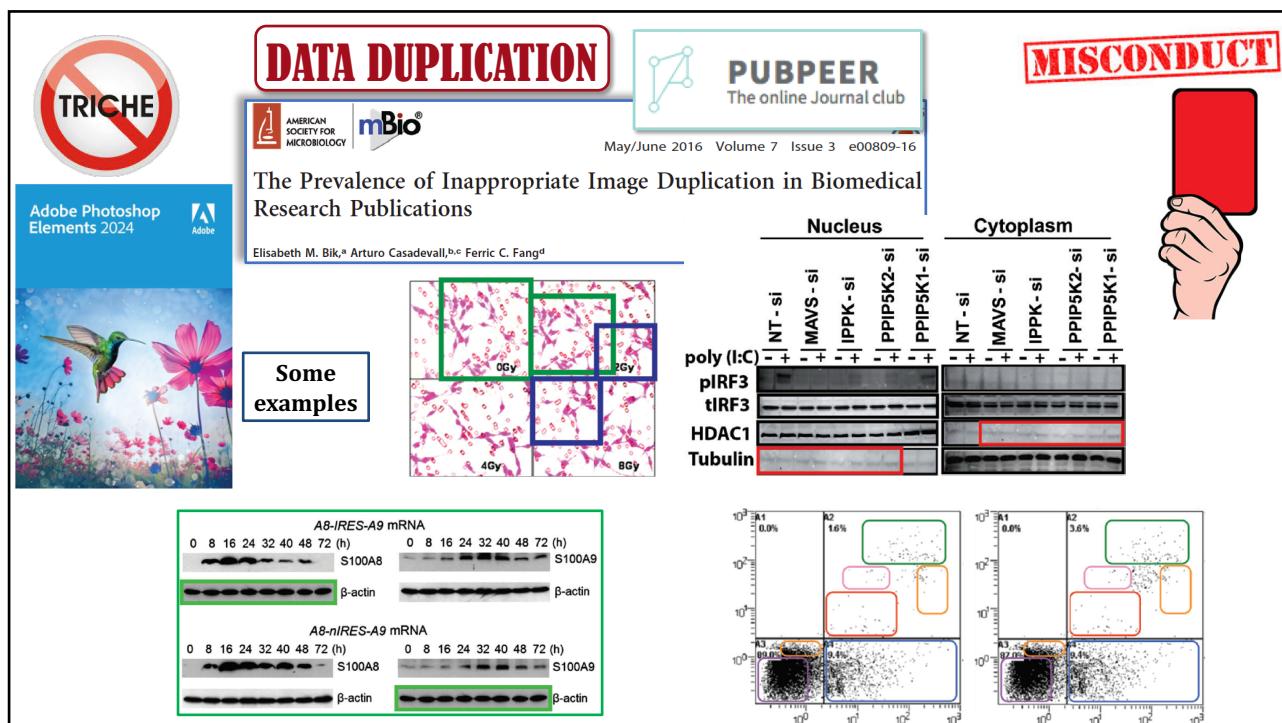
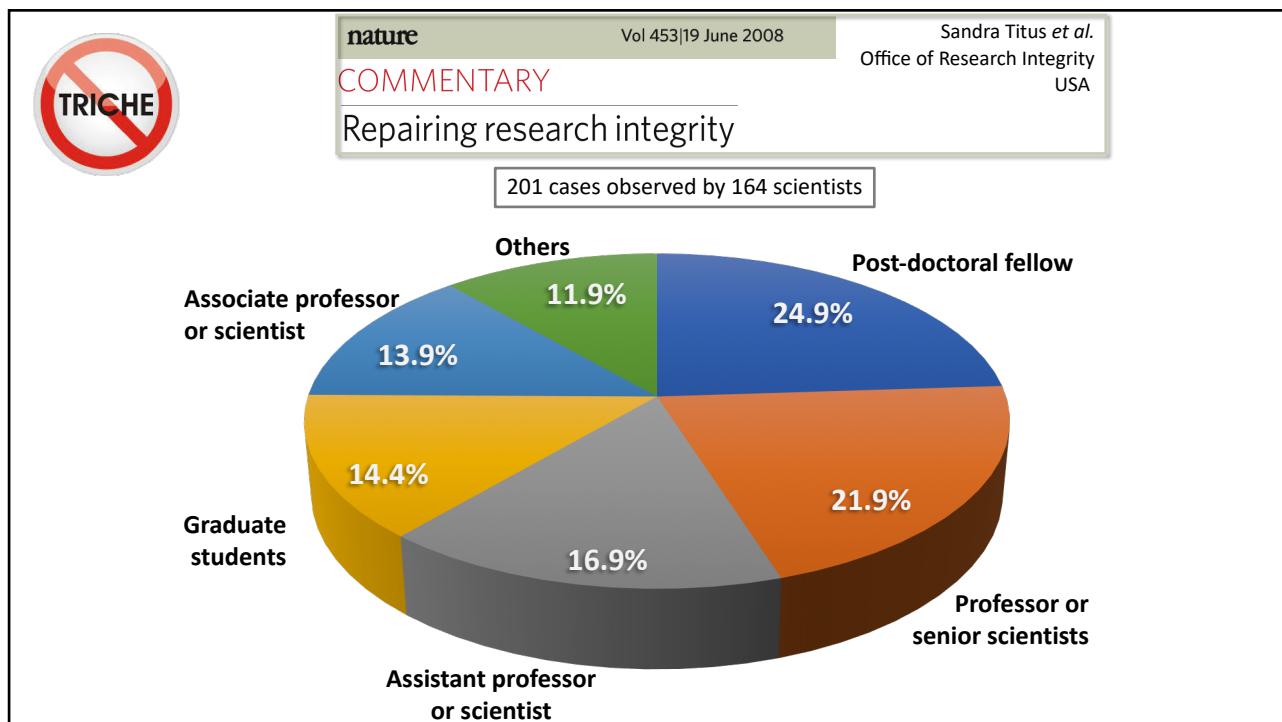
Jean-Marc Cavaillon, Minou Adib-Conquy, Isabelle Cloëz-Tayarani, Catherine Fitting



