

Cycle
BIOLOGIE
ET SANTE

MARDI 17 OCTOBRE 2023
Les cytokines : le langage de nos cellules
Jean-Marc CAVALLON,

VENDREDI 8 DECEMBRE 2023
Thérapie génique : résultats, promesses et difficultés
Alain FISCHER

VENDREDI 26 JANVIER 2024
Histoire d'eau : les eaux usées, témoins des pandémies
Vincent MARECHAL

VENDREDI 9 FÉVRIER 2024
Neurosciences : la plasticité du système nerveux central
Gabriel LEPOUSEZ

VENDREDI 15 MARS 2024
Des mouches et des hommes : sentir le danger microbien
Bruno LEMAÎTRE

VENDREDI 23 AVRIL 2024
Conséquences de l'apésanteur sur le corps humain
Marc-Antoine CUSTAUD

VENDREDI 3 MAI
Intelligence artificielle au service de la santé
Jean CHARLET



Université Libre de Saint-Germain-en-Laye

Unité de Recherche
Cytokines
et Inflammation

Biologie et Santé
2023- 2024

Chief d'unité : Jean-Marc CAVALLON



LES CYTOKINES :

LE LANGAGE DE NOS CELLULES

1993 & 1996



Université Libre de Saint-Germain-en-Laye

Biologie et Santé
2023- 2024

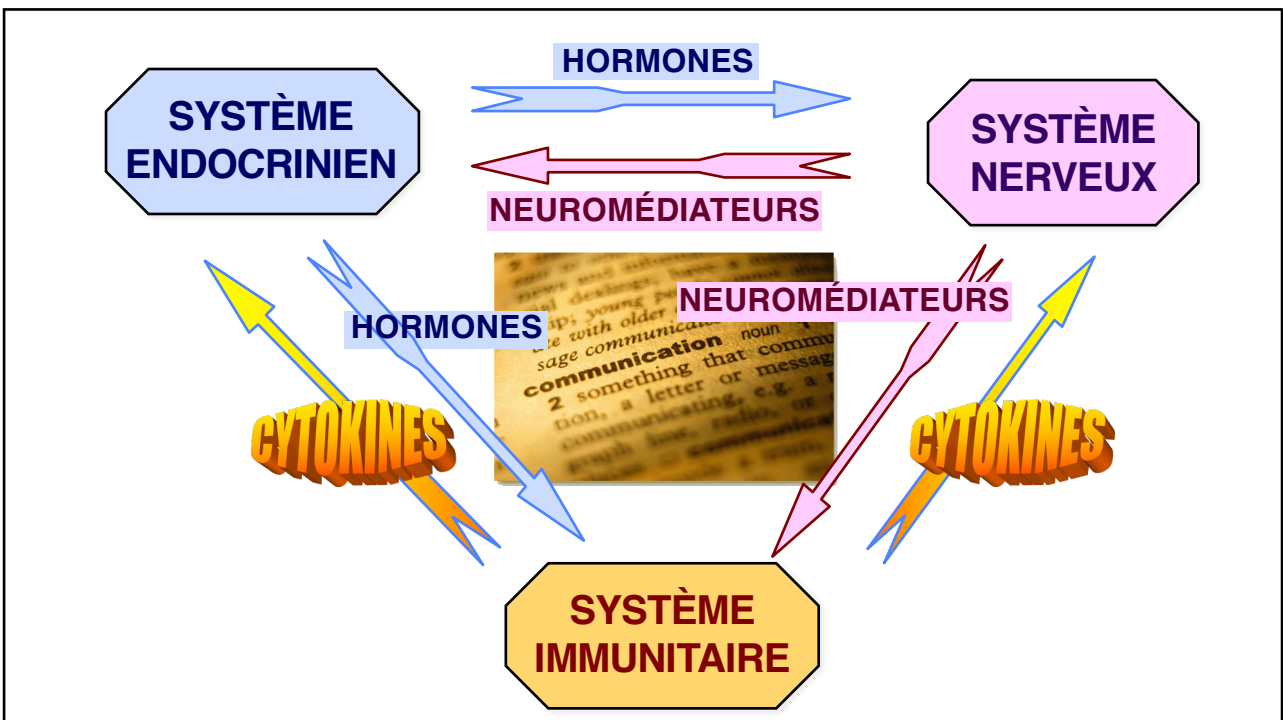
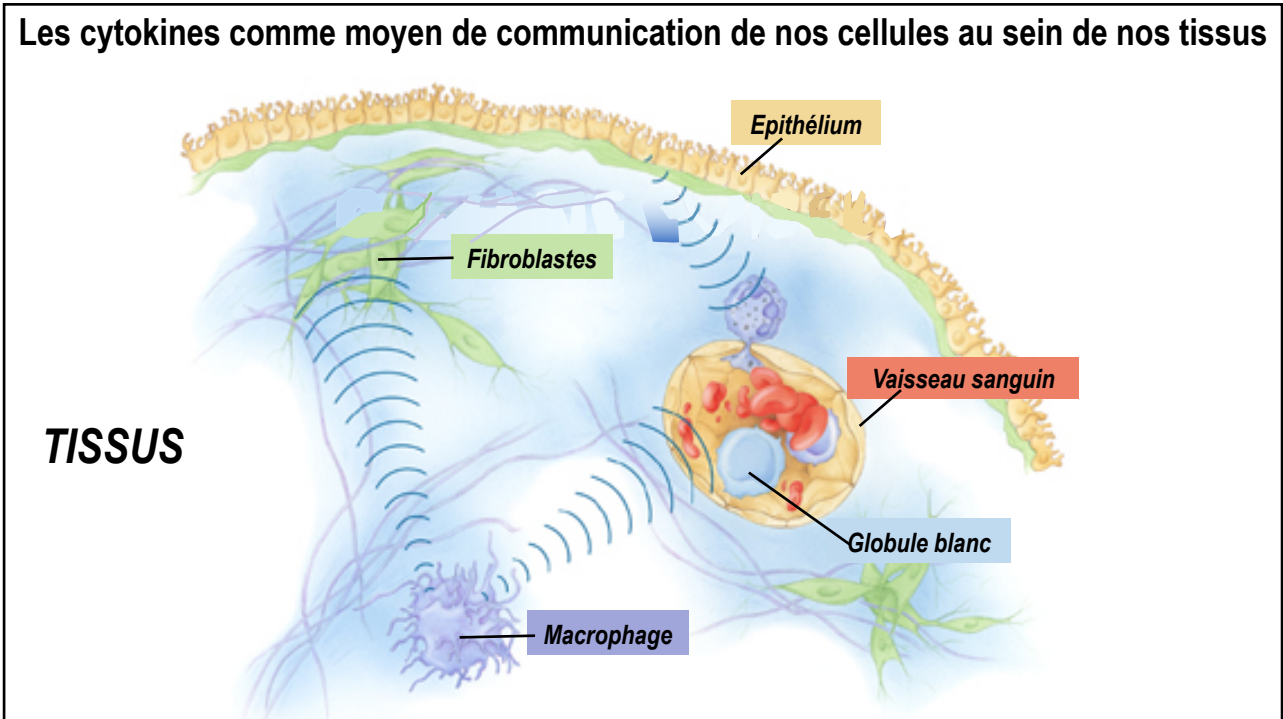
LES CYTOKINES : LE LANGAGE DE NOS CELLULES DÉFINITION



Le repas des canotiers

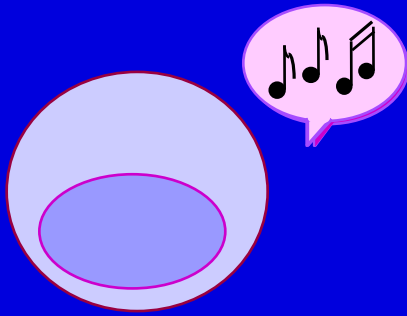
Auguste Renoir, 1881

Les cytokines comme moyen de communication de nos cellules au sein de nos tissus




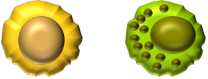












LA FAÇON DE COMMUNIQUER DES CELLULES IMMUNITAIRES : UN LANGUAGE UNIVERSEL

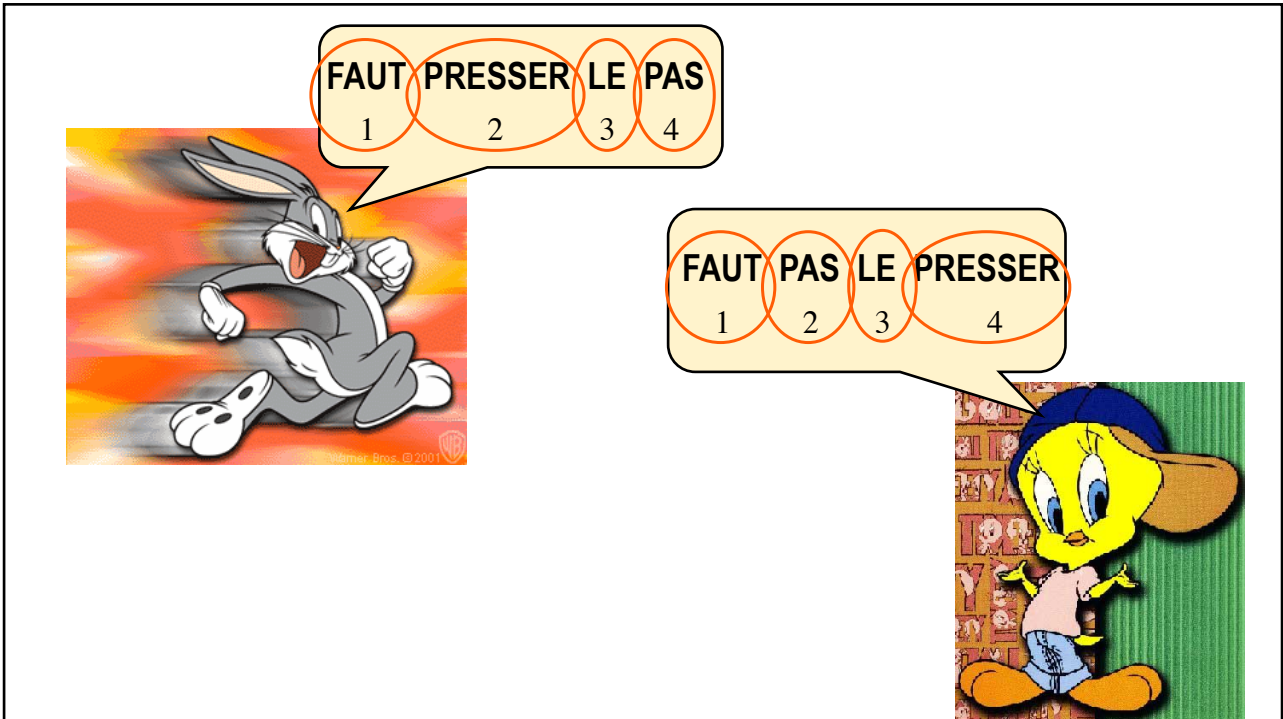
CYTOKINES



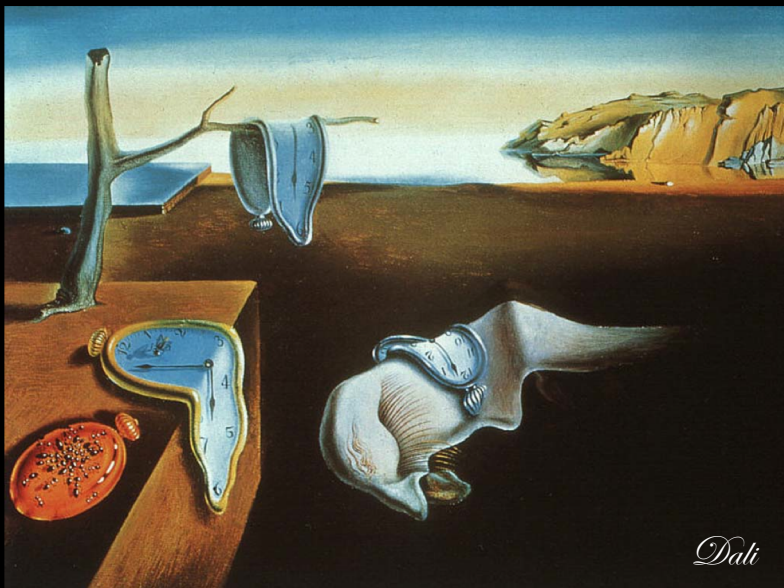
RECEPTORS

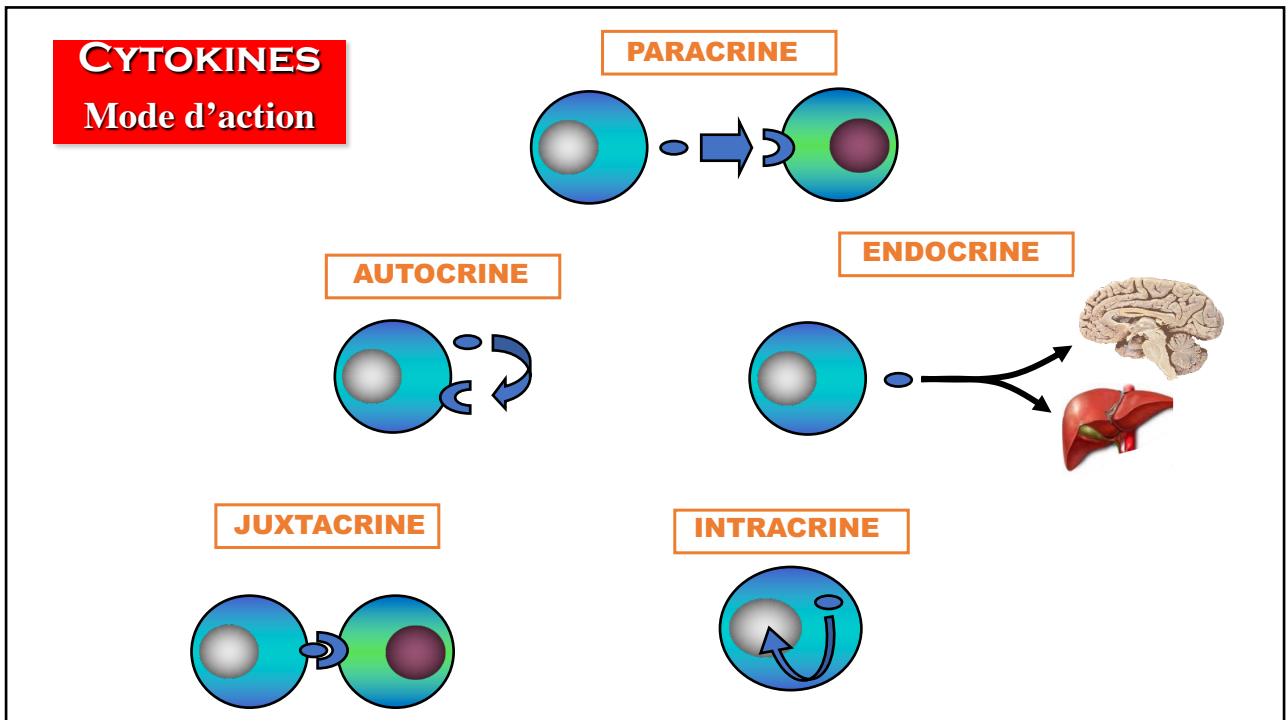
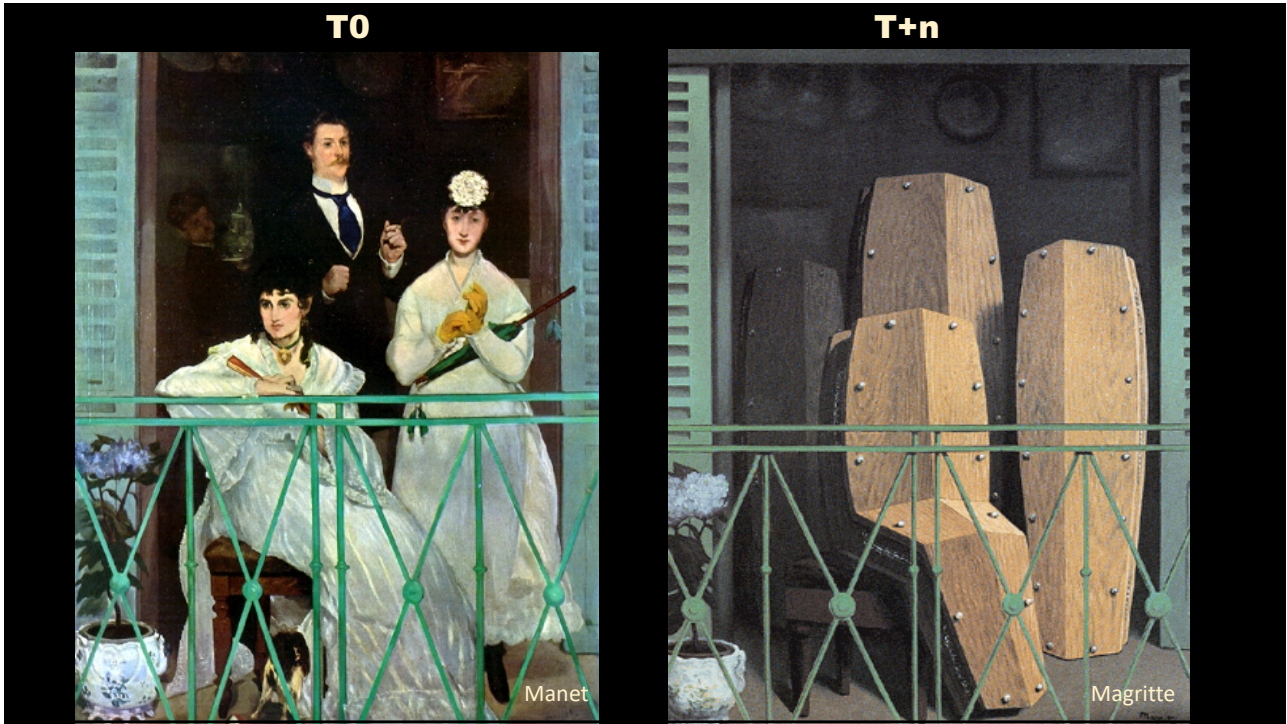


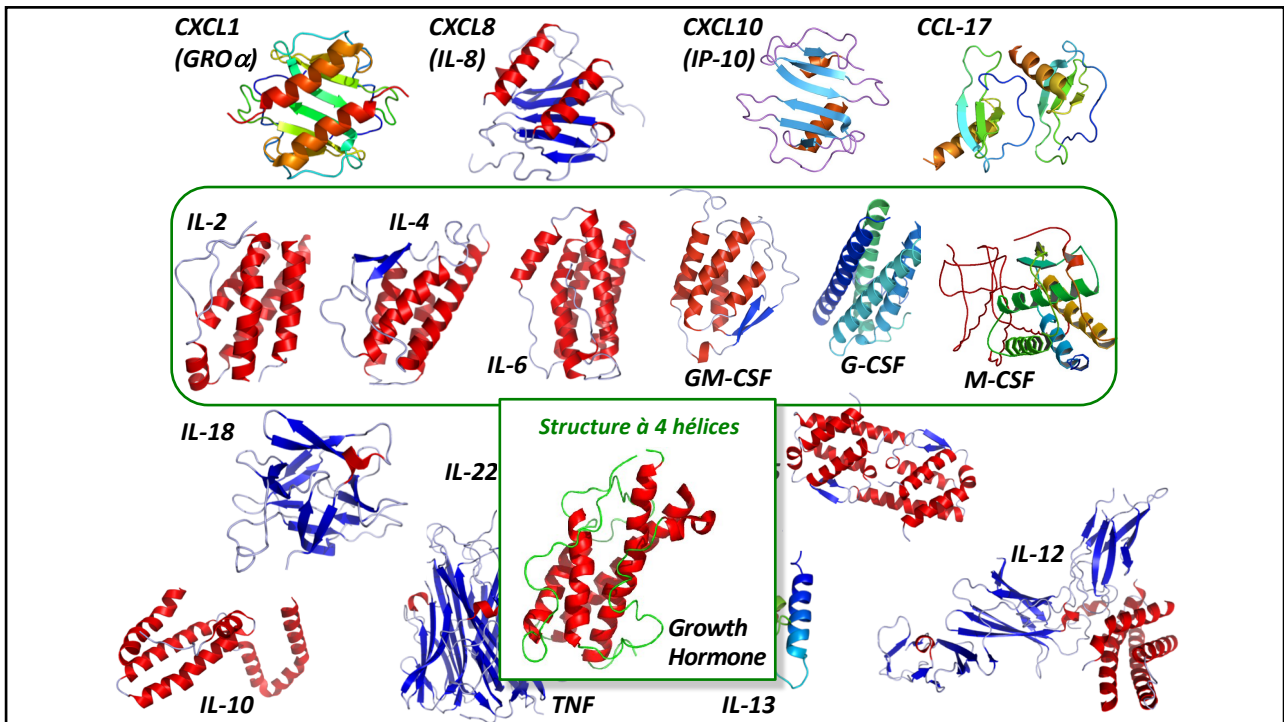
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LA SÉQUENCE DANS LE TEMPS « TIMING »








Université Libre de Saint-Germain-en-Laye

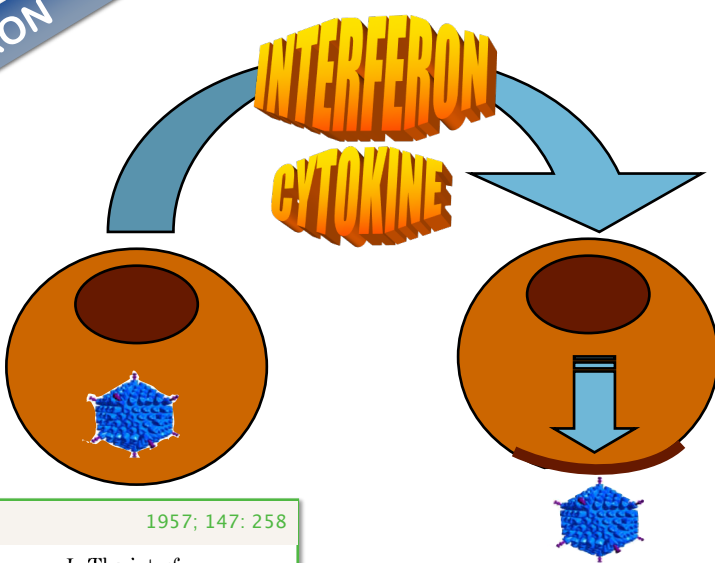
Biologie et Santé
2023- 2024

LES CYTOKINES : LE LANGAGE DE NOS CELLULES LEURS DÉCOUVERTES

1957





LONDON





INTERFERON
CYTOKINE

Infection Virale

ALICK ISAACS
(1921-1967)

JEAN LINDENMANN
(1924-2015)

PROCEEDINGS OF THE ROYAL SOCIETY 1957; 147: 258
BIOLOGICAL SCIENCES

Virus interference. I. The interferon

By A. ISAACS AND J. LINDENMANN*

National Institute for Medical Research, London

(Communicated by C. H. Andrewes, F.R.S.—Received 7 March 1957)

2007 **50TH ANNIVERSARY**

Jean Lindenmann collects the European Virology award on 2 September in Nuremberg, Germany.