Enhanced ex vivo cytokine production
Enhanced NF-κB expression in nucleus of - alveolar macrophages - lung neutrophils - liver cells

Reduced ex vivo cytokine production
Reduced NF-κB expression in nucleus of peripheral blood mononuclear cells of patients and trauma patients

Penser hors des sentiers battus ne pourra déboucher sur un accord consensuel qu'une fois les ténors du domaine auront fait l'idée leur.



Proc. Natl. Acad. Sci. USA
Vol. 81, pp. 7907–7911, December 1984
Immunology

Nucleotide sequence of human monocyte interleukin 1 precursor cDNA
(monokine/T-lymphocyte activation/hybrid selection/oocyte translation)

PHILIP E. AURON*†‡, ANDREW C. WEBB*‡§, LANNY J. ROSENWASSER‡, STEVEN F. MUCCI‡,
ALEXANDER RICH*, SHELDON M. WOLFF‡, AND CHARLES A. DINARELLO*‡

*Biology Department, Massachusetts Institute of Technology, Cambridge, MA 02139; †Harvard-M.I.T. Division of Health Sciences and Technology, Cambridge, MA 02139; ‡Department of Medicine, The New England Medical Center, Tufts University School of Medicine, Boston, MA 02111; and §Department of Biological Sciences, Wellesley College, Wellesley, MA 02181



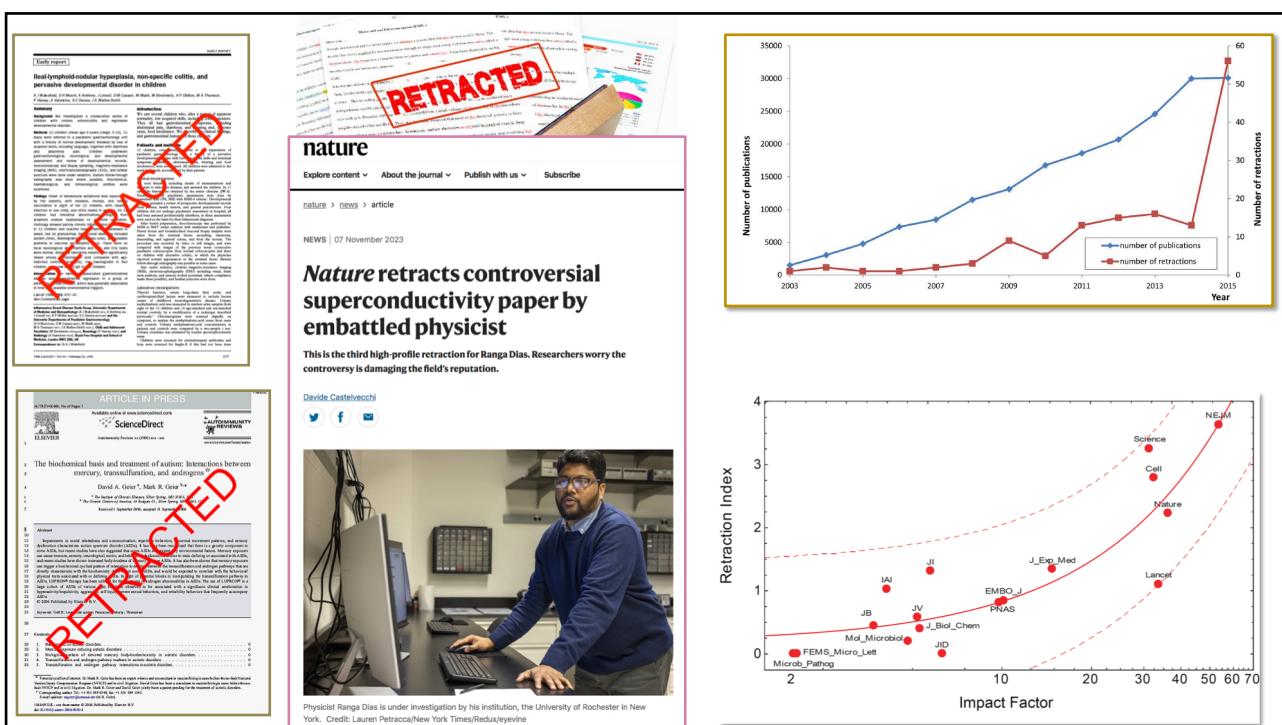
Mai 1984 Le groupe de Charles Dinarello soumet le clonage de l'interleukine-1 humaine au journal *Nature*

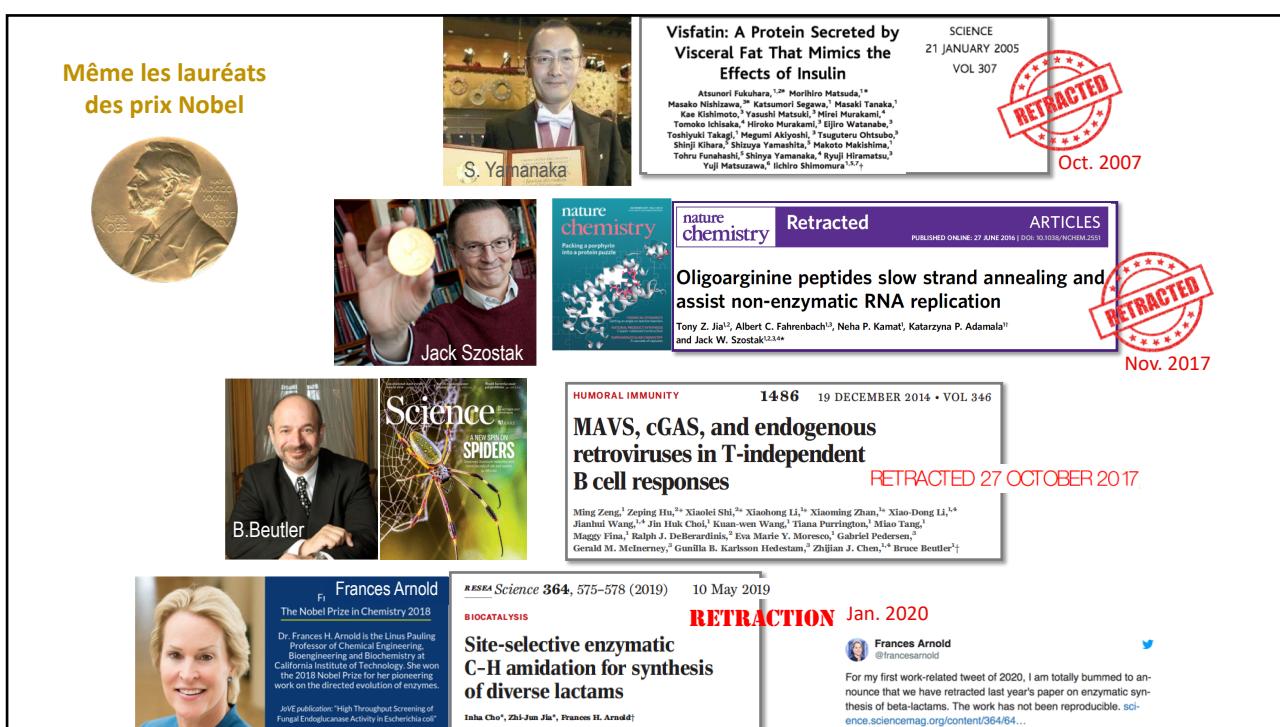
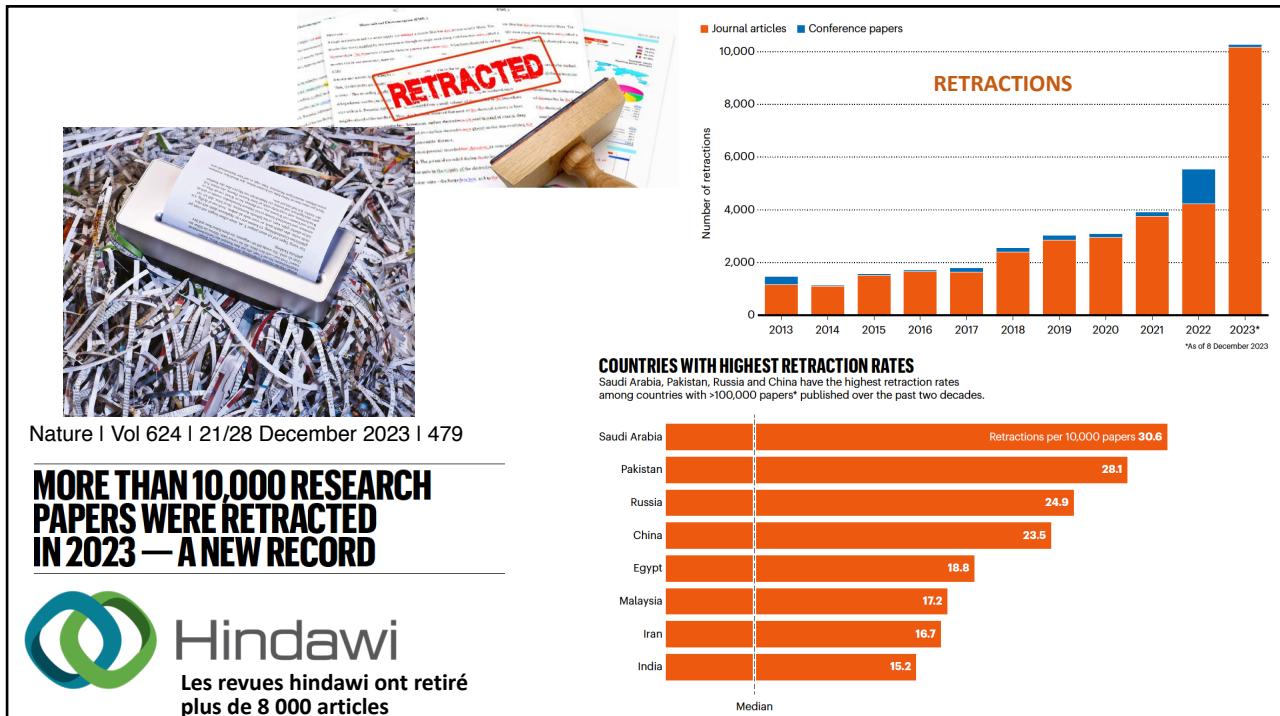
 *Nature* rejette le manuscript