2015 **Infection Virale**

Vol. 35, No. 4, April 2015
ISSN 1078-9907

Journal of Interferon & Cytokine Research

An Official Journal of the International Cytokine and Interferon Society

35TH ANNIVERSARY



Jean Lindenmann, MD
1924–2015

Mary Ann Liebert, Inc. publishers
www.liebertpub.com/jir

Virus interference. II. Some properties of interferon

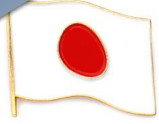
By A. ISAACS, J. LINDENMANN* AND R. C. VALENTESE

National Institute for Medical Research, London


(Communicated by C. H. Andrewes, F.R.S.—Received 7 March 1957)

Interferon could be stimulated by the action of interference induced in fragments of chloro-
allergic membranes challenged with influenza A virus. Over a ten-fold range, inverse
proportion between interferon concentration and haemagglutination titre reached by the
challenge virus was observed.


1954



INTERFERON

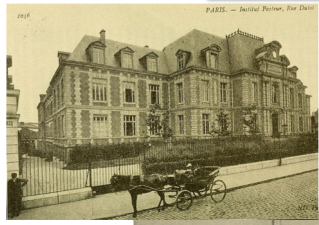



Yasu-ichi Nagano
(1906-1998)

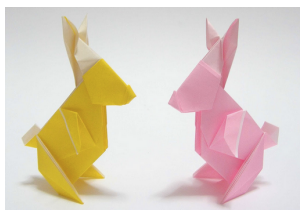


Yasuhiko Kojima
(1928-

Viral infection








Il fut envoyé à l'Institut Pasteur de Paris pour étudier la virologie pendant 2 ans (1936-1938)

Pouvoir immunisant du virus vaccinal inactivé par des rayons ultraviolets,
par Y. NAGANO et Y. KOJIMA.



Y. Nagano & Georges Stefanopoulo



Exploring Living a Longer & Healthy Life

Don't we all want to live longer, healthier lives? A little change can be a good thing!

Aging starts at 20! There's never been a better time to do something different!



1980

8 bonnes raisons de renforcer votre système immunitaire avec NutriFeron



Yasuhiko Kojima, M.D.
President and Chairman of the Board
Interferon Herb Research Institute

1. Augmente naturellement les niveaux d'interféron
2. Créé par le découvreur de l'interféron
3. 40 ans de recherche
4. Mélange breveté d'extraits de plantes stimulant l'interféron
5. Soutenu par quatre études cliniques humaines
6. Formule exclusive protégée par 3 brevets
7. Fabriqué selon les normes de qualité les plus élevées
8. Les fleurs printanières vous font pleurer





ADDITIFS

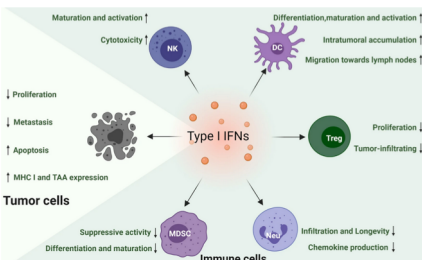


CLONAGE

1980 : INTERFÉRON alpha : 1^{ère} Cytokine humaine à avoir été clonée

Homo sapiens interferon, alpha 2 (IFNA2), mRNA
 GAGAACTGACGCTAAGGTTTACGGCTACCCATTTCAACGAGTCTAGGACATCTGGAACATCTACAATGGCTTGACCTTTGCTTACTGGTGGCCCTCTGGTCTCAGCTGCAAGCTCAAGCTCTCTCTGTGGCTGTGATCTGCTCAAAAGCCAGACGCTGGTAGCAGGAGGACCTTGTGCTCTGGCAGACA
 TGAGGAAATCTCTTTCTCTCTGCTTGAAGCAGACAGACACTTGGATTTCCAGGAGGAGGTTTGGCAACGACTTCCAAAGGCTGAAACCATCCCTCTCTCATGAGATGATCAAGCAGATCTCAATCTTTCAGCACAAAGACCTCATCTCTGCTGGATGAGACCTCTCAACAAATCTACACTGA
 ACTTACGACAGCTAATGACCTGGAAAGCTGTGTGTATACAGGGGGTGGGGTGACAGACACTCCCTGATGAAGAGGACTCCATTCTGGCTGTGAAGAAATCTTCAAAAGATCACTCTCTATCTGAAAGAGAAATACAGCCCTTGTGGCTGGGAGGTTGTGACAGAGAAATCATGACATCTTTCTTT
 GTCACAAACTTGGCAAGAGTTTAAAGAGTAAAGCAATCAAAAGCTGTTCAACATGGAATGATTTTATTGATTCATGATGCACTTCTTTATGATGCTCAATTCAGACACTCAGTTTCTGCTATGACCATGACAGCAATTAAATCTTTCAAAATGTTTAAAGCATTAAATCAACATGATTTACCTTTA
 AGCCACTGCTCTTACAGAGCAGCTGCTGACTGATGCTATTATTAATATTTTAAATATTATTATTAACTATTATTAAGAAAGCACTTTATTTGTCATATTGCTATGCACTGCTGATGCTGATGATTAATTAAGAAATGTTGTTCTGTATTTGGTAAATTTATTTGTGTGCTGATGCACTTTG
 TATGGAATTTGTACTGTTTATCTTTAAATGAAATCCAGCCTAATTTGCCAACCATTACAGAATACTGGTCACTCTATTGTCATCAATATTATTAATCAAGATATAAGTAAATAAATCTTCTGTAACCA

1982 : INTERFERON alpha : 1^{ère} cytokine utilisée chez des patients



Horning et al.
Clinical and immunologic effects of recombinant leukocyte A interferon in eight patients with advanced cancer.
 JAMA 1982 Mar 26; 247: 1718-22

Sherwin et al.
A multiple-dose phase I trial of recombinant leukocyte A interferon in cancer patients.
 JAMA 1982 Nov 19; 248: 2461-6.





CLONAGE

1980 : INTERFÉRON alpha : 1^{ère} Cytokine humaine à avoir été clonée

Homo sapiens interferon, alpha 2 (IFNA2), mRNA

GACAGCTGGACCTAAGGTTACGGCTACCGATTTCACACTCTAGCAGGATCTGCAGAACTACAAAGCCCTGACCTTTCTTTACTGTGGCCCTCTGCTGCTCAGCTGCAAGTCAAGCTCTCTGTGGCTGTGATCTGCCTCAAAAGCAGAGCTGGGTAGGAGGAGCTTGTCTCTGGACAGATCGAGGAACTCTCTTTCTCTCTCTCAAGCAGACATCACTTTCGATTTCCAGCAGCAGCTTTCGCAAGCAGCTTCCAAAGCCCTGCAAAAGCCCTGCTCTCATGATGATGATCAGCAGATCTCAATCTCTTCAGCACAAAGCAGCTCTCTCTCTGGATCAGACCTCTAGACAAATCTACACTGACTCTACCCAGCAGCTGAATGACCTGGAAAGCTGTGTGATACAGGGGGTGGGGGTGACAGAGCCTCCCTGATGAAGGAGGACTCCATTCTGGCTGTGAGGAAATCTTCCAAAGATCACTCTCTACTGAAAGAGAAATACAGGCCCTTGTCCCTGGAGGTTGTGACAGGAGAAATCATGAGATCTTTCTTTGTCAACAACCTTCCAAAGGTTTAAAGAGTACCAATCAAACTGCTTCACATCGAAATGATTTTCATTTGATTCGATCCAGCTCAGCTTTTATGATCTGCCATTTTCAAGACTCATGTTTCTGCTATGACCATGACAGCATTAAATCTTTCAAAATGTTTATAGGAGTATTAATCAACATTTGATTCAGCTTTAAGGACTTCTCTTACAGAGCAGCTGCTGACTGATCCGATATCTAATTAATATTTTAAATATTTTAAATATTTTAACTATTTTAAAGAACTTATTTTGTGATATGATGATGATGACCTTTGACAGCTGTTTAAATGTTTGTGATTTGGTAAATTTTGTGTTGATTCAGCTTTGCTATGGAATTTGACTGTTTATCTTTAAATCAAAATCCAGCCTAATTTGCAACCTGATACAGAACTGCTGACACTCTATTGCTCATCAATATATATATCAAGATAACTAAATAAATCTTCTGTAAGCA

1993 : INTERFERON beta : utilisée dans la sclérose en plaques



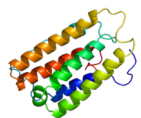
Knobler et al.
Systemic recombinant human interferon-beta treatment of relapsing-remitting multiple sclerosis: pilot study analysis and six-year follow-up.
J Interferon Res. 1993; 13: 333-40



SARS-COV-2

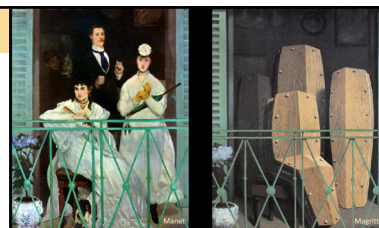
COVID-19

2020 : INTERFERON alpha : utilisée dans le COVID-19



Cell Host & Microbe 2020 Sep 9;28(3):455
Retrospective Multicenter Cohort Study Shows Early Interferon Therapy Is Associated with Favorable Clinical Responses in COVID-19 Patients

Nan Wang,^{1,15} Yan Zhan,^{2,5,15} Linyu Zhu,^{4,15} Zhibing Hou,⁵ Feng Liu,⁵ Pinhong Song,⁵ Feng Qiu,⁵ Xiaolin Wang, Xiaofei Zou,⁷ Deyun Wan,⁵ Xiaosong Qian,⁵ Shanshan Wang,² Yabi Guo,² Hao Yu,² Miao Cui,⁵ Gangling Tong,¹⁰ Yunsheng Xu,^{1,4} Zhihua Zheng,¹¹ Yingying Lu,^{1,15} and Peng Hong^{1,15,14,15*}



PRÉCOCE

TARDIF

L'administration précoce d'interféron-α2b a été associée à une réduction de la mortalité hospitalière. En revanche, le traitement tardif par interféron a augmenté la mortalité et retardé la récupération, ce qui suggère que le moment du traitement par interféron est crucial pour des réponses favorables chez les patients COVID-19.



BÉNÉFIQUE

DÉLÉTÈRE

#2

Macrophage Migration Inhibitory Factor (MIF)

1 JULY 1966

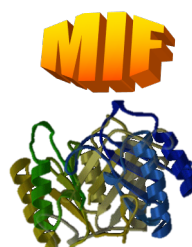

SCIENCE, VOL. 153

Mechanism of a Reaction in Vitro Associated with Delayed-Type Hypersensitivity

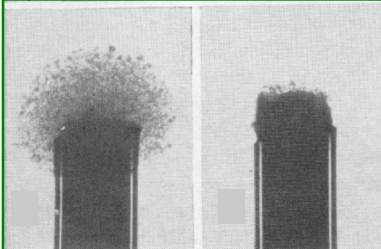
Abstract. The cell type responsible for inhibition by antigen of migration in vitro of peritoneal exudate cells obtained from tuberculin-hypersensitive guinea pigs was studied. Exudate populations were separated into component cell types, the lymphocyte and the macrophage. Peritoneal lymphocytes from sensitive donors were the immunologically active cells in this system, the macrophages being merely indicator cells which migrate. Sensitized peritoneal lymphocyte populations, upon interaction with specific antigen in vitro, elaborated into the medium a soluble material capable of inhibiting migration of normal exudate cells.

BARRY R. BLOOM
BOYCE BENNETT

Department of Microbiology and Immunology and Department of Pathology, Albert Einstein College of Medicine, New York 10461

HARVARD
School of Public Health



38 NATURE VOL. 224 OCTOBER 4 1969

"Lymphokines": Non-Antibody Mediators of Cellular Immunity generated by Lymphocyte Activation

by
D. C. DUMONDE
R. A. WOLSTENCROFT
G. S. PANAYI
MARGARET MATTHEW
J. MORLEY
W. T. HOWSON*

*Division of Immunology, Kennedy Institute of Rheumatology, Hammersmith, London W6, and Department of Immunology, Wright-Fleming Institute, London W2

Four principal features of cellular immunity in the 'guinea-pig' are mediated by a group of soluble factors generated by antigen-activated lymphocytes. These "lymphokines" are different from classical antibodies.

Lymphokine

Dumonde et al
Nature 1969, 224, 38

#2


Macrophage Migration Inhibitory Factor (MIF)

The American Journal of **PATHOLOGY**
Cellular and Molecular Biology of Disease

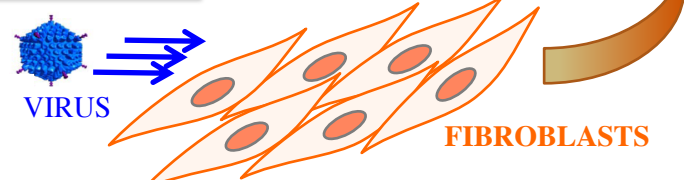
1975; 80(1): 69-78.

Production of Lymphokine-Like Factors (Cytokines) by Simian Virus 40-Infected and Simian Virus 40-Transformed Cells

Pierluigi E. Bigazzi, MD, Takeshi Yoshida, MD, Peter A. Ward, MD, and Stanley Cohen, MD



Macrophage migration inhibitory factor



FIBROBLASTS


1974

CELLULAR IMMUNOLOGY 12, 150-159 (1974)


COMMENTARY

Similarities of T Cell Function In Cell-Mediated Immunity and Antibody Production¹

STANLEY COHEN, PIERLUIGI E. BIGAZZI, AND TAKESHI YOSHIDA
Departments of Microbiology and Pathology, State University of New York at Buffalo, Buffalo, New York 14214




CYTOKINE




Stanley Cohen
Pathologist

2004




Founded 1989



CYTOKINE
The Official Journal of the International Cytokine Society

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National Institute for Biomedical Research, United Kingdom



CYTOKINE
www.elsevier.com/locate/cytokine

Cytokine 28 (2004) 242–247

Cytokine: more than a new word, a new concept proposed by Stanley Cohen thirty years ago

In 1974, Cohen et al. (Cohen S, Bigazzi PE, Yoshida T. Similarities of T cell function in cell-mediated immunity and antibody production. *Cell Immunol* 1974;12:150–9) introduced for the first time the word “cytokine”. To commemorate this 30-year anniversary, we interviewed him.

Could you remind us the main steps of your career?


I attended Columbia University (BA and MD) and trained in Pathology at Harvard, followed by a fellowship with Drs. Baruj Benacerraf and Robert McCluskey at NYU. My initial research was done at the University of Buffalo and the University of Connecticut. Currently I am Chair of the Department of Pathology at the University of Medicine and Dentistry-New Jersey Medical School. I Co-chaired five of the International Lymphokine Workshops, and served on NIH and DOD Study Sections, as well as the editorial boards of several journals. I won the Parke–Davis Award in 1977 for work on the in vivo role of lymphokines, and for the work that led to the identification of cytokines as a new category of biologic mediator. In 1986, I received a seven-year “Outstanding Investigator Award” from the NIH for research in these areas. I am currently the Secretary–Treasurer of the American Society of Investigative Pathology.

What was your main field of investigation in 1974?

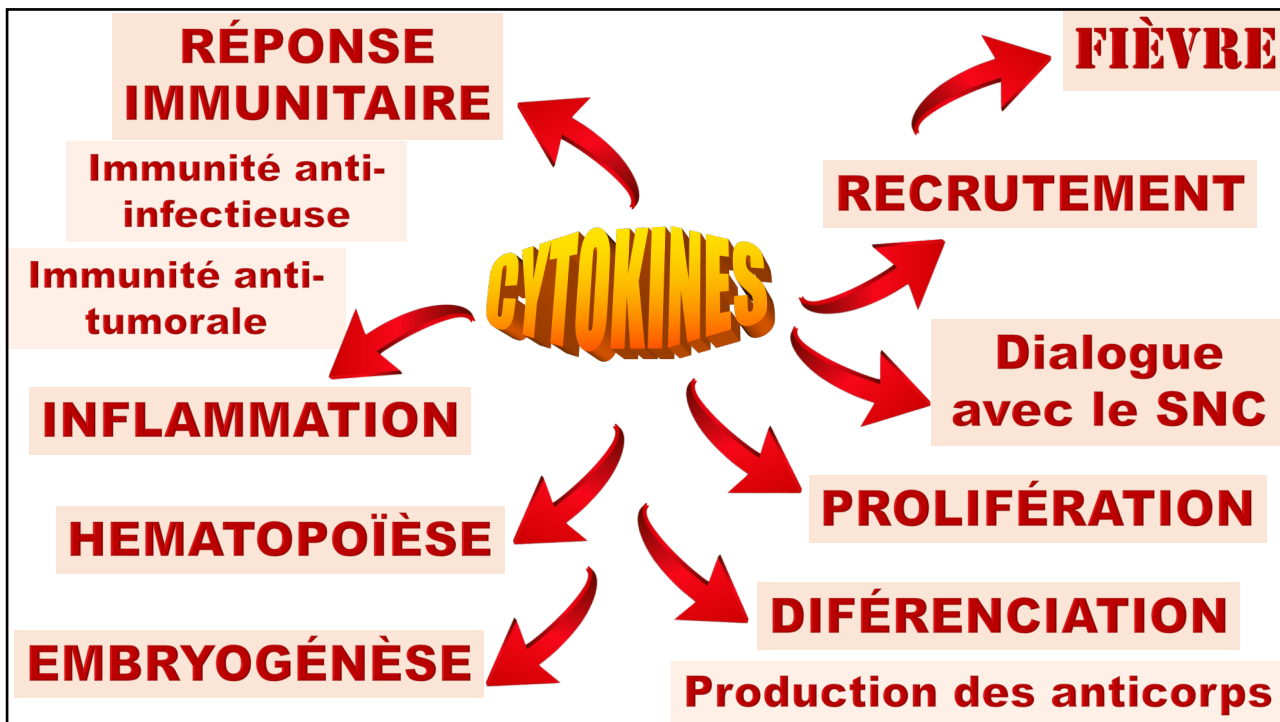
my work therefore focused on demonstrating in vivo roles for them. Takeshi Yoshida and I were able to demonstrate that lymphokines were produced in vivo, that they could be identified at reaction sites of cellular immunity, and that the injection of these factors into intact animals induced physiologic or pathologic responses, depending upon experimental conditions. Mine was also one of two laboratories (the other being that of Carolyn Gezcy and Alain deWéck) to simultaneously first describe the successful production of anti-lymphokine antibodies, and my group was able to use these to confirm in vivo presence and activity of lymphokines.

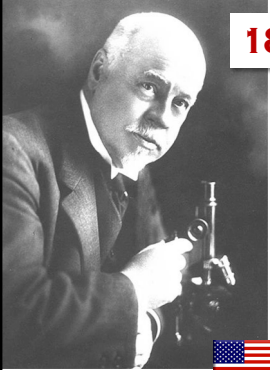
Do you remember how you went to work? Was it long before it appeared in other words could you tell how occurred the word “cytokine”?

In the course of the above work, cells, as well as T cells, could not be identified from either source had been described, and antigenic products of lymphocytes could make such mediators, but what was special about lymphocytes was their capacity to make mediators, but antigen could stimulate them to do so. I described MIF-like activity in fibroblasts those days. MIF was quantitated by



Stanley Cohen
Pathologist





1888

A quoi ça sert ?