Mai 1985 *Nature* publie la séquence de l'IL-1 β humaine par des scientifiques de la société Immunex

Les avocats découvrent que le brevet Immunex sur l'IL-1 β (déc. 1984) contenait les mêmes neuf erreurs nucléotidiques aux mêmes endroits que dans l'article de Dinarello (NB les erreurs avaient été corrigées dans l'article publié par Immunex dans *Nature*)

! 





Même les lauréats des prix Nobel



GREGG L. SEMENZA

THE NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE 2019



nature

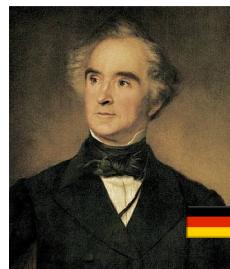
NEWS | 21 October 2022

Dozens of papers co-authored by Nobel laureate raise concerns

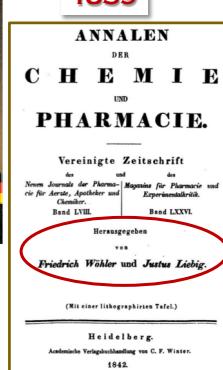
Concerns about image integrity have so far led to 17 retractions, corrections or expressions of concern for papers co-authored by geneticist Gregg Semenza.

Le lauréat du prix Nobel fait l'objet d'une enquête sur l'intégrité de ses papiers : Dix-sept études co-écrites par le prof. Gregg Semenza (Johns Hopkins School of Medicine) ont été rétractées, corrigées ou mentionnées pour des problèmes liés à des images manipulées, et 15 autres sont actuellement en cours d'investigation.

Les liens incestueux entre les scientifiques et la presse scientifique



JUSTUS FREIHERR VON LIEBIG
(1803 – 1873)



1839

**ANNALEN
DER
CHEMIE
UND
PHARMACIE.**

Vereinigte Zeitschrift
und
Neues Journal der Pharmacie
für Aerzte, Apotheker und
Chemiker.
Band LXIX.
Band LXIX.
Herausgegeben
von
Friedrich Wöhler und Justus Liebig.

(Mit einer lithographirten Tafel.)

Heidelberg
Akademische Verlagsanstalt von C. F. Winter.
1842.



FRIEDRICH WÖHLER
(1800 – 1882)

Fermentation alcoolique



→ Les levures sont d'origine animale

Liebig et Wöhler soutenaient l'idée selon laquelle la fermentation est un processus mécanique. Ils n'avaient aucune preuve expérimentale pour réfuter la base cellulaire de la fermentation ; au lieu de cela, ils ont eu recours à la moquerie et à la controverse ; Ils ont publié dans "Annalen der Chemie und Pharmacie" dont ils étaient les rédacteurs-en-chef

1887

Les liens incestueux entre les scientifiques et la presse scientifique

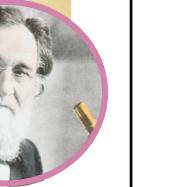


**ANNALES
DE L'INSTITUT PASTEUR**
(JOURNAL DE MICROBIOLOGIE)
PUBLIÉES SOUS LE PATRONAGE DE M. PASTEUR
PAR
E. DUCLAUX
PROFESSEUR À LA SORBONNE
Et un Comité de rédaction composé de MM.
CHAMBERLAND, directeur du laboratoire de M. Pasteur.
GRANCHIER, professeur à la Faculté de médecine.
NOGARD, directeur de l'École vétérinaire d'Alfort.
D. ROUX, sous-directeur au laboratoire de M. Pasteur.
D. STRAUS, professeur agrégé à la Faculté de médecine.

TOME PREMIER
1887
AVEC XX PLANCHES







1890

**ANNALES
DE L'INSTITUT PASTEUR**
(JOURNAL DE MICROBIOLOGIE)
PUBLIÉES SOUS LE PATRONAGE DE M. PASTEUR
PAR
M. E. DUCLAUX
MEMBRE DE L'INSTITUT
PROFESSEUR À LA SORBONNE
Et un Comité de rédaction composé de MM.
CHAMBERLAND, chef du service à l'Institut Pasteur.
D. GRANCHIER, professeur à la Faculté de médecine.
METZENHOPF, chef du service à l'Institut Pasteur.
NOGARD, directeur de l'École vétérinaire d'Alfort.
D. ROUX, chef du service à l'Institut Pasteur.
D. STRAUS, professeur à la Faculté de médecine.