FIÈVRE

Vol. CXVIII, No. 17.] *BOSTON MEDICAL AND SURGICAL JOURNAL.* 413

Lecture.

CARTWRIGHT LECTURES.1
THE GENERAL PATHOLOGY OF FEVER.

BY WILLIAM H. WELCH, M.D.,
Professor of Pathology, Johns Hopkins University, Baltimore.



WILLIAM H. WELCH
(1850 - 1934)

Physician, pathologist,
bacteriologist

" Le véritable ennemi dans la plupart des fièvres est la substance nocive qui envahit le corps, et rien n'empêche de penser que la fièvre est une arme employée par la Nature pour combattre les assauts de cet ennemi."

" Selon cette conception, les agents qui induisent la fièvre allument le feu qui les consume. Il n'est pas incompatible avec cette conception de la fièvre, de supposer que l'incendie peut également s'avérer préjudiciable aux patients et nécessiter la main salvatrice du médecin."



1944

Un médiateur endogène ?


FIÈVRE

Isolation à partir d'exudats inflammatoires

PYREXIN

VALY MENKIN
(1901-1960)

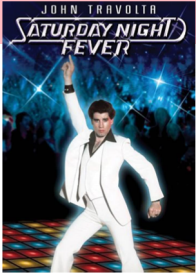


HARVARD
MEDICAL SCHOOL

Science 1944, 100, 337

Chemical basis of fever

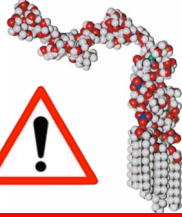

Vally Menkin
*Harvard University Medical school,
Boston*




The Lancet 1958, Jul 12 : 53-7

The role of endogenous pyrogen in the genesis of fever

Barry Wood
John Hopkins University, Baltimore



→ Contamination en endotoxines bactériennes

1953

Un médiateur endogène ?

FIÈVRE

Extraction d'une substance pyrogène à partir des neutrophiles de lapin.



Ivan L. Bennet Jr
1922 - 1990



Paul Beeson
1908 - 2006

J. Exp. Med. 1953, 98, 493

STUDIES ON THE PATHOGENESIS OF FEVER

II. CHARACTERIZATION OF FEVER-PRODUCING SUBSTANCES FROM POLYMORPHONUCLEAR LEUKOCYTES AND FROM THE FLUID OF STERILE EXUDATES*

BY IVAN L. BENNETT, JR., M.D., AND PAUL B. BEESON, M.D.
WITH THE TECHNICAL ASSISTANCE OF ELIZABETH ROBERTS

From the Department of Internal Medicine, Yale University School of Medicine, New Haven)

IL-1

1955

Pyrogène endogène circulant dans le sang après l'injection du vaccin contre la typhoïde.



Elisha Atkins
1921 - 2005



W. Barry Wood Jr.
1910 - 1971

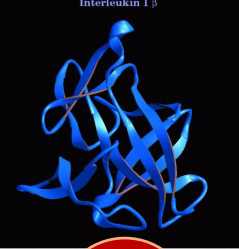
J. Exp. Med. 1955, 101, 519

STUDIES ON THE PATHOGENESIS OF FEVER

I. THE PRESENCE OF TRANSFERABLE PYROGEN IN THE BLOOD STREAM FOLLOWING THE INJECTION OF TYPHOID VACCINE*

BY ELISHA ATKINS, M.D., AND W. BARRY WOOD, JR., M.D.

(From the Department of Medicine, Washington University School of Medicine, and the Barnes and Wohl Hospitals, St. Louis)

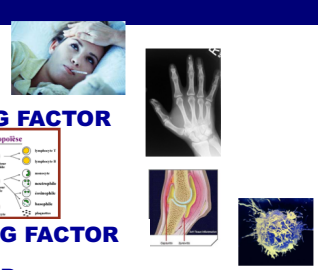


Interleukin 1 β

INTERLEUKINE-1

ACTIVITÉS
BIOLOGIQUES

- 1953 **ENDOGENOUS PYROGEN**
- OSTEOCLAST ACTIVATING FACTOR**
- HEMOPOIETIN-1**
- CATABOLIN**
- 1972 **LYMPHOCYTE ACTIVATING FACTOR**
- EPIDERMAL-CELL DERIVED THYMOCYTE ACTIVATING FACTOR**
- 1981 **EPIDERMAL-CELL DERIVED THYMOCYTE ACTIVATING FACTOR**

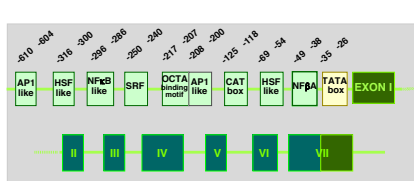



IL-1

1977 - Caractérisation biochimique
=> 17.5 kDa ; 2 l.p. = 5.0 & 7.0


1984 / 85 - Clonage des gènes
(6 coding exons)
Chromosome 2 [Humain & Souris]
PRECURSEUR = 30 kDa
2 GÈNES IL-1 α & IL-1 β (26% homologie)

1979 - INTERLEUKINE-1



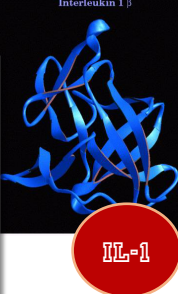


CHARLES DINARELLO



CHARLES DINARELLO

INTERLEUKINE-1

Interleukin 1 

PNAS Proceedings of the National Academy of Sciences of the United States of America

December 1984, Vol.81, pp.7907-11

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 a soumis à Nature le clonage de l'IL-1 humaine

↳ Le journal Nature rejeta le manuscrit!

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

Les avocats ont découvert que le brevet d'Immunex sur l'IL-1β (déc. 1984) contenait les mêmes neuf erreurs nucléotidiques aux mêmes endroits que dans l'article de Dinarello ! (les erreurs avaient été corrigées dans l'article Immunex Nature)





CHARLES DINARELLO

INTERLEUKINE-1

Search by name or affiliation		Immunology	All countries
4	3	 Charles A. Dinarello University of Colorado Anschutz Medical Campus, United States	224 189,803 1,064
1	1	 Shizuo Akira Osaka University, Japan	226 241,364 754



CARLOS MUÑOZ

IL-1β & TNFα radio-immunoassays

Institut Pasteur
Jean-Marc Cavallion, DRSc
 Unit "Cytokines & Inflammation"
 28 rue du Dr. Roux, 75015 Paris
 jean-marc.cavallion@pasteur.fr
 331 45 68 62 38

Prof. Eric M. Poeschla, M.D.
 Till Gill Professor
 Chief, Division of Infectious Diseases
 University of Colorado Denver
 12700 East 19th Ave., B168
 Aurora, CO 80045 - USA

Re. Nomination of Prof. Charles Dinarello for "Distinguished Professor"

Dear Prof. Poeschla,

It is a great honor for me to write this recommendation letter for the nomination of Prof. Charles Dinarello for "Distinguished Professor" at the University of Colorado. As a scientist working in the same field of research as Charles Dinarello, I have known his work for more than three decades. Interestingly, I indirectly owe him my best paper, when I welcomed a post-doc who had acquired in his lab the mastering of radioimmunoassays to measure IL-1 and TNF, at a time ELISA did not exist. We have even been in competition to demonstrate that chronic hemodialysed patients were making IL-1 during their dialysis session!

Of course, reading his CV is sufficient to be convinced that Charles Dinarello is one of the most outstanding and famous world scientists. He has been regularly awarded by his peers from all over the world for his key contributions in the field of innate immunity, cytokines and inflammation, linking basic investigations to clinical research. Among his many awards, let's mention the "Paul Ehrlich and Ludwig Darmstaedter Prize" (2010), the most prestigious German award, and the "Albany Medical

16

INTERLEUKINE-1

1982

Une des toutes premières démonstrations concernant la présence d'IL-1 dans un fluide biologique lors d'une inflammation

INFECTION AND IMMUNITY, Dec. 1982, p. 1190-1195
0019-9567/82/121190-06\$02.00/0
Copyright © 1982, American Society for Microbiology

Vol. 38, No. 3

Increased Thymocyte-Activating Factor in Human Gingival Fluid During Gingival Inflammation

JACQUES A. CHARON, THOMAS A. LUGER, STEPHAN E. MERGENHAGEN,* AND JOOST J. OPPENHEIM

Laboratory of Microbiology and Immunology, National Institute of Dental Research, Bethesda, Maryland 20205



INTERLEUKINE-1

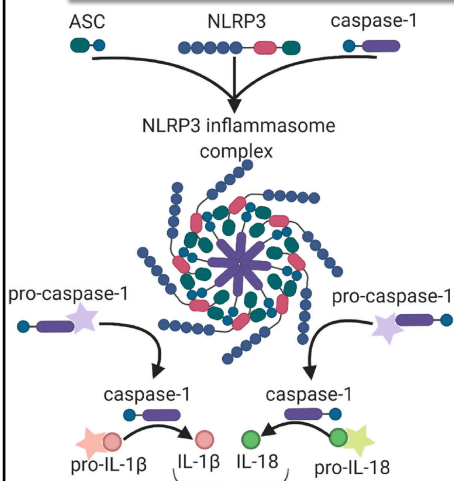
Molecular Cell, Vol. 10, 417-426, August, 2002

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)



ADDITIFS




1984, Vol., pp.



PNAS
Proceedings of the National Academy of Sciences of the United States of America

IDENTIFICATION OF A NEW BIOACTIVITY IN LYMPHOCYTES SUPERNATANTS

THE X FACTOR : a new cytokine ?
7 publications till 1990



... Un artefact du à une contamination en mycoplasmes



Université Libre de Saint-Germain-en-Laye

Biologie et Santé
2023- 2024

LES CYTOKINES :
LE LANGAGE DE NOS CELLULES
LEURS NATURES

CYTOKINES

INTERFERONS

INTERLEUKINS

TUMOR NECROSIS FACTOR & Co

CHEMOKINES

HEMATOPOIETIC FACTORS

INTERFERONS

1954 → "Facteur inhibiteur"

1957 → "INTERFERON" : IFN Type I

IFN α (n=13), **IFN β** (n=1), **IFN ϵ** (n=1), **IFN ω** (n=5), **IFN τ** (n=0)

1975 → "Macrophage activating factor"

→ "immune interferon" (≡ 1982)

IFN Type II : IFN γ

2003 → IFN Type III : IFN $\lambda_{2,3,1}$ (IL-28A,B, IL-29)

2013 → Human IFN λ_4 gene / pseudogene

→ Murine IFN λ_1 & IFN λ_4 pseudogenes

CYTOKINES

INTERLEUKINES :

1979 → IL-1 & IL-2

2023 → IL-1 → IL-41



TUMOR NECROSIS FACTOR

1975 → TNF



Beutler et al. Identity of tumour necrosis factor and the macrophage-secreted factor **CACHECTIN**.
Nature 1985; 316:5 52-4

2023 → 19 members
of the TNF superfamily



TUMOR NECROSIS FACTOR

1898

LA TOXINE DE COLEY : ACTIVITÉ ANTI-TUMORALE



WILLIAM B. COLEY
(1862–1936)

Les propriétés anti-tumorales des toxines bactériennes ont été démontrées par William Coley à New York

J. Am. Med. Ass. 1898, **31**: 465.
THE TREATMENT OF INOPERABLE SARCOMA WITH THE MIXED TOXINS OF Erysipelas and Bacillus prodigiosus.
 IMMEDIATE AND FINAL RESULTS IN ONE HUNDRED AND FORTY CASES.
 Presented to the Section on Surgery and Anatomy, at the Forty-ninth Annual Meeting of the American Medical Association, held at Denver, Colo., June 7-10, 1898.
 BY WILLIAM B. COLEY, M.D.
 ATTENDING SURGEON TO THE NEW YORK CANCER HOSPITAL; ASSISTANT SURGEON TO THE HOSPITAL FOR RUPTURED AND CRIPPLED. NEW YORK, N. Y.

S. pyogenes

Serratia marcescens

ENDOTOXINE BACTÉRIENNE

1975



10 - 14 jours



2 h – Récolte du sérum



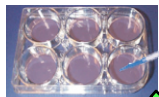
Proc. Nat. Acad. Sci. USA
 Vol. 72, No. 9, pp. 3666-3670, September 1975
 Immunology

An endotoxin-induced serum factor that causes necrosis of tumors (activated macrophage)

E. A. CARSWELL, L. J. OLD, R. L. KASSEL, S. GREEN, N. FIORE, AND B. WILLIAMSON

La découverte du 'tumor necrosis factor'

MACROPHAGES IN CULTURE

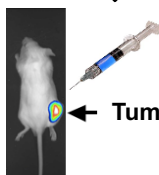


Endotoxine

Récolte du milieu de culture



TEST DE L'ACTIVITÉ TNF



Tumeur

1 Jour

NECROSE DE LA TUMEUR



Lignée de cellules fibroblastique

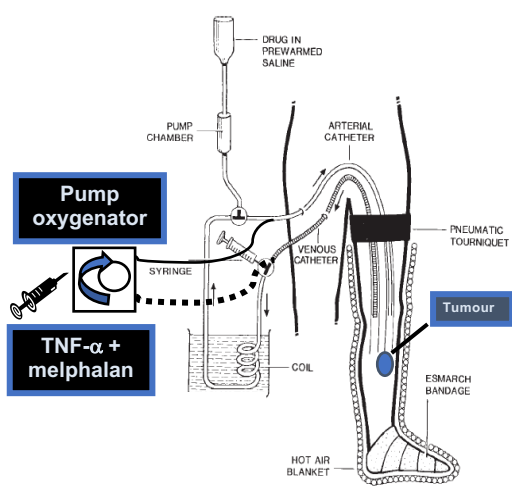


48 h

LYSE CELLULAIRE



Perfusion de membres isolés pour les sarcomes de membres localement avancés avec TNF et melphalan



Before TNF- α

Merkel's tumor

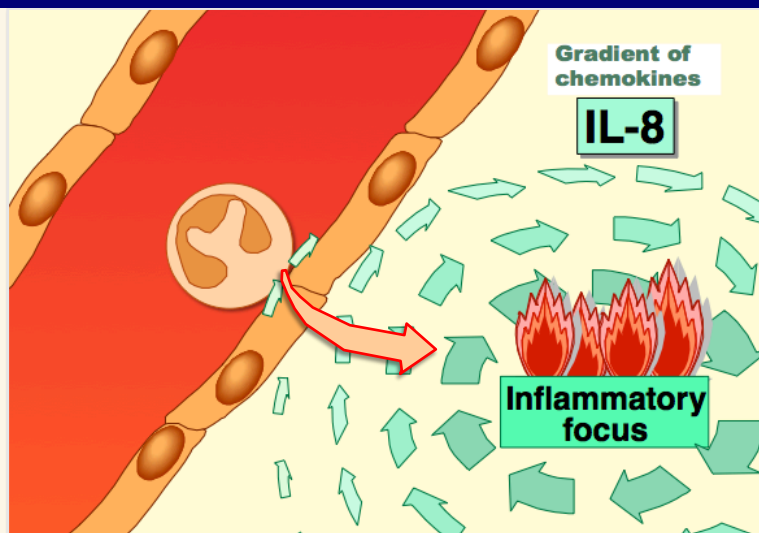
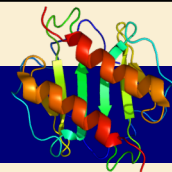


After TNF- α

n = 100 patients
 4 different doses \rightarrow 36% complete remission
Bonvalot et al. Ann of Oncol 2005

**CHIMIOTACTISME
 CHÉMOKINES**

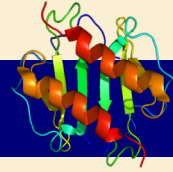
(1992)



CHIMIOTACTISME

(1992)

CHÉMOKINES



1957 → anti-heparin factor (1964 = PF4)

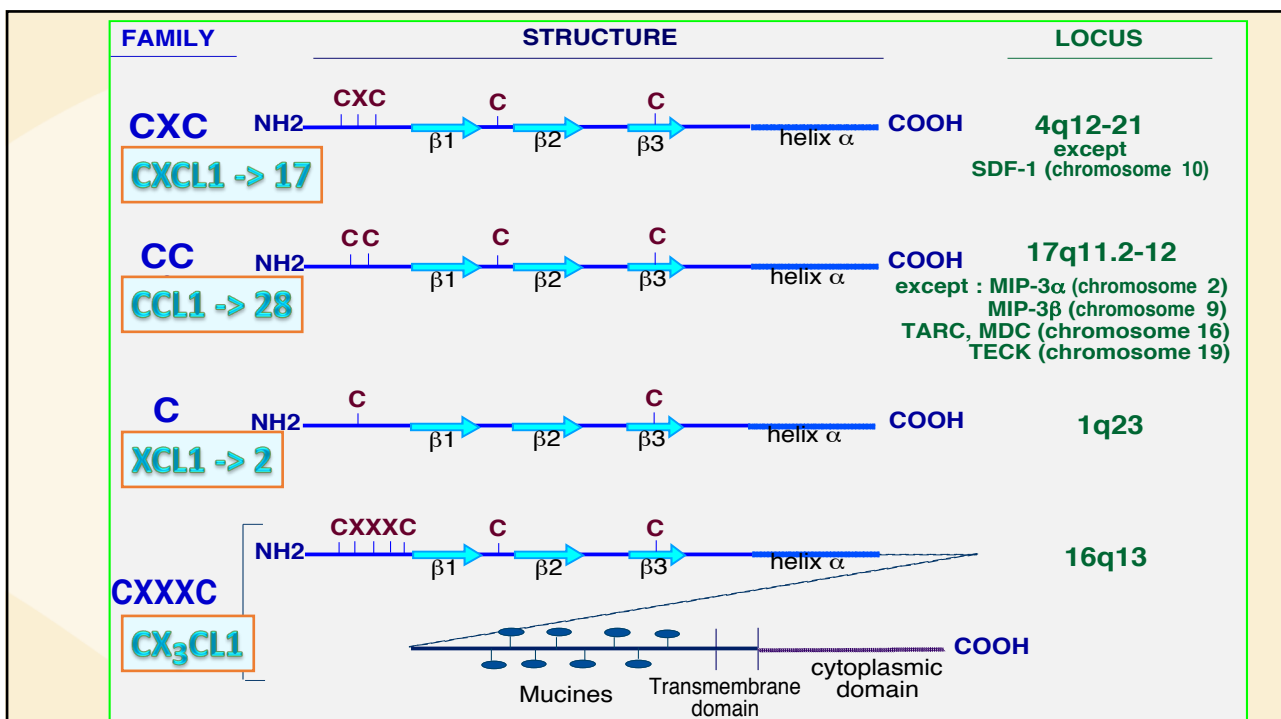
1985 → IP-10

1987 → MIP & IL-8

1995 → New nomenclature:

2023 → CXCL1 - 17 ; CCL1 - 28

..... XCL1 & 2 ; CX₃CL

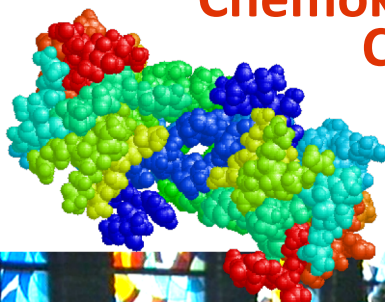


RANTES

Schall TJ et al. *J. Immunol.* 1988; 141: 1018-25.

Regulated upon **A**ctivation, **N**ormal T-cell
Expressed and (presumably) **S**ecreted

Chemokine
CCL5



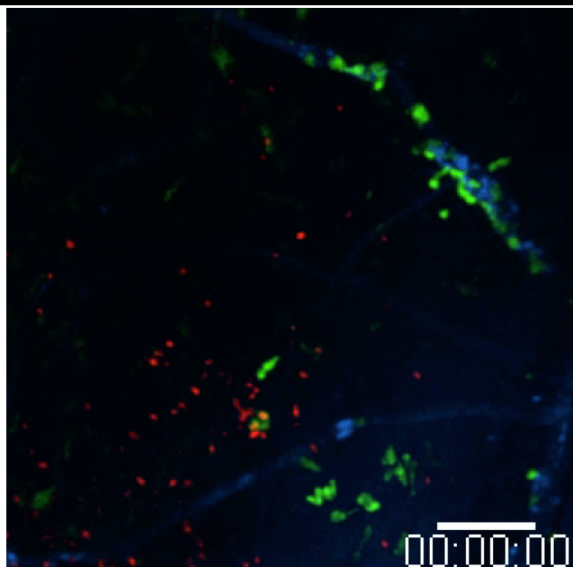
Argentine movie
(1986)
by Eliseo Subiela

Cast:
Lorenzo Quinteros
(Dr Julio Denis),
Hugo Sato (**Rantes**)



CHIMIOTACTISME

RECRUTEMENT DE NEUTROPHILES



Blue : blood vessels
Green : neutrophils
red : *Leishmania major*
(intradermal injection in ears)

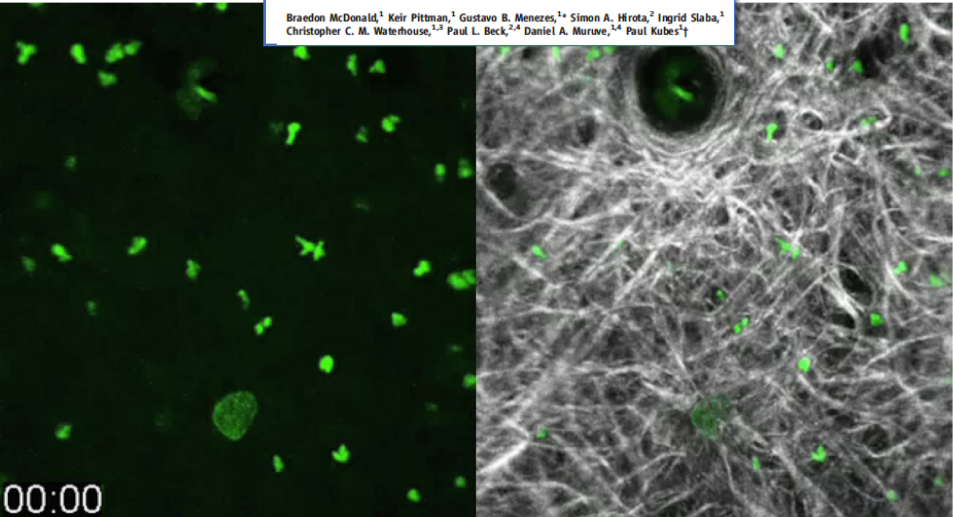
Peters et al. *Science* 2008, 321, 970

CHIMIOTACTISME

362 15 OCTOBER 2010 VOL 330 SCIENCE

Intravascular Danger Signals Guide Neutrophils to Sites of Sterile Inflammation


Bradron McDonald,¹ Keir Pittman,¹ Gustavo B. Menezes,^{1*} Simon A. Hirota,² Ingrid Slaba,¹ Christopher C. M. Waterhouse,^{1,3} Paul L. Beck,^{2,4} Daniel A. Muruve,^{1,4} Paul Kubisz^{1†}



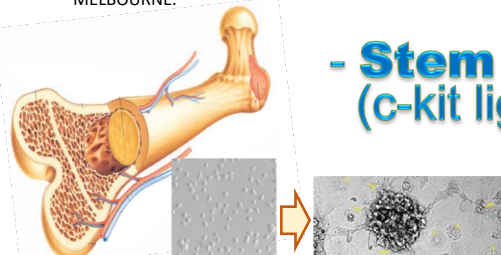
00:00

30

FACTEURS HÉMATOPOÏÉTIQUES



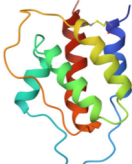
DONALD METCALF
(1929-2014)
Walter and Eliza Hall Institute of Medical Research (WEHI)
MELBOURNE.



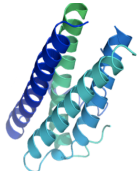
De 1965 à 1985, Metcalf et son équipe ont identifié et purifié quatre facteurs stimulant les colonies :

L'équipe clona également le gene du GM-CSF

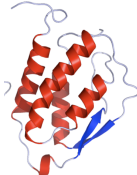
- **Colony Stimulating Factors (M-, G-, GM-CSF)**
- **IL-3 (multi-CSF)**
- **Stem Cell Factor (c-kit ligand)**




IL-3



G-CSF



GM-CSF



M-CSF



Université Libre de Saint-Germain-en-Laye

Biologie et Santé
2023- 2024

LES CYTOKINES : LE LANGAGE DE NOS CELLULES LEURS PRODUCTIONS



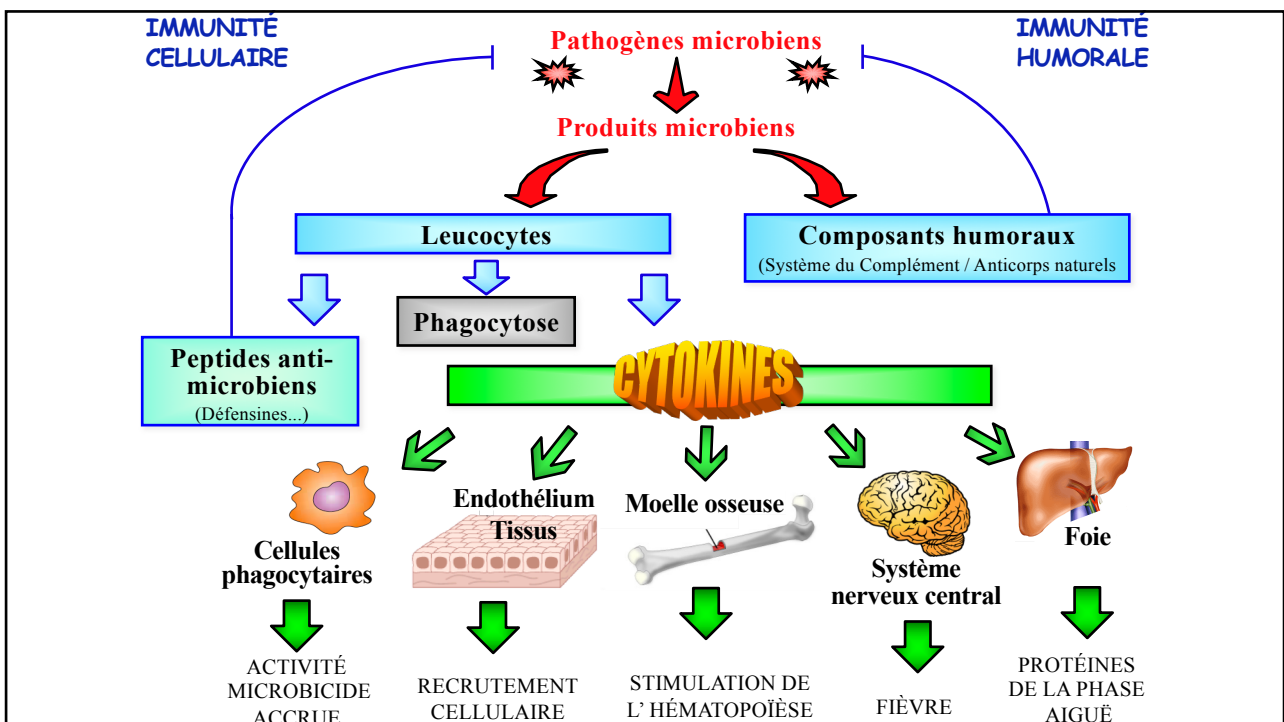
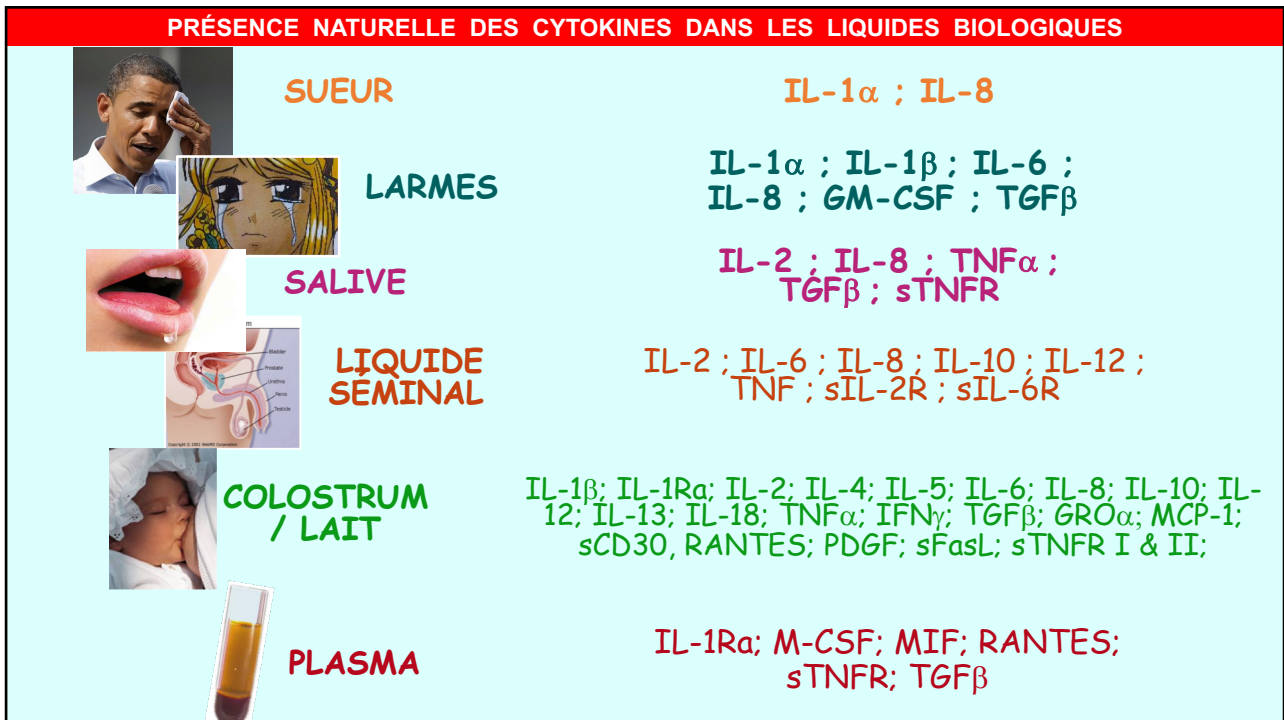
PRODUCTIONS

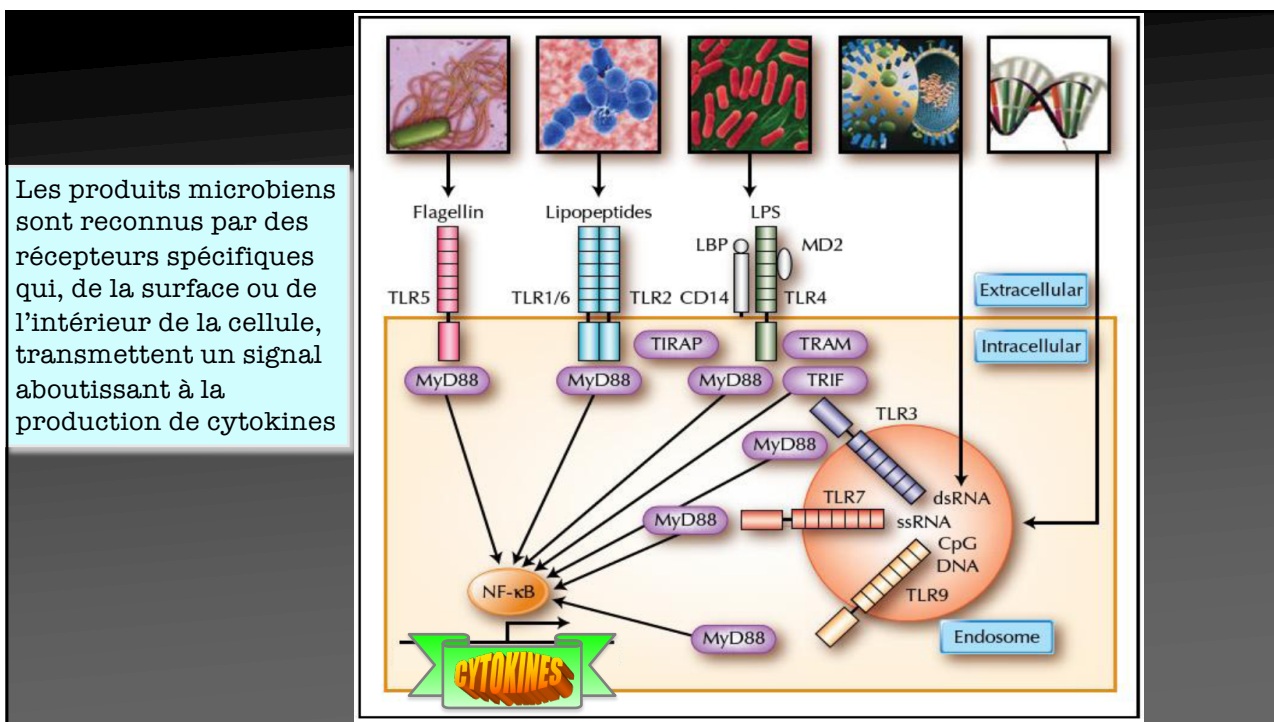
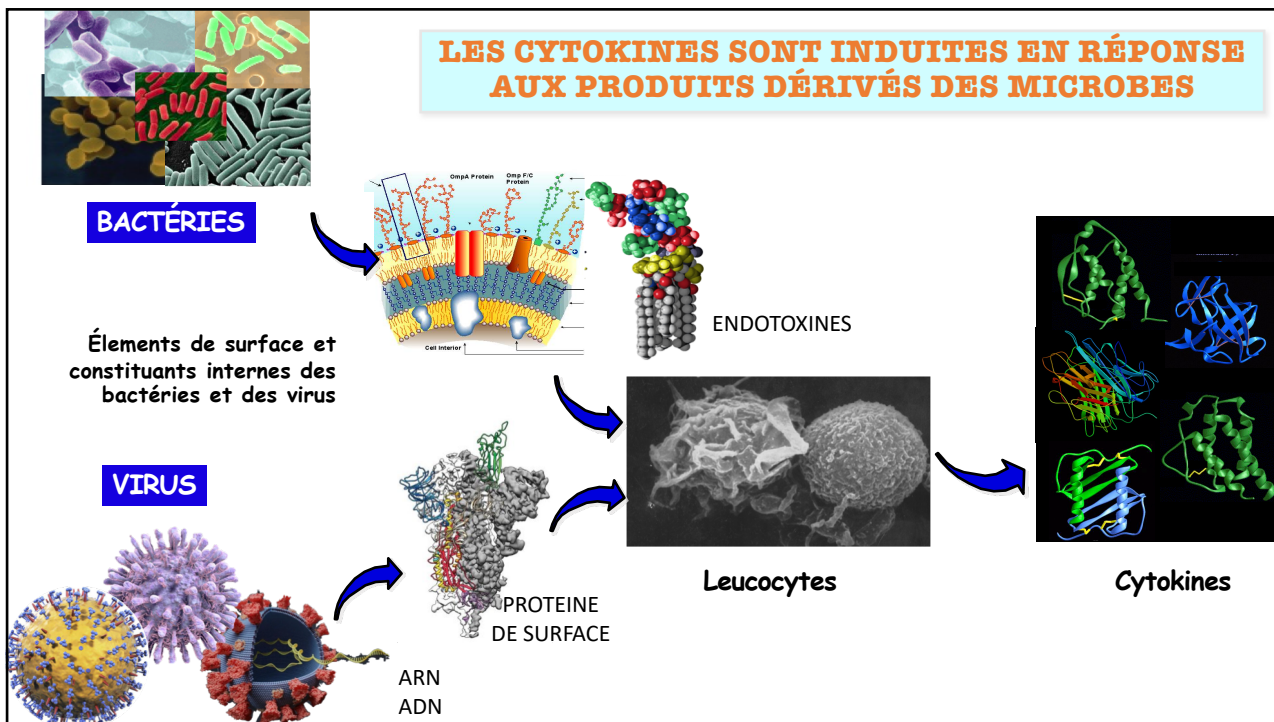
Spontanée à
l'homéostasie

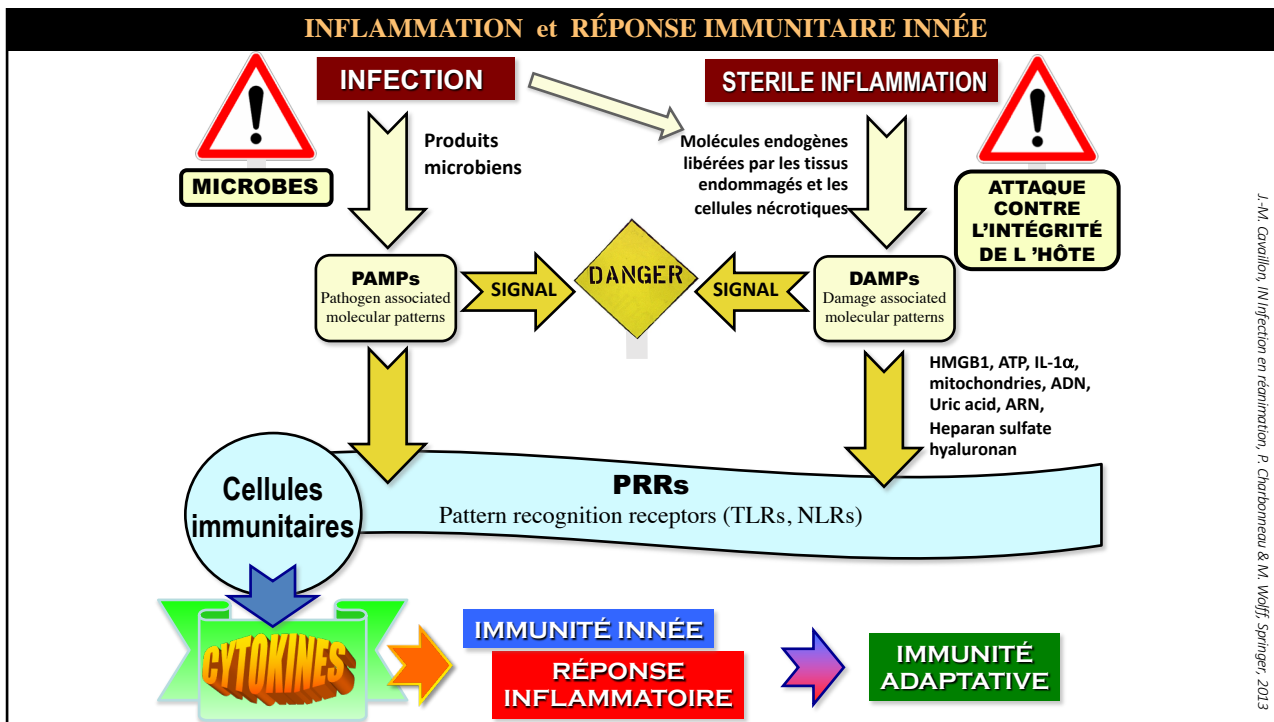
↳ **Microenvironnement spécifique
des tissus**

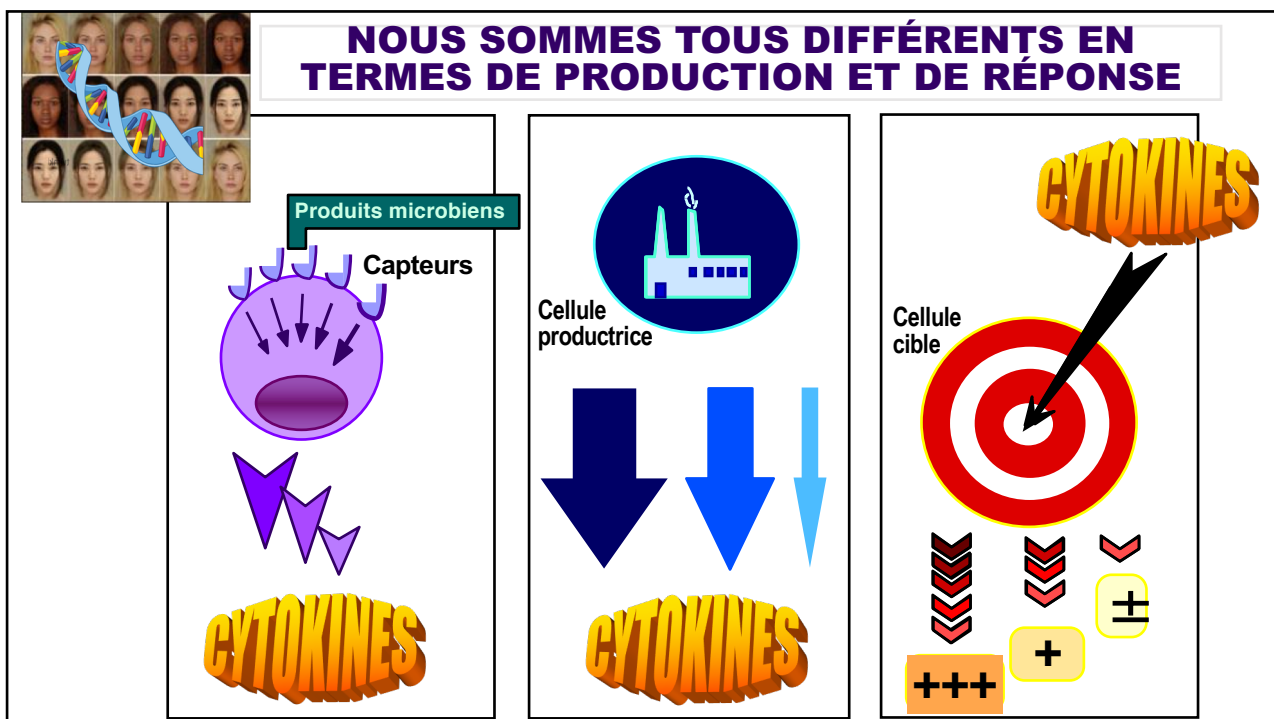


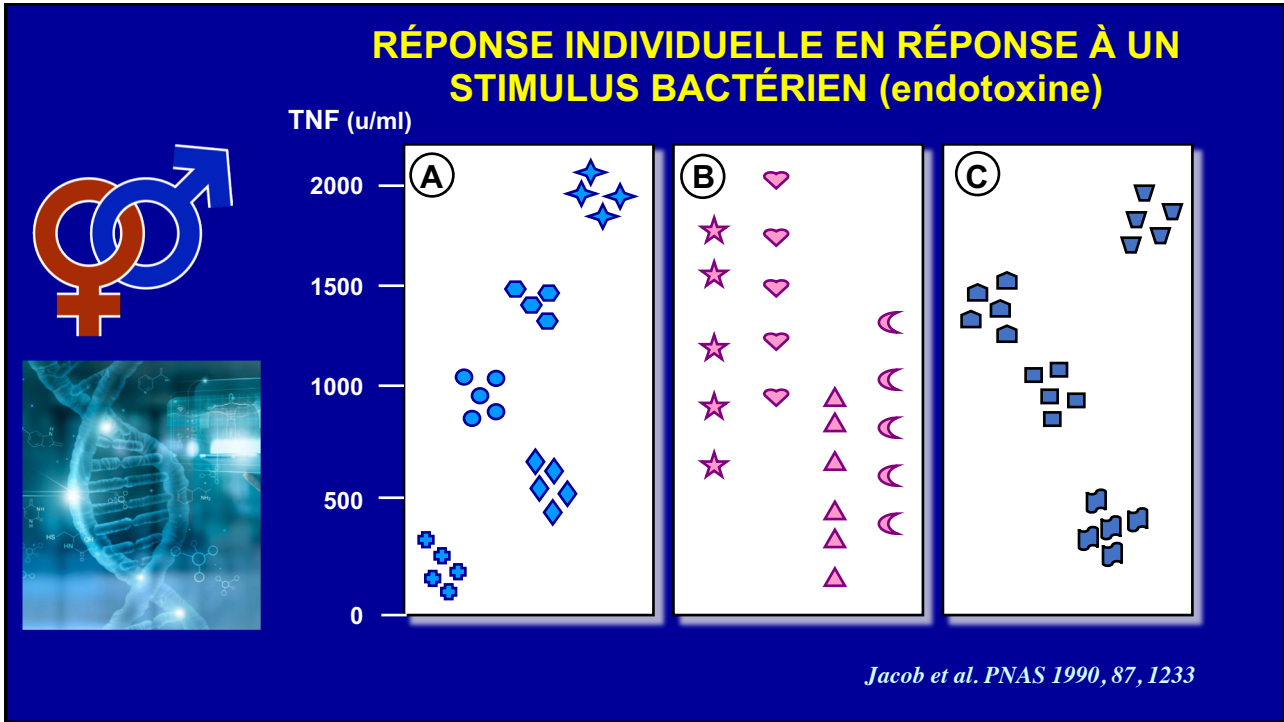
**Suite à une agression
(infectieuse ou non)**