SIXIÈME ANNÉE
1892
Avec douze planches

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1892



Les liens incestueux entre les scientifiques et la presse scientifique

Les Revues dans lesquelles Didier Raoult (IHU Marseille) publie




Revue	Nombre d'articles publiés par Raoult	Editeur
New Microbes New Infect	235	Editeur : Michel Drancourt (IHU Marseille) 259 publications avec Raoult
Emerging Infect. Dis.	167	Associate Editeur : Didier Raoult
J. Clin. Microbiol.	140	
Clin. Microbiol. Infect.	135	Editeur jusqu'en 2016 : Didier Raoult
Clin. Infect. Dis.	100	
PLoS ONE	80	
Am. J. Trop. Med. Hyg.	60	
Eur. J. Clin. Microbiol. Infect...	55	
Stand Genomic Sci	55	
Int. J. Antimicrob. Agents	55	Editor-in-Chief : J.M. Rolain (IHU Marseille) 291 publications avec Raoult

7 [Complications of peripheral venous catheters: The need to propose an alternative route of administration](#). Mailhe M, Aubry C, Brouqui P, Michelet P, Raoult D, Parola P, Lagier JC. *Int J Antimicrob Agents*. 2020 Mar;55(3):105875. doi: 10.1016/j.ijantimicag.2020.105875. Epub 2020 Jan 8. PMID: 31926285

8 [New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19?](#) Devaux CA, Rolain JM, Colson P, Raoult D. *Int J Antimicrob Agents*. 2020 May;55(5):105938. doi: 10.1016/j.ijantimicag.2020.105938. Epub 2020 Mar 12. PMID: 32171740 Free PMC article.

9 [Pattern of SARS-CoV-2 infection among dependant elderly residents living in long-term care facilities in Marseille, France, March-June 2020](#). Ly TDA, Zanini D, Laforge V, Arlotto S, Gentile S, Mendizabal H, Finaud M, Morel D, Quenette O, Malfuson-Clot-Faybesse P, Midejean A, Le-Dinh P, Daher G, Labarriere B, Morel-Roux AM, Coquet A, Augier P, Parola P, Chabriere E, Raoult D, Gautret P. *Int J Antimicrob Agents*. 2020 Nov 13:106219. doi: 10.1016/j.ijantimicag.2020.106219. Online ahead of print.

Les liens incestueux entre les scientifiques et la presse scientifique



International Journal of Antimicrobial Agents
Available online 20 March 2020, 105949
In Press, Journal Pre-proof

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial

Philippe Gautret ^{a, b, c, d}, Jean-Christophe Lagier ^{a, c, e}, Philippe Parola ^{a, b}, Van Thuan Hoang ^{a, b, d}, Line Meddeb ^a, Morgane Malhe ^a, Barbara Douvier ^a, Johan Courjon ^{c, f, g}, Valérie Giordanengo ^b, Vera Esteves Vieira ^a, Hervé Tissot Dupont ^{a, h}, Stéphane Honoré ^{i, j}, Philippe Colson ^{a, c}, Eric Chabrière ^{a, c}, Bernard La Scola ^{a, c}, Jean-Marc Rolain ^{a, c}, Philippe Brouqui ^{a, c}, Didier Raoult ^{a, c, k}

^a IHU-Méditerranée Infection, Marseille, France
^b Aix Marseille Univ, IRD, AP-HM, SSA, VITROME, Marseille, France
^c Aix Marseille Univ, IRD, APHM, MEPHI, Marseille, France
^d Thai Binh University of Medicine and Pharmacy, Thai Binh, Viet Nam
^e Infectiologie, Hôpital de l'Archet, Centre Hospitalier Universitaire de Nice, Nice, France
^f Université Côte d'Azur, Nice, France
^g U1065, Centre Méditerranéen de Médecine Moléculaire, C3M, Virulence Microbienne et Signalisation Inflammatoire, INSERM, Nice, France
^h Department of Virology, Biological and Pathological Center, Centre Hospitalier Universitaire de Nice, 06200 Nice, France
ⁱ Service Pharmacie, Hôpital Timone, AP-HM, Marseille, France
^j Laboratoire de Pharmacie Clinique, Aix Marseille Université, Marseille, France

Received 16 March 2020, Accepted 17 March 2020, Available online 20 March 2020.