PNAS | July 3, 2001 | vol. 98 | no. 14 | 7904-7909

Increased sexual activity reduces male immune function

Kurt A. McKean* and Leonard Nunney
Department of Biology, University of California, Riverside, CA 92521

Science is fun

NeuroImmunoModulation
Neuroimmunomodulation 2004;11:293-298
DOI: 10.1159/000079409

Effects of Sexual Arousal on Lymphocyte Subset Circulation and Cytokine Production in Man

Philip Haake^a Tillmann H.C. Krueger^a Marion U. Goebel^a
Katharina M. Heberling^a Uwe Hartmann^b Manfred Schedlowski^a

^aDepartment of Medical Psychology, University Clinic of Essen, Essen, and ^bDepartment of Clinical Psychiatry, University of Hannover Medical School, Hannover, Germany

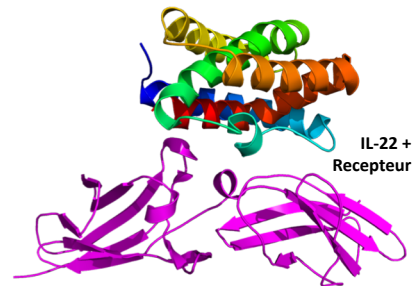


Université Libre de Saint-Germain-en-Laye

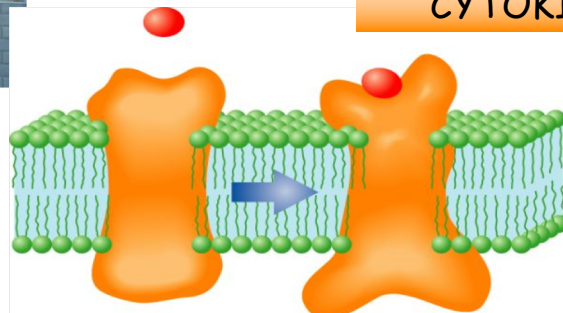
Biologie et Santé
2023- 2024

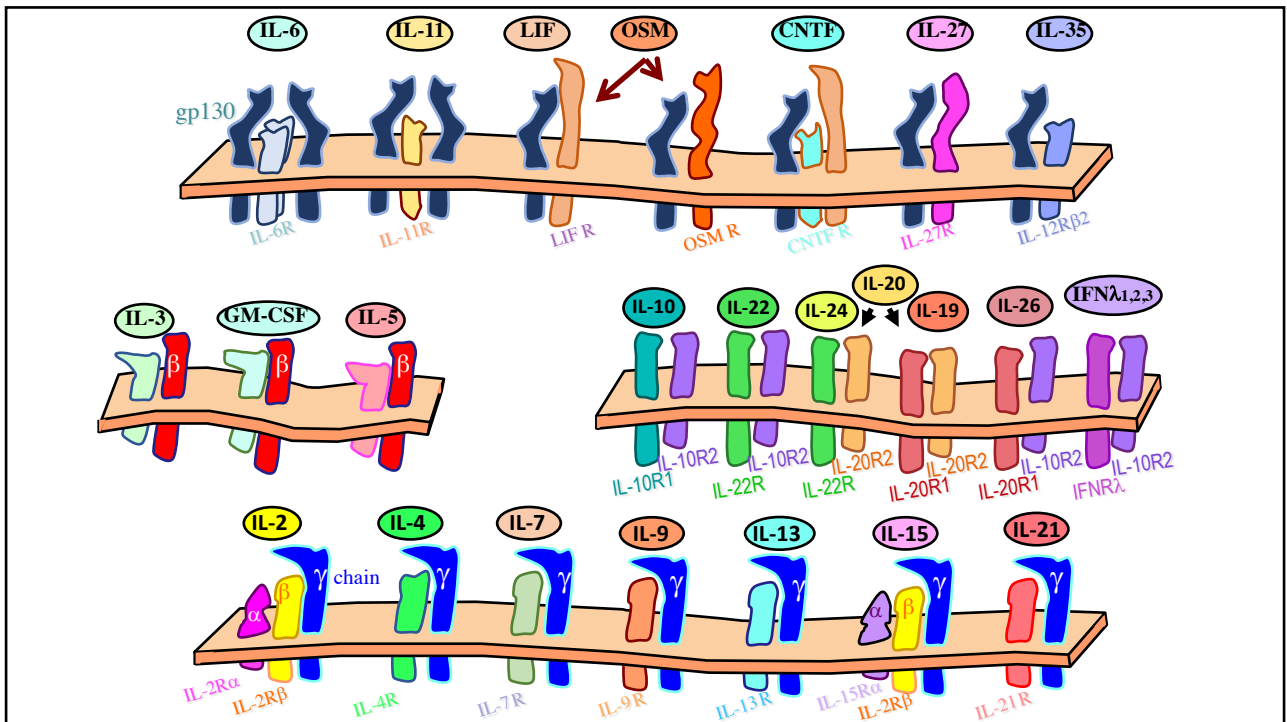
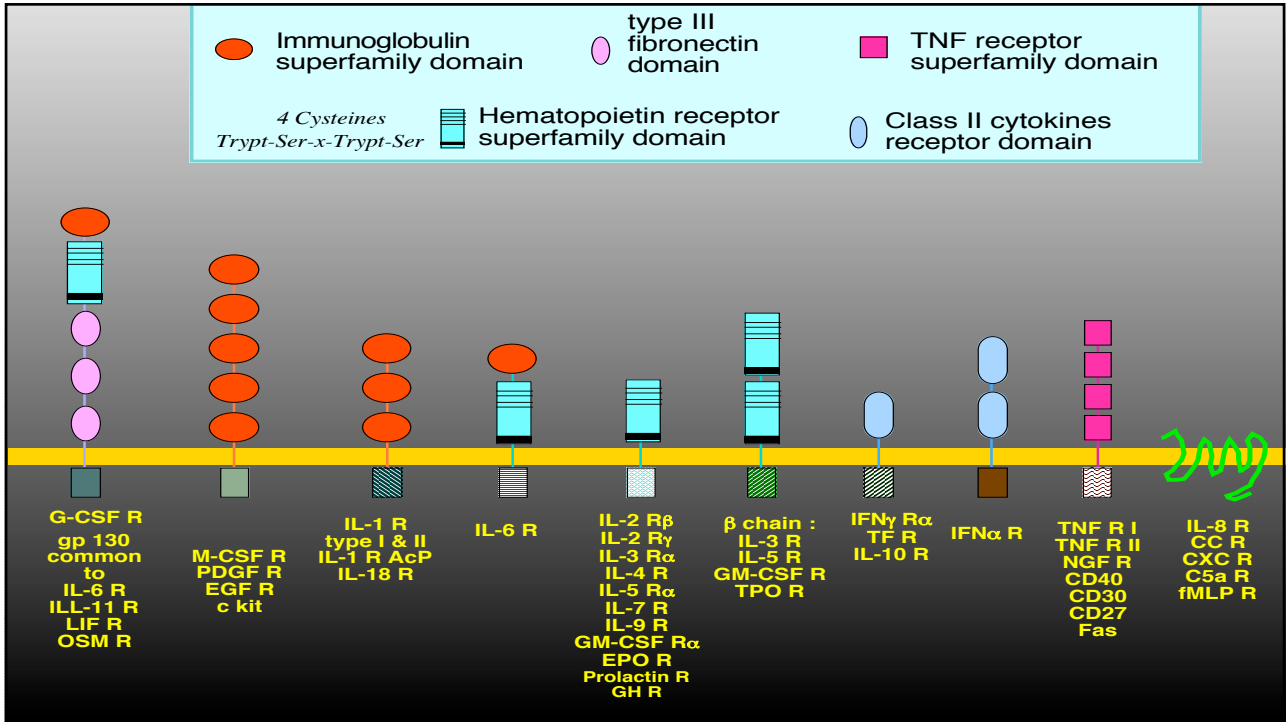
LES CYTOKINES : LE LANGAGE DE NOS CELLULES LEURS RÉCEPTEURS

COMMENT ENTENDRE CES MESSAGES ?



RÉCEPTEURS DES
CYTOKINES





Enfant bulle
immunodéficient



Traitement par thérapie génique

The New England
Journal of Medicine

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VOLUME 346

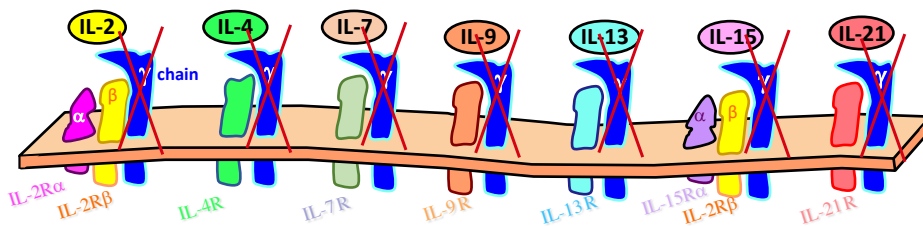
APRIL 18, 2002

NUMBER 16



SUSTAINED CORRECTION OF X-LINKED SEVERE COMBINED
IMMUNODEFICIENCY BY EX VIVO GENE THERAPY

SALIMA HACEIN-BEY-ABINA, PH.D., FRANÇOISE LE DEIST, M.D., PH.D., FRÉDÉRIQUE CARLIER, B.S., CÉCILE BOUNEAUD, PH.D.,
CHRISTOPHE HUE, B.S., JEAN-PIERRE DE VILLARTAY, PH.D., ADRIAN J. THRASHER, M.D., PH.D., NICOLAS WULFFRAAT, M.D.,
RICARDO SORENSEN, M.D., SOPHIE DUPUIS-GIROD, M.D., ALAIN FISCHER, M.D., PH.D.,
AND MARINA CAVAZZANA-CALVO, M.D., PH.D.

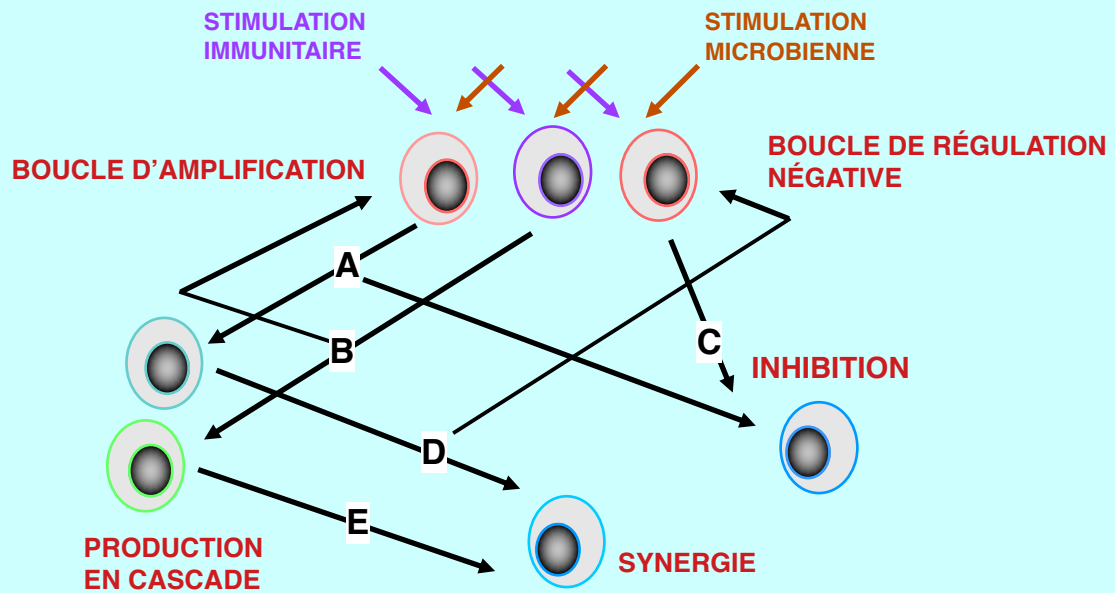


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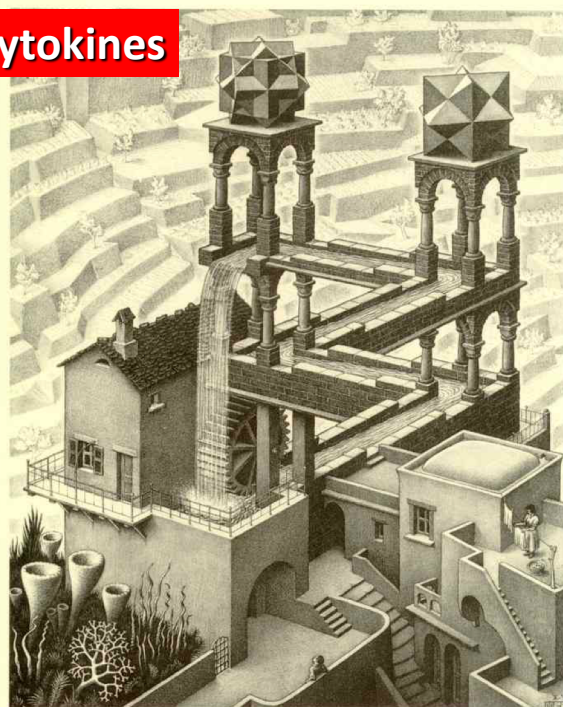
Biologie et Santé
2023- 2024

LES CYTOKINES :
LE LANGAGE DE NOS CELLULES
LE RÉSEAU

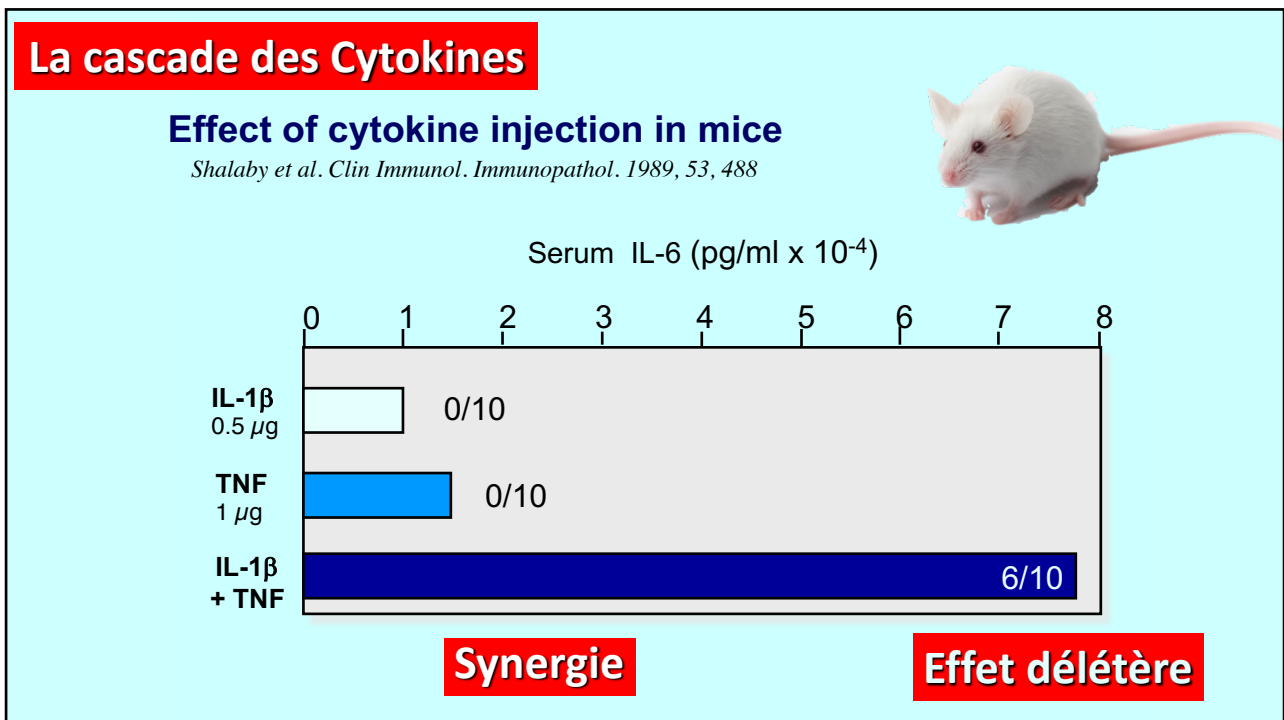
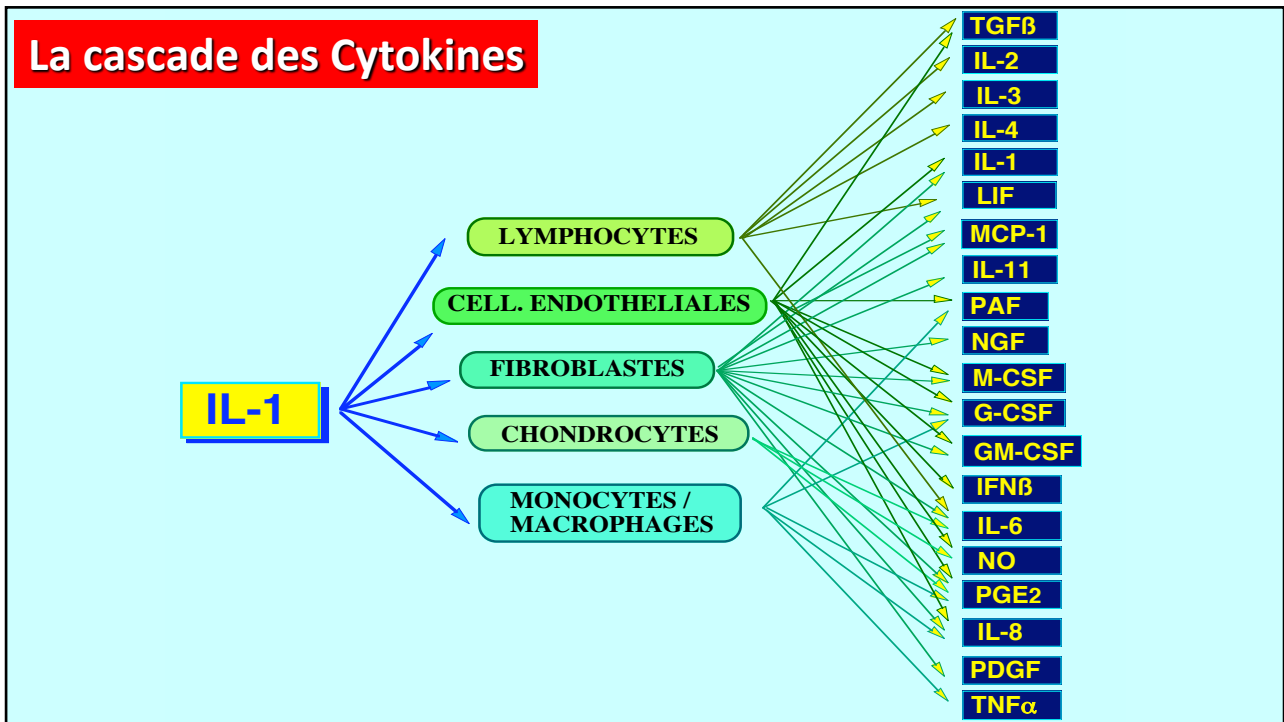
LE RÉSEAU DES CYTOKINES



La cascade des Cytokines



Escher





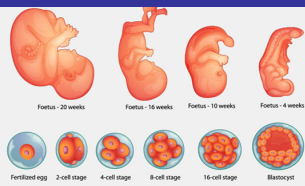
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Biologie et Santé
2023- 2024

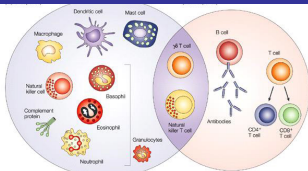
LES CYTOKINES : LE LANGAGE DE NOS CELLULES

LEURS FONCTIONS

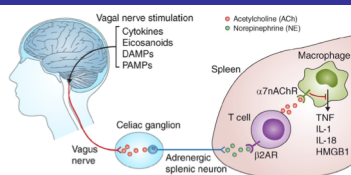
GESTATION & EMBRYOGENESIS



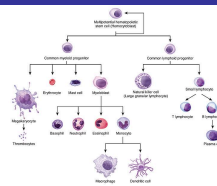
RÉPONSE IMMUNITAIRE



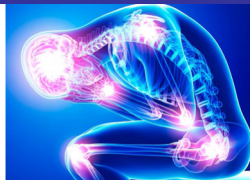
DIALOGUE AVEC LE SNC



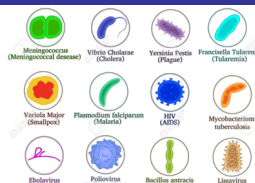
HÉMATOPOÏÈSIS

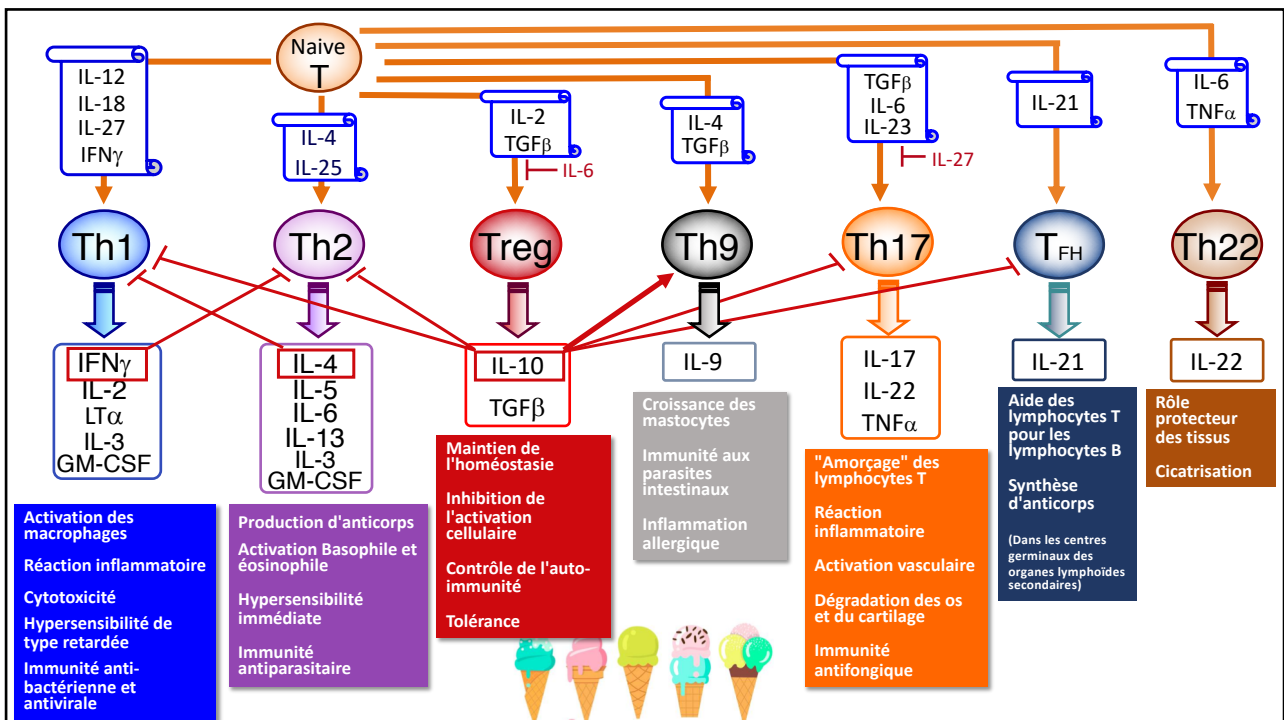
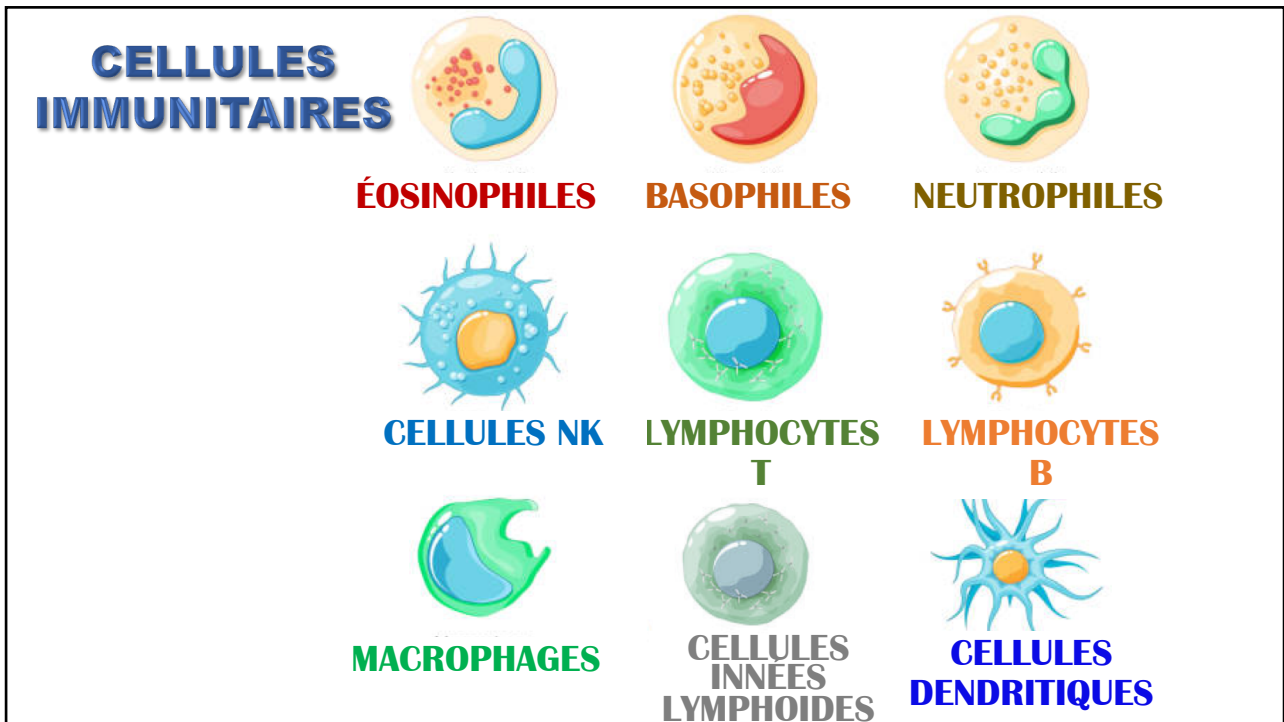


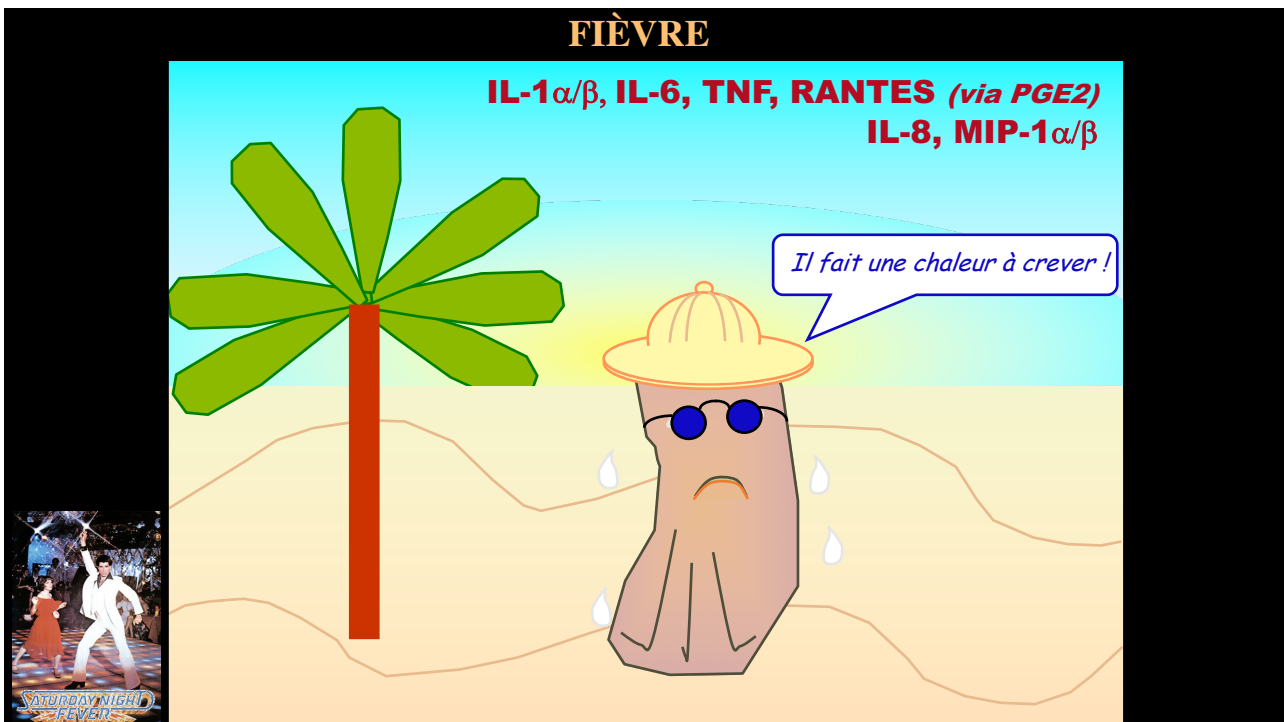
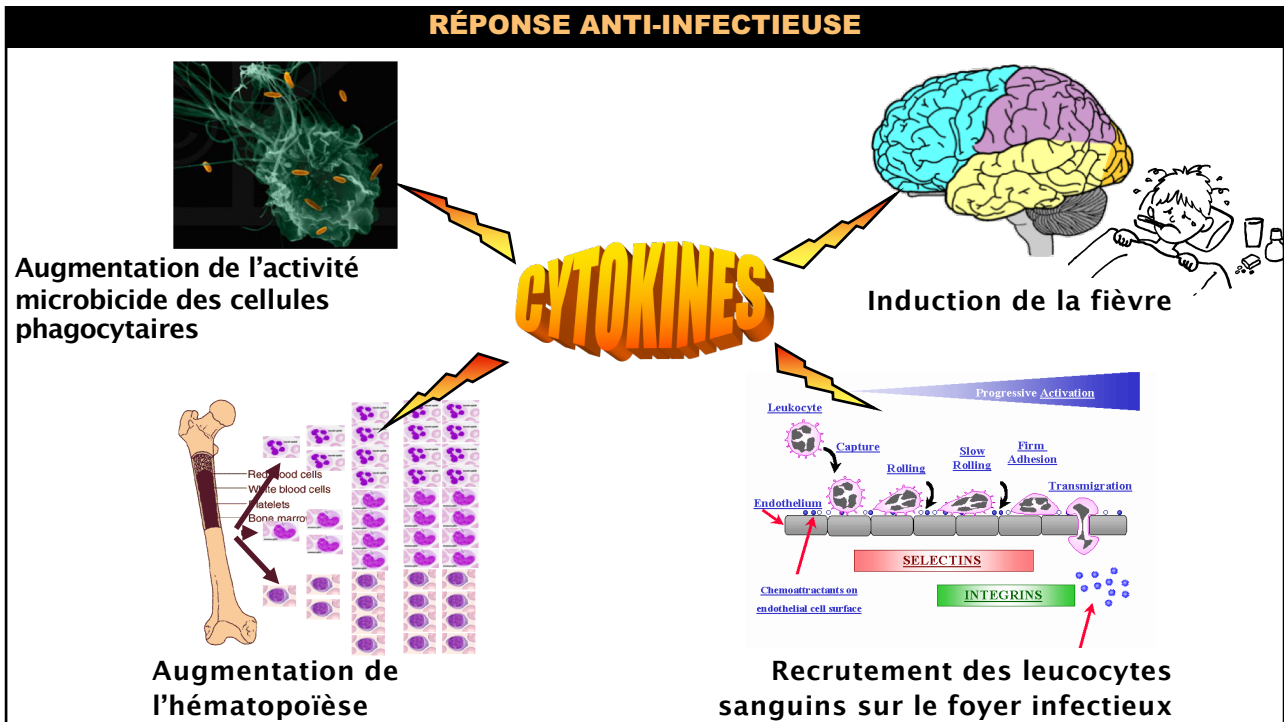
INFLAMMATION

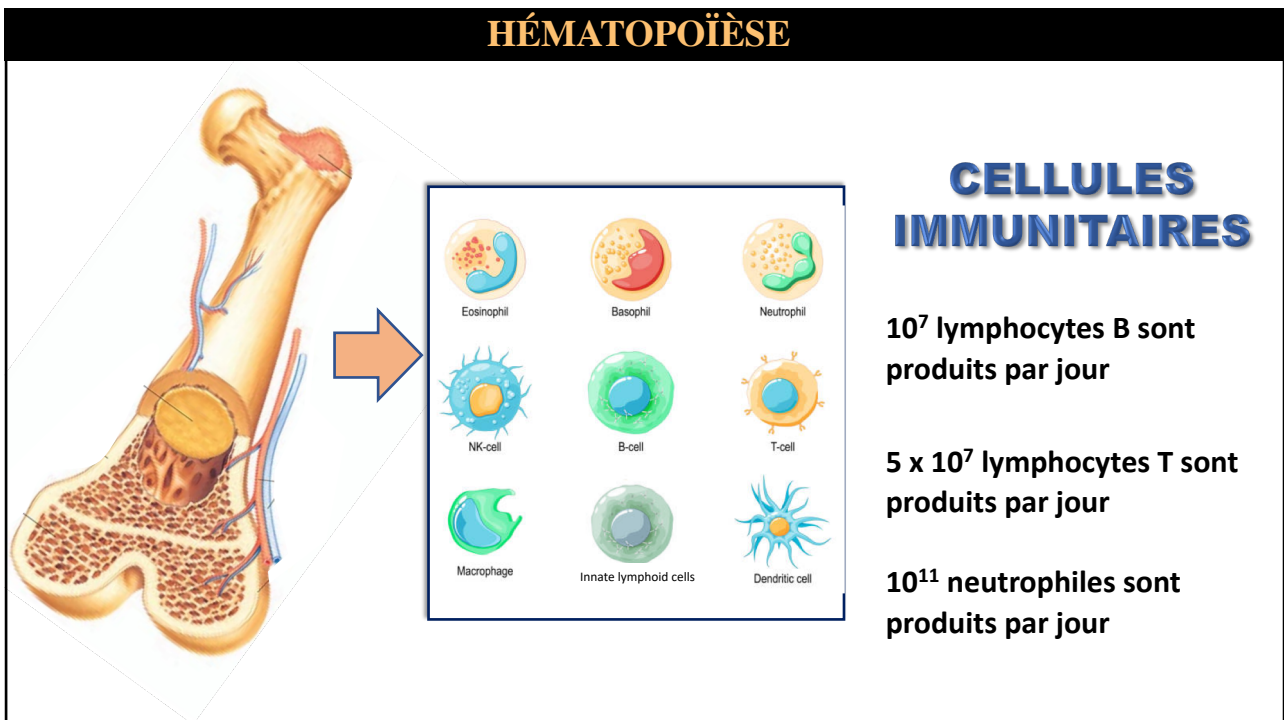
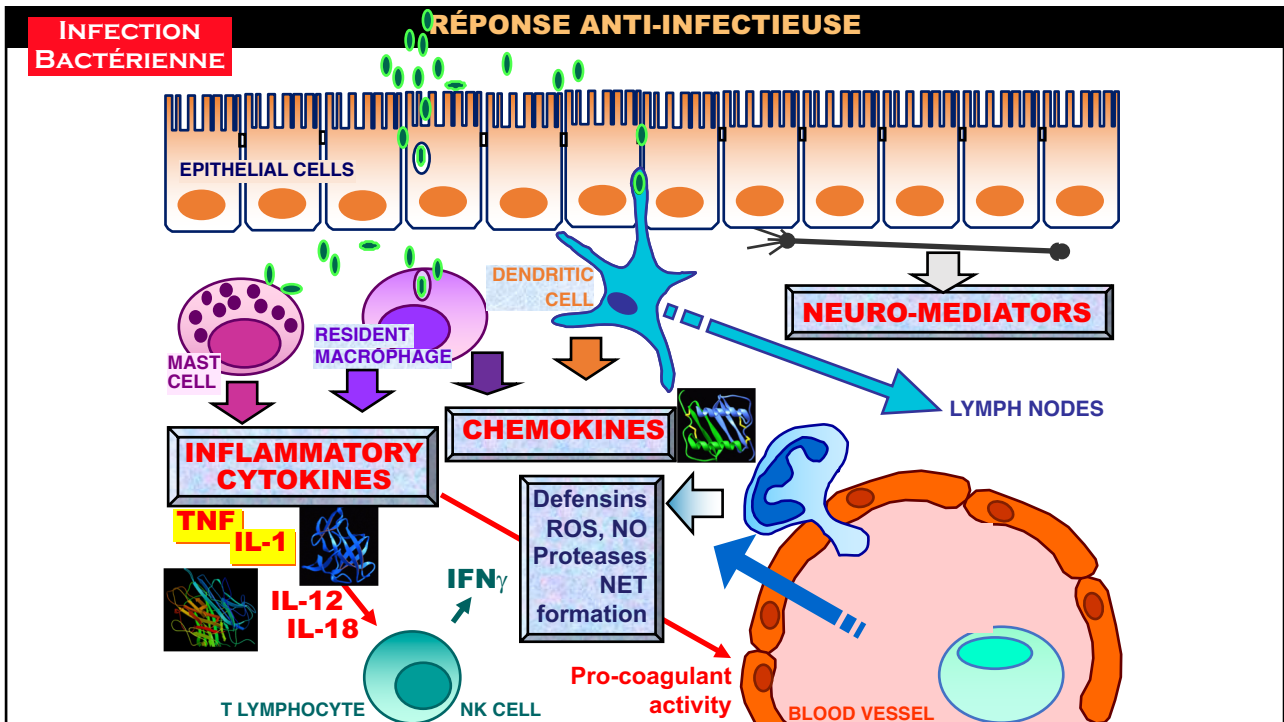


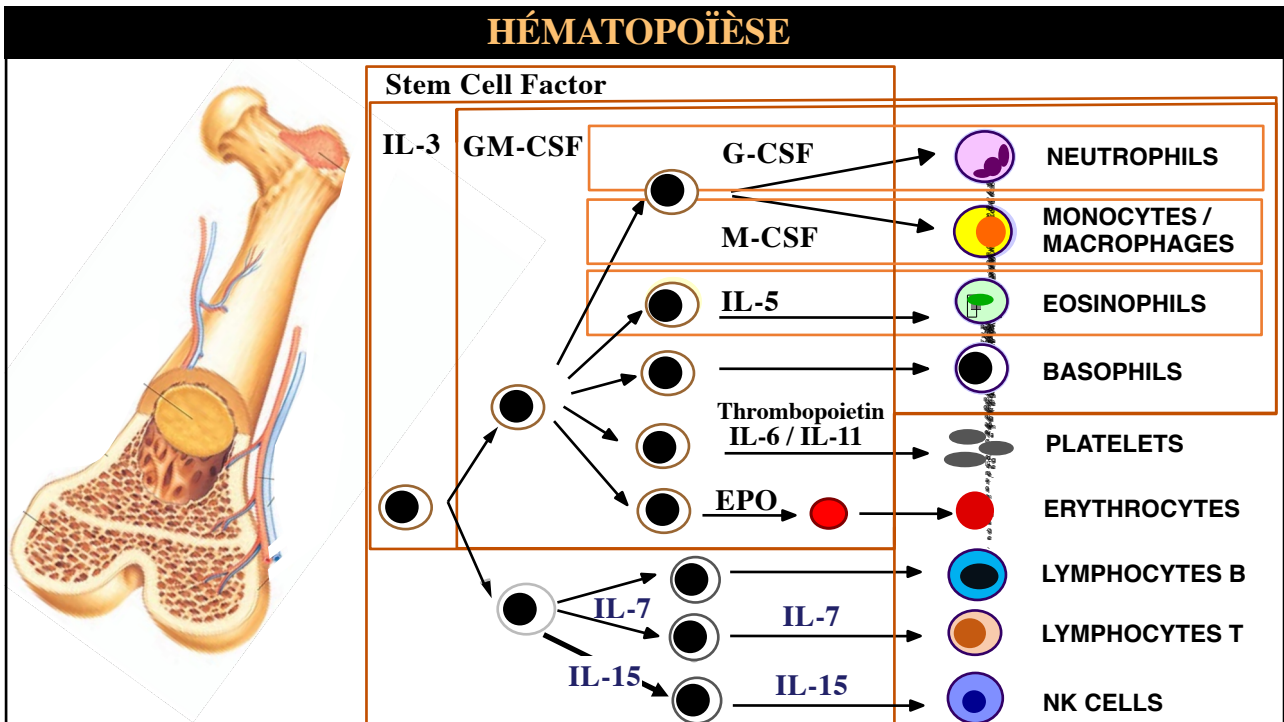
MALADIES INFECTIEUSES











L'IMMUNITÉ INNÉE
CYTOKINES
L'INFLAMMATION

JAMES BOND CONTRE DARK VADOR

LICENCE TO KILL

SPECIAL 007th EDITION

Nécessité d'être rapidement efficace

LA FORCE OBSCURE DU SYSTÈME IMMUNITAIRE

L'IMMUNITÉ INNÉE **CYTOKINES** **L'INFLAMMATION**

MI-ANGE/ MI-DÉMON



Escher

This section features a collage of four images. On the left is a sword with a decorative hilt. Next to it is a microscopic view of green, rod-shaped bacteria with flagella. To the right is a black and white illustration of the Grim Reaper holding a scythe. On the far right is a large circular mandala with intricate, repeating patterns of birds and floral motifs, characteristic of M.C. Escher's work.