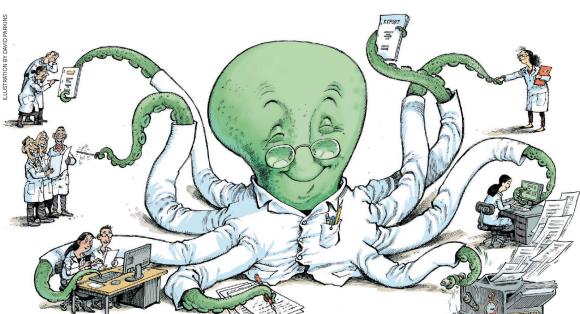
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^c Aix Marseille Univ, IRD, APHM, MEPHI, Marseille, France
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^e Infectiologie, Hôpital de l'Archet, Centre Hospitalier Universitaire de Nice, Nice, France
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^g U1065, Centre Méditerranéen de Médecine Moléculaire, C3M, Virulence Microbienne et Signalisation Inflammatoire, INSERM, Nice, France
^h Département de Virologie, Biologique et Pathologique Center, Centre Hospitalier Universitaire de Nice, 06200 Nice, France
ⁱ Service Pharmacie, Hôpital Timone, AP-HM, Marseille, France
^j Service Pharmacie Clinique, Aix Marseille Université, Marseille, France

13 SEPTEMBER 2018 | VOL 561 | NATURE | 167



The scientists who publish a paper every five days

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→ 265 hyperprolific authors

FÉVRIER 2020

Coronavirus : vers une sortie de crise ?
« L'infection respiratoire la plus facile à traiter »

Coronavirus : fin de partie !

Nombre de publications / an

Année	Nombre de publications
2008	~100
2009	~150
2010	~100
2011	~150
2012	~200
2013	~180
2014	~190
2015	~160
2016	~280
2017	~220
2018	~180
2019	~170
2020	~180
2021	~60
2022	~40
2023	~20

de 105 à 285 / an soit de 2 à 5.5 articles par semaine

TOTAL 3171 publications ; moyenne 44 citations / article

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Allied Journals	Astern Journals	Cloud Journals	EPRA Journals	EPH Journal (Engineers Publication House)
Astorn Journals	Astorn Journals	Cloud Publications	EPIX PUB (EPIX PUB)	EPRA Journals
Bonfire Publishing	Bonfire Publishing	Cloud Research & Educational In	DI Publications	EPRA Journals
Bonfire Publishing	Bonfire Publishing	Cloud Research Institute	Dorma Journals	EPRA Journals
Bonfire Publishing	Bonfire Publishing	Cloud Access	DR.BGR Publications.	EPRA Journals
Bonfire Publishing	Bonfire Publishing	Cotharis Institute	DRUNPP Sarajevs (Society for Develop	EPRA Journals
Bonfire Publishing	Bonfire Publishing	Columbia International Publishing	Dynamical Publishers	EPRA Journals
Bonfire Publishing	Bonfire Publishing	Comparative Journals	e-Century Publishing Corporation	EPRA Journals
Bonfire Publishing	Bonfire Publishing	Comprehensive Research Journals	e-Cronicon	EPRA Journals
Bonfire Publishing	Bonfire Publishing	Computer Science Journals	e-journal (shankargraph.org) also (we	EPRA Journals
Bonfire Publishing	Bonfire Publishing	CONFAB Journals	e-Science Central	ETA Maths Journals
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Bonfire Publishing	Bonfire Publishing	Conferences	e-Science Central	Eurasian Publications
Bonfire Publishing	Bonfire Publishing	Conferences	e-Science Central	Eurasian Research Publishing
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Sujet :
Hepatology healthcare partnerships

De :
Jennifer Shiflet <publisher@gastromediresonline.com>
Date :
16/01/2024 12:46

Research Gastric Management and Hepatology (ISSN: 2836-6204)

Dear Dr. Jean-Marc Cavailon

I trust this message finds you well. I am writing to you on behalf of the **“Research of Gastric Management and Hepatology”**. I hope you have had a positive experience with the recent publication of your manuscript titled "Natural Killer (NK) Cells in Antibacterial Innate Immunity: Angels or Devils? Your contribution to our journal has been invaluable.

We are continually seeking high-quality submissions to enhance the diversity and depth of our content. Given the impact of your previous contribution, we would be delighted if you could consider submitting manuscripts to the **“Research of Gastric Management and Hepatology”**.

We're excited to announce that we are planning to release our next issue by **January 31st, 2024**.

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Should you have any questions or require further information, please do not hesitate to contact me.
We genuinely appreciate your consideration and look forward to the prospect of receiving additional manuscripts from you.

Thank you for your continued support of the **“Research of Gastric Management and Hepatology”**.

Warm regards,

Jennifer Shiflet,

Editorial Coordinator,
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July 15, 2020

Asian Journal of Medicine and Health
18(7): 45-55, 2020; Article no.AJMAH.59198
ISSN: 2456-8414

Azithromycin and Hydroxychloroquine Accelerate Recovery of Outpatients with Mild/Moderate COVID-19

Violaine Guérin^{1*}, Pierre Lévy², Jean-Louis Thomas¹, Thierry Lardenois¹, Philippe Lacrosse¹, Emmanuel Sarrazin¹, Natacha Regensberg-de Andreis¹ and Martine Wonner¹

¹Collectif Laissons Les Médecins Prescrire, France.
²Département de Santé Publique, Institut Pierre-Louis de Santé Publique (INSERM UMR S 1136, EPAR Team), Sorbonne Université, Assistance Publique-Hôpitaux de Paris, Hôpital Tenon, 75020 Paris, France.