LA FORCE OBSCURE DU SYSTÈME IMMUNITAIRE **TEMPÊTE CYTOKINIQUE**



Munch *Hokusai*

This section features a collage of three images. On the left is 'The Scream' by Edvard Munch, showing a figure in a dark boat against a turbulent, orange and red sky. In the center is a digital illustration of Darth Vader from Star Wars, holding a glowing red lightsaber. On the right is 'The Great Wave off Kanagawa' by Katsushika Hokusai, a woodblock print depicting a massive blue wave crashing over a small boat.



TEMPÊTE CYTOKINIQUE

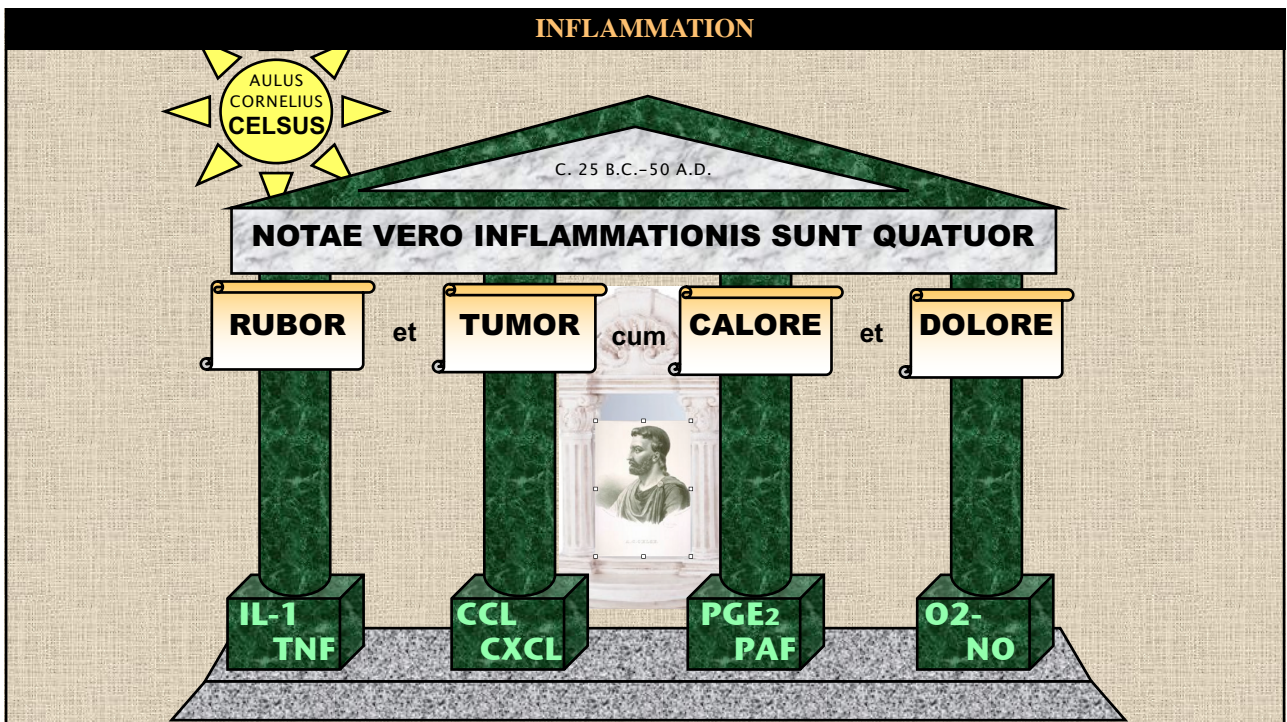
UN EXCÈS DE CYTOKINES ABOUTIT A UNE DÉFAILLANCE DES ORGANES

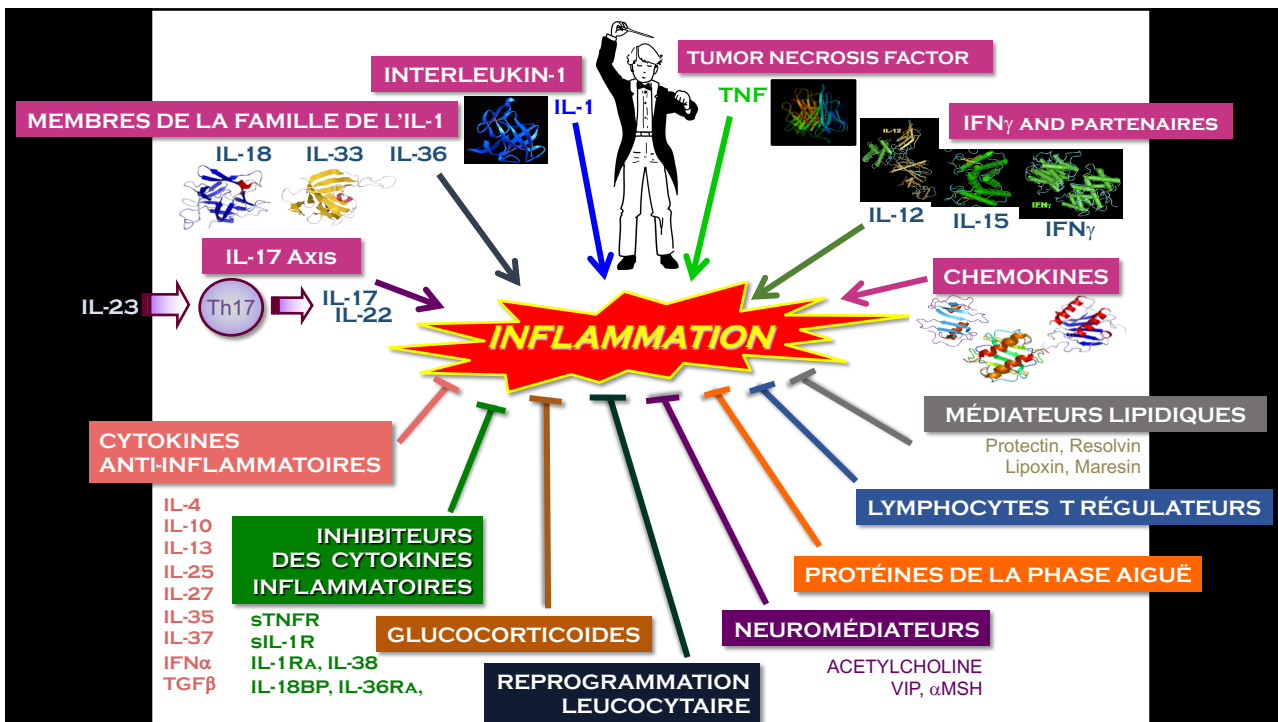
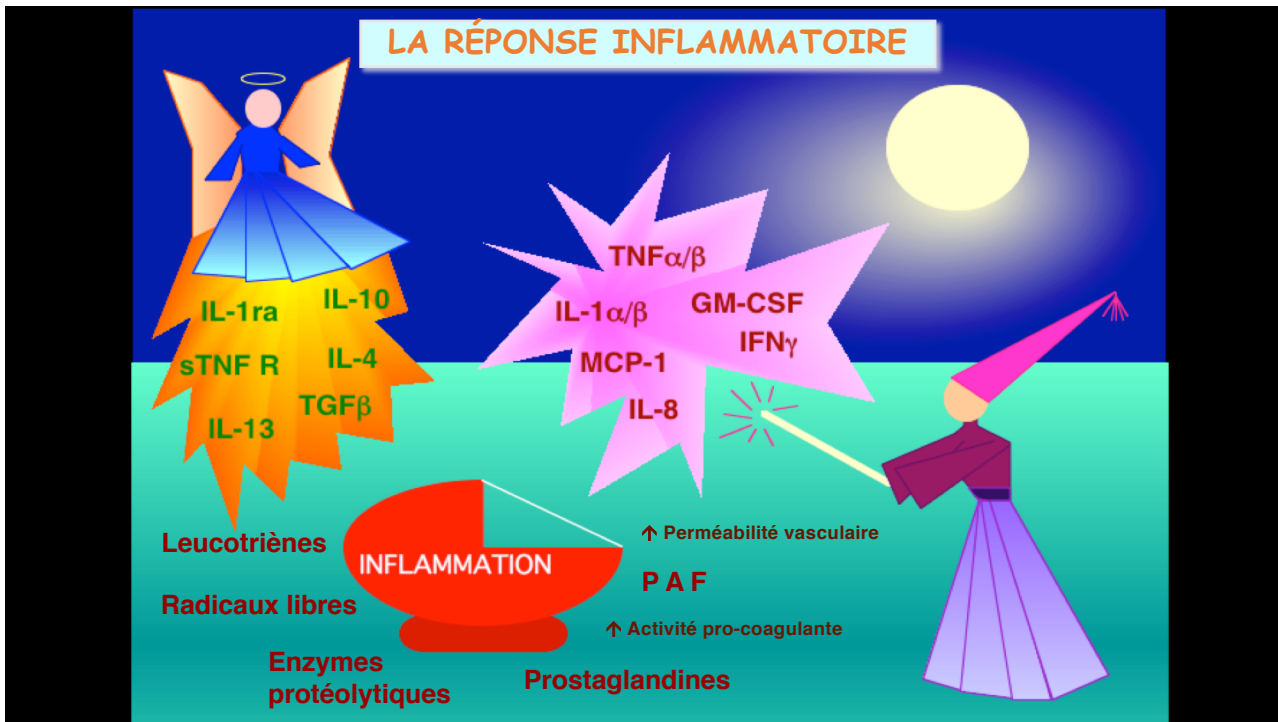


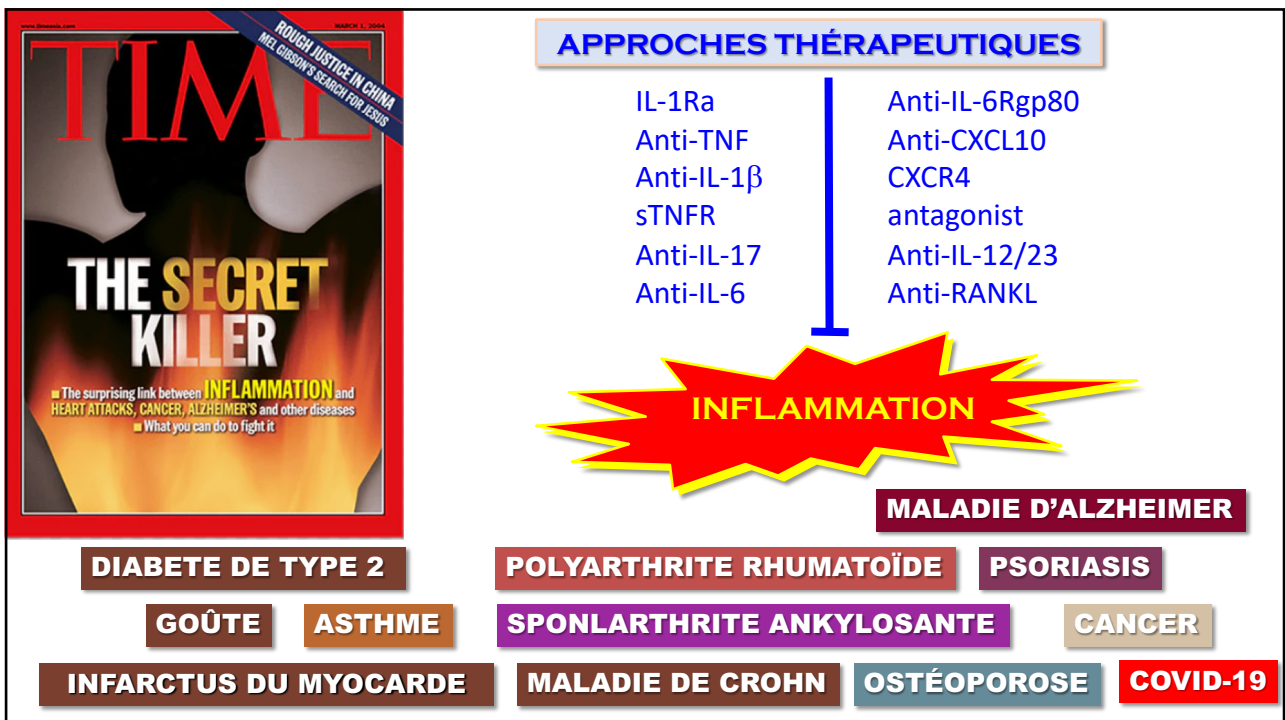
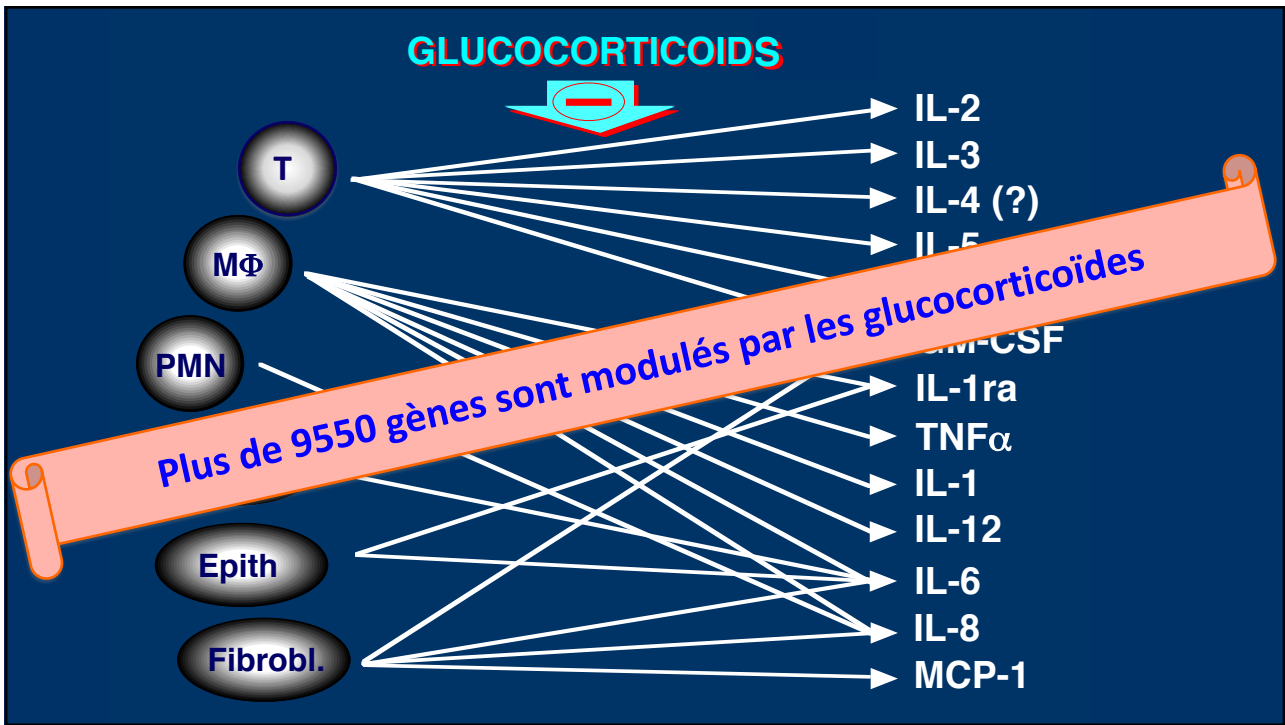
Season 1 / Episode 21

DR. HOUSE

70

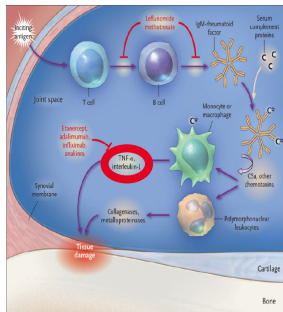
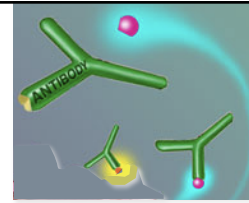




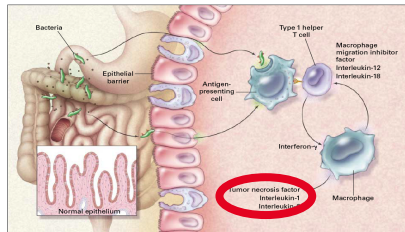




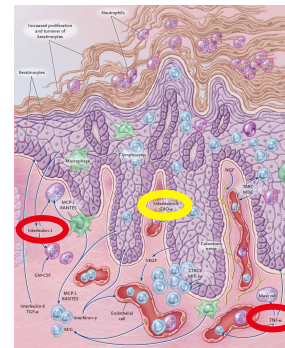
Un médicament disponible : anticorps anti-TNF



INFLAMMATION ARTICULAIRE :
La polyarthrite rhumatoïde

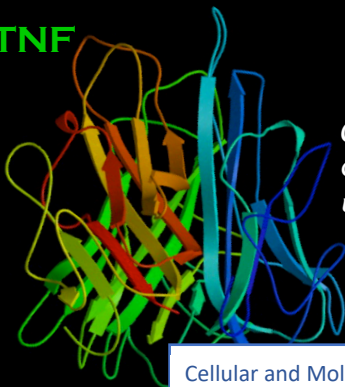


MALADIES INFLAMMATOIRES DU TUBE DIGESTIF :
La maladie de Crohn



PSORIASIS

TNF



Ceci n'est pas une cytokine pro-inflammatoire



Ceci n'est pas une pipe.

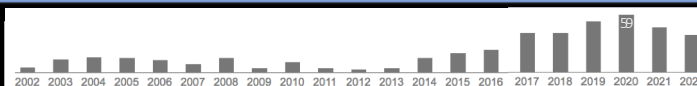
Cellular and Molecular Biology 2001, 47: 695

Review

Magritte

**PRO- versus ANTI-INFLAMMATORY CYTOKINES:
MYTH OR REALITY**

Jean-Marc CAVAILLON





Université Libre de Saint-Germain-en-Laye

Biologie et Santé
2023- 2024

LES CYTOKINES : LE LANGAGE DE NOS CELLULES COVID-19

SARS-COV-2

COMORBIDITÉ

frontiers in Immunology October 2020 | Volume 11 | Article 570251

NLRP3 Inflammasome: The Stormy Link Between Obesity and COVID-19

Alberto López-Reyes^{1,2*}, Carlos Martínez-Armenta³, Rocio Espinosa-Ortega¹, Paola Vázquez-Cárdenas⁴, Marlid Cruz-Ramos⁵, Berenice Palacios-Cruz⁶, Luis Enrique Gomez-Quiroz⁷ and Gabriela Angélica Martínez-Nava⁸

OBÉSITÉ

L'infection par le SARS-CoV-2 pourrait potentialiser l'état de maladie inflammatoire systémique chez les personnes obèses, via l'activation de l'inflammasome NLRP3 et la libération de cytokines pro-inflammatoires.

COVID-19

JEM Journal of Experimental Medicine 2020 Vol. 218 No. 3 e20201707

Inflammasomes are activated in response to SARS-CoV-2 infection and are associated with COVID-19 severity in patients

Tamara S. Rodrigues et al.

Lung histopathological analysis and NLRP3 activation in fatal cases of COVID-19.