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Asian Journal of Medicine and Health
18(9): 14-21, 2020; Article no. AJMAH.60013
ISSN: 2456-8414

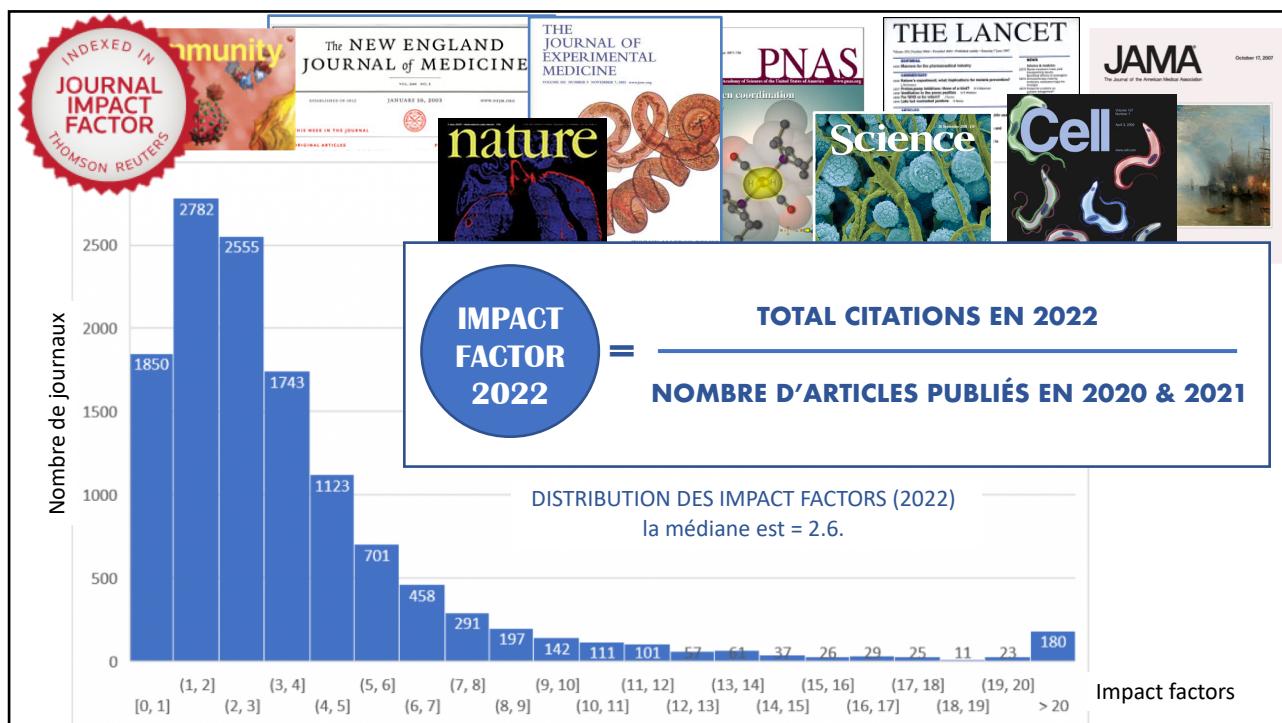
SARS-CoV-2 was Unexpectedly Deadlier than Push-scooters: Could Hydroxychloroquine be the Unique Solution?

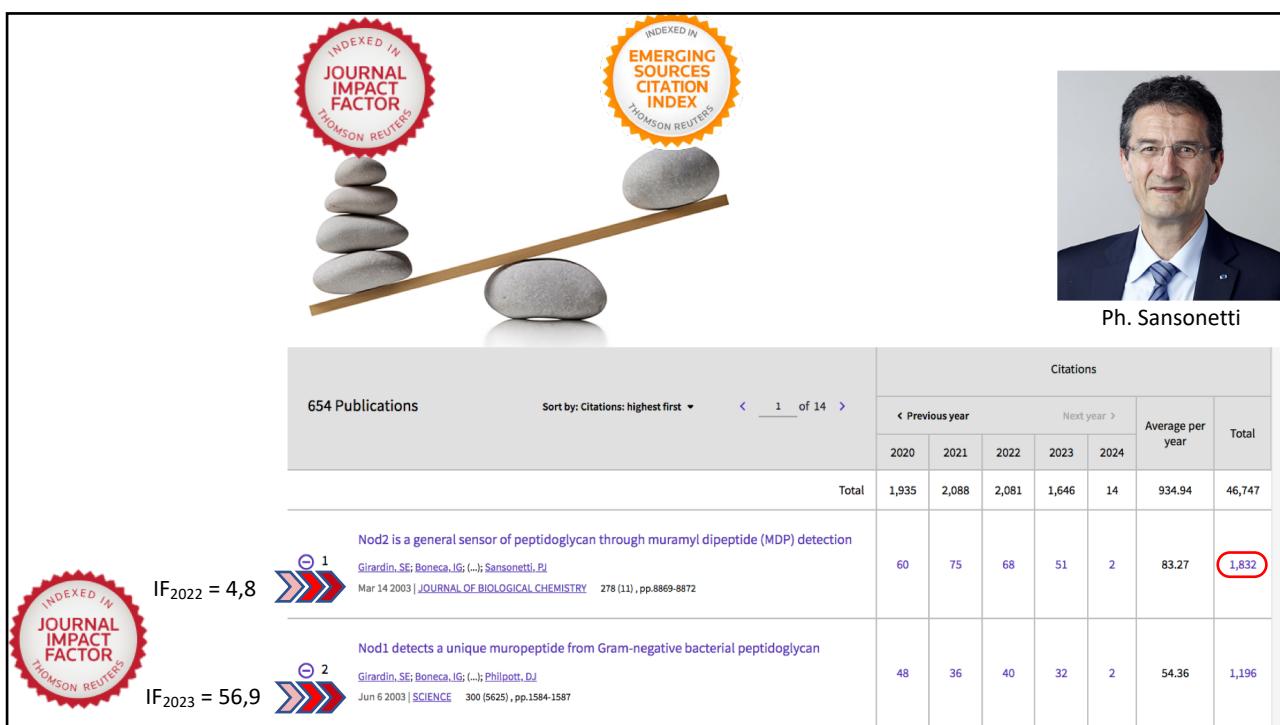
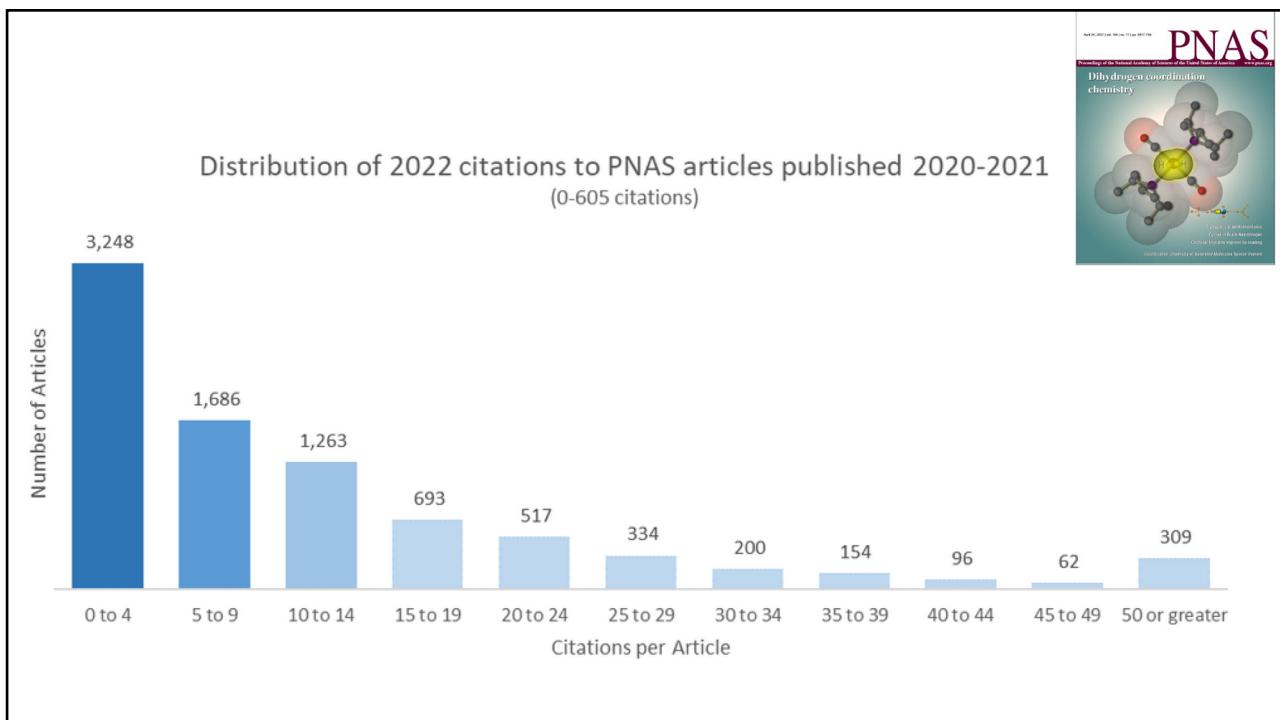
Willard Oodendijk¹, Michaël Rochoy², Valentin Ruggeri³, Florian Cova⁴, Didier Lembrouille⁵, Sylvano Trottinetta⁶, Otter F. Hantome⁷, Nemo Macron⁸ and Manis Javanica⁹

¹Belgian Institute of Technology and Education (BITE), Couillet, Belgium.
²General Practitioner and Independent Seeker of Science, Ankl, Morpork, France.
³Observatoire de Zéététique, Grenoble, France.
⁴Institute for Quick and Dirty Science, Neuchâtel, Switzerland.
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⁶Collectif Laissons les Vendeurs de Trottinette Prescrire, France.
⁷University of Melon, Melon, France.
⁸Palais de l'Elysée, Paris, France.
⁹Institute of Chiropteran Studies, East Timor.

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MA VÉRITÉ SUR LA « MÉMOIRE DE L'EAU »

Albin Michel

SCIENTIFIC PAPER
NATURE VOL. 333 30 JUNE 1988

Human basophil degranulation triggered by very dilute antiserum against IgE

E. Davenas, F. Beauvais, J. Amara*, M. Oberbaum*, B. Robinzon‡, A. Miadonna‡, A. Tedeschi‡, B. Pomeranz§, P. Fortner§, P. Belon, J. Sainte-Laudy, B. Poitevin & J. Benveniste|