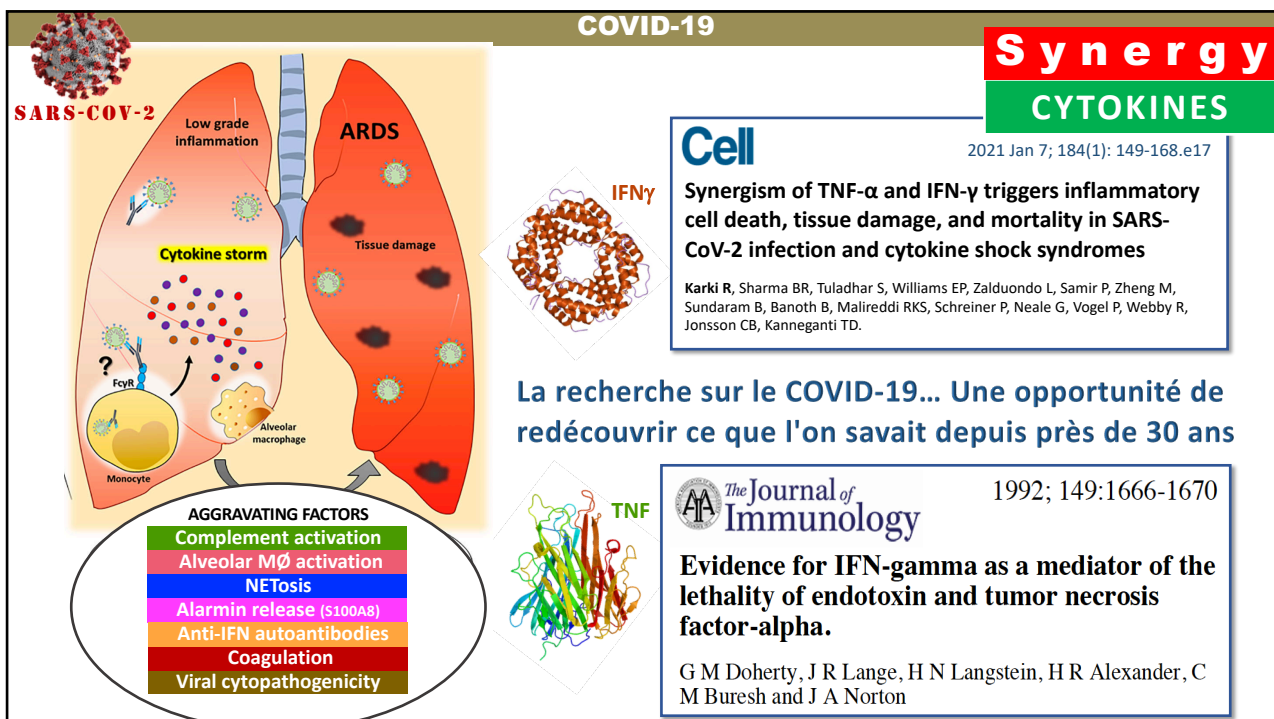
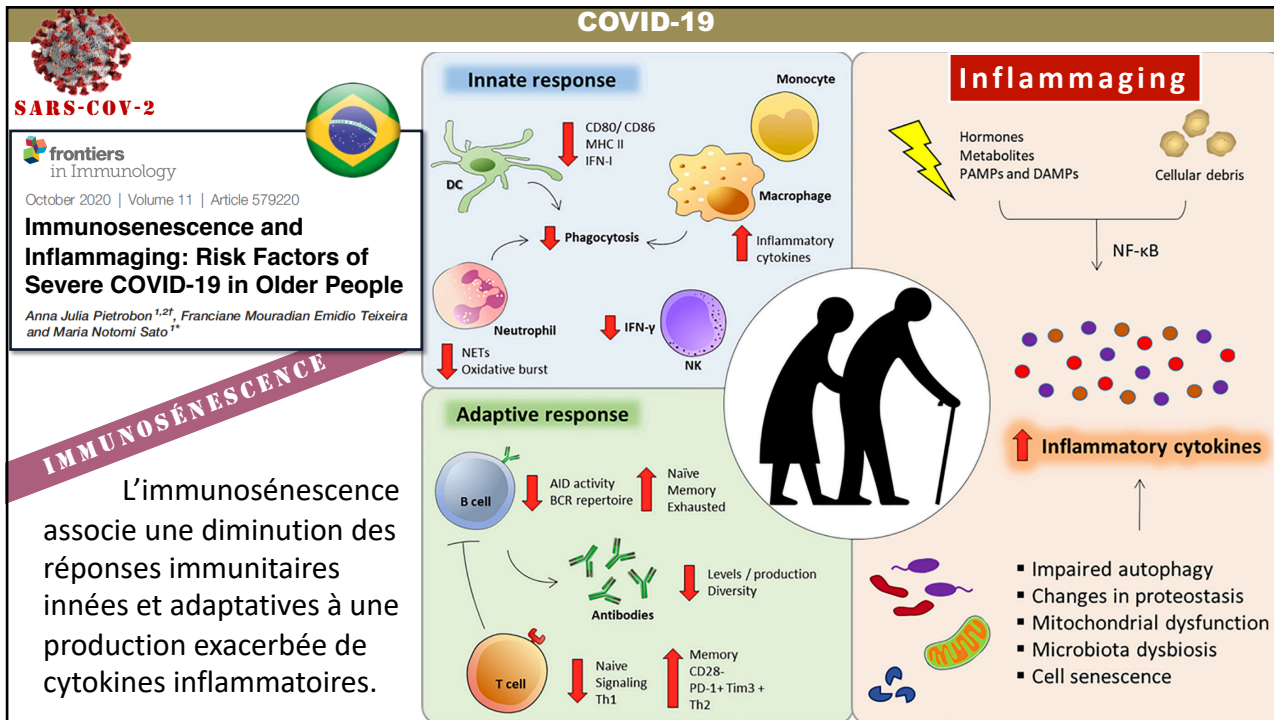
E

Cells with NLRP3 puncta/mm²

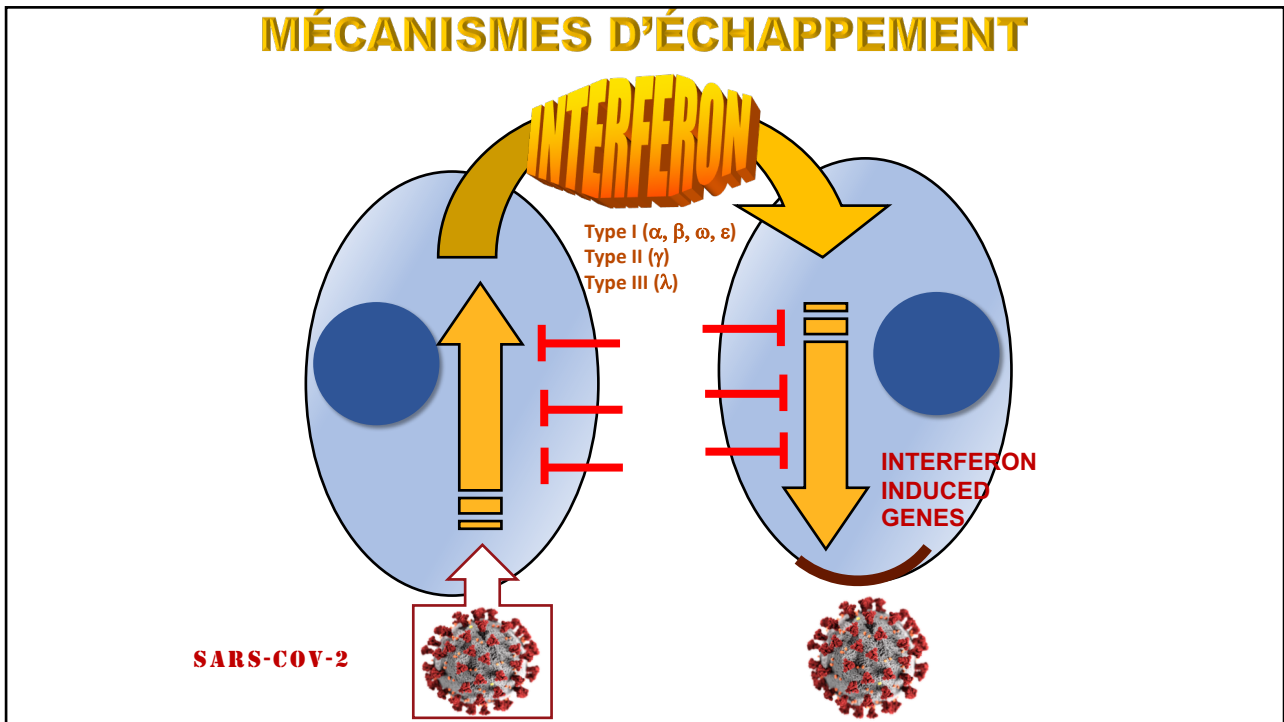
Group	Mean Value
CT	~20
COVID-19	~160

Cells with ASC puncta/mm²

Group	Mean Value
CT	~20
COVID-19	~160



MÉCANISMES D'ÉCHAPPEMENT



COVID-19

Asymptomatic/mild

0/663 (0%)

Life-threatening

101/987 (10.2%)

Neutralizing auto-Abs impair type I IFN immunity

Type I IFN immunity

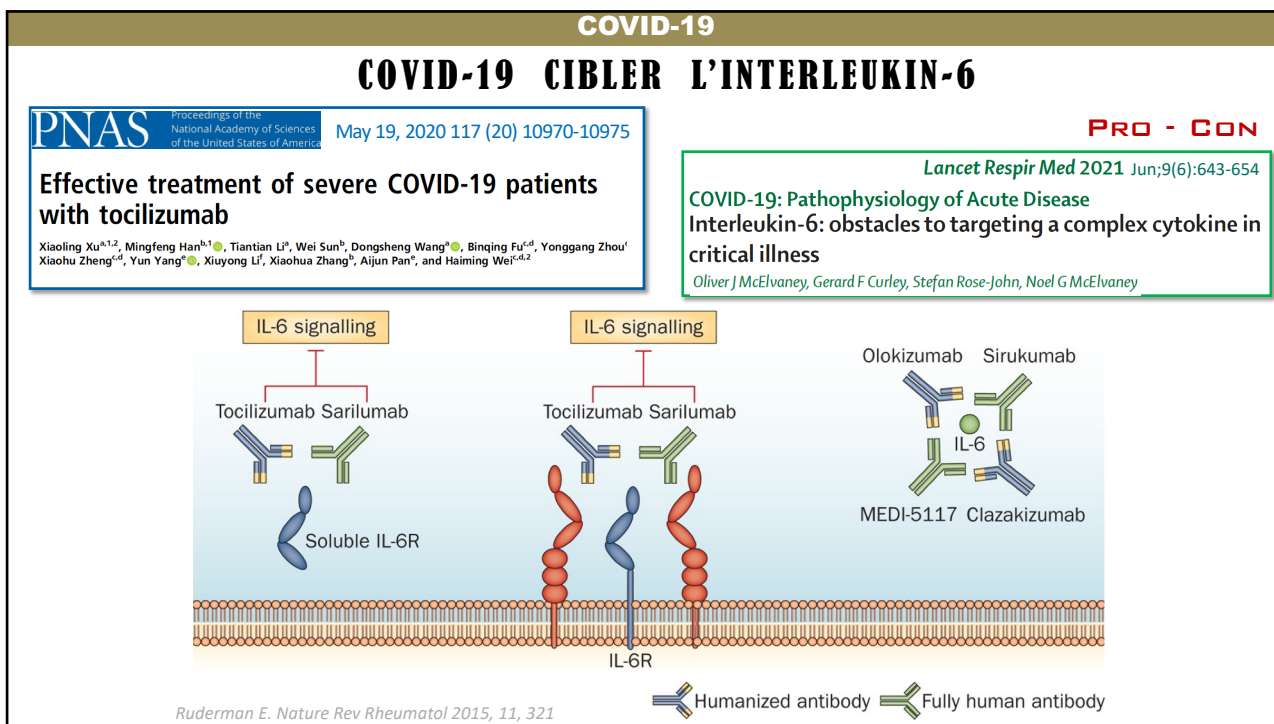
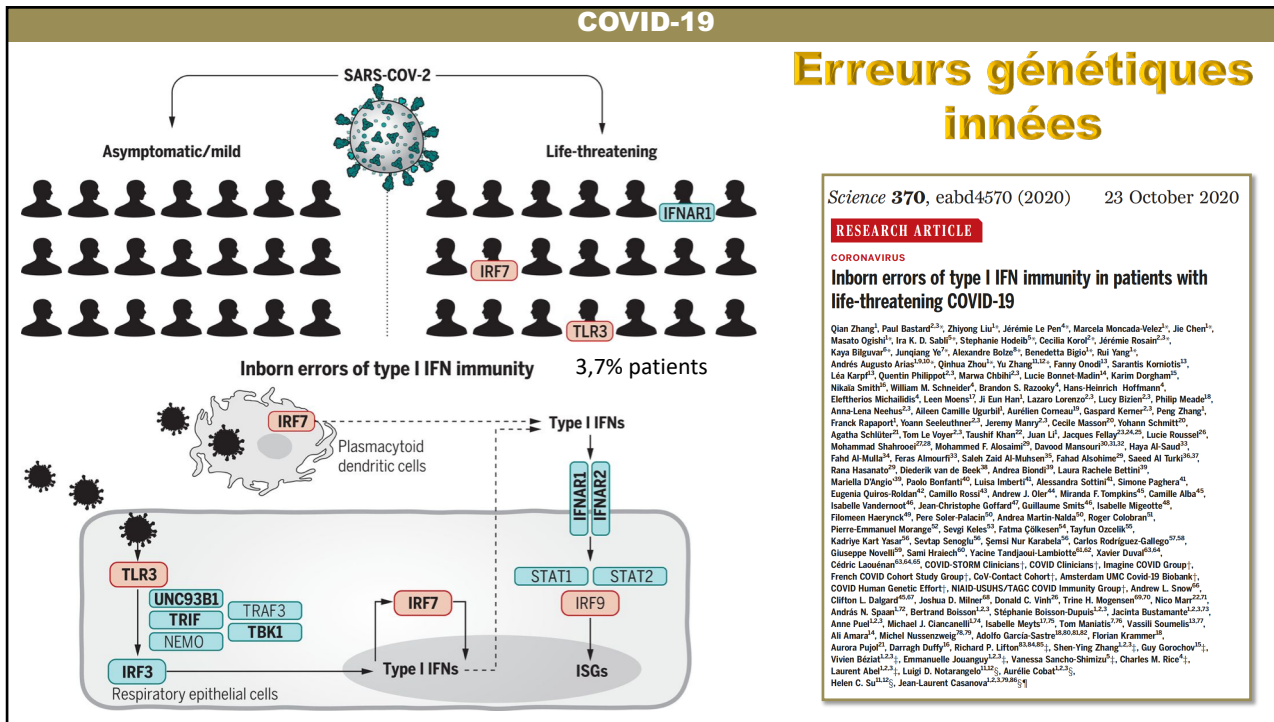
Auto-Abs to type I IFNs

Auto-anticorps anti-interferon

Science **370**, eabd4585 (2020) 23 October 2020

Autoantibodies against type I IFNs in patients with life-threatening COVID-19

Paul Bastard^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000}





FRANCE 24 Katalin Kariko, la chercheuse derrière le vaccin Pfizer : de sa fuite de Hongrie à un futur Nobel

December 23, 2020



University of Pennsylvania mRNA biology pioneers receive COVID-19 vaccine enabled by their foundational research



ARNm Liposomes

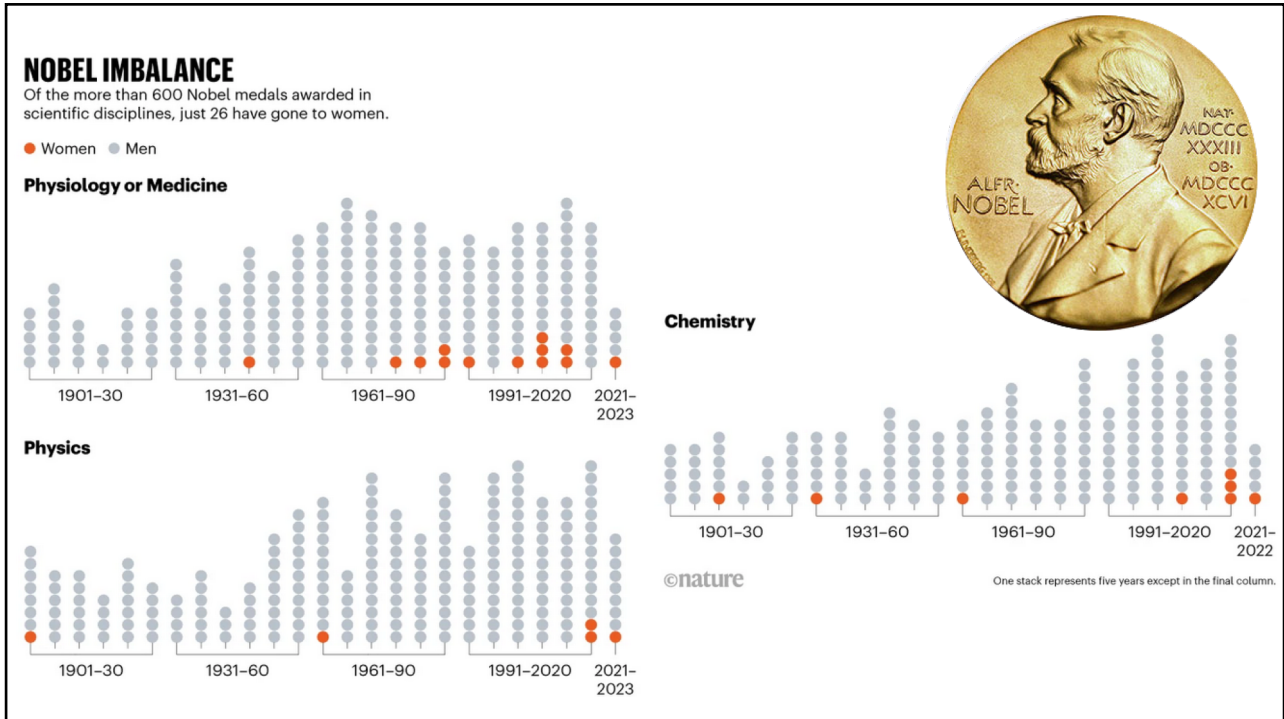


THE NOBEL PRIZE
IN PHYSIOLOGY OR MEDICINE 2023



Illustrations: Niklas Elmehed

Katalin Karikó Drew Weissman



La recherche : C'est voir au-delà de la première observation évidente.



Octavio Ocampo



Dalí

Fotos.org



Jean-Marc
CAVAILLON

**LA FLAMME
SALVATRICE**
IL ÉTAIT UNE FOIS L'INFLAMMATION

Éditions **DOCSIS**

Jean-Marc Cavaillon

**LA FLAMME SALVATRICE :
IL ÉTAIT UNE FOIS L'INFLAMMATION**

Dans cet ouvrage, l'auteur cherche à faire découvrir au lecteur la fascinante histoire de l'inflammation, sa beauté quand elle rime avec immunité et protection contre les infections, sa laideur quand elle rime avec maladies, voire avec mort. En faisant références au cinéma et aux œuvres d'art, l'auteur illustre la dualité de cette inflammation, son aspect mi-ange mi-démon, le yin et le yang de la vie, le bien et le mal... Au gré de ses recherches bibliographiques, l'auteur emmène le lecteur de l'âge des dinosaures aux découvertes les plus récentes du XXI^e siècle. Il nous détaille les nombreux paramètres qui influencent la qualité de la réponse inflammatoire, le stress, le sexe, la vieillesse, le système nerveux... de l'effet placebo à l'effet nocébo. Il décrypte les étapes qui permettent de faire le lien entre miasmes, microbes et maladies infectieuses. Il évoque les luttes contre ces dernières, et salue les précurseurs de l'hygiène. Il s'incline devant la tombe du scientifique inconnu, rend hommage aux pionniers célèbres ou oubliés, aux savants qui déchiffrèrent les mécanismes de l'inflammation, à ceux qui proposèrent de nouvelles thérapies, ou mirent fin à des approches thérapeutiques millénaires inutiles telle que la saignée. Il témoigne de son admiration pour ces précurseurs qui en avance sur leur temps luttèrent contre les préjugés, les dogmes, et l'égo de leurs collègues. Au gré du récit, l'auteur sème des anecdotes de sa vie de chercheur et d'enseignant, ses rencontres avec des prix Nobel, mais aussi avec des escrocs de la science. Enfin, il nous livre ses commentaires que l'amènent à formuler des décennies confrontées au long chemin escarpé de la recherche.

La flamme c'est le feu, le feu qui brûle, le feu qui dévore, détruit et réduit en cendres, mais la flamme, c'est celle que l'on déclare, c'est aussi la passion de celui qui est tout feu tout flamme et qui se consume d'amour. Dans cet ouvrage, Jean-Marc Cavaillon nous déclare sa flamme pour cette inflammation si étroitement associée à la vie, le fil rouge de sa carrière scientifique.

Jean-Marc Cavaillon est professeur à l'Institut Pasteur où il aura exercé l'ensemble de sa carrière de chercheur. Enseignant l'immunologie, il aura dispensé ses cours tant au Pérou qu'à Hong Kong, au Mexique, en Algérie, en Colombie ou en Corée du Sud. Ses présidences successives de sociétés savantes internationales (International Endotoxin and Innate Immunity Society, 1998-2000 ; European Shock Society, 2015-2017), illustrent la visibilité de ses recherches tant fondamentales que médicales, avec un intérêt toujours affiché pour les maladies humaines.

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Le mauvais air

Il était une fois les infections
et les combattants de l'ombre

Jean-Marc Cavaillon



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Le mauvais air

Il était une fois les infections
et les combattants de l'ombre

Jean-Marc Cavaillon

Jean-Marc Cavaillon nous retrace l'histoire de l'humanité confrontée aux pandémies, et la contribution de quelques savants célèbres et de beaucoup d'autres injustement oubliés qui identifièrent les miasmes, les animalcules, les virus, les germes responsables de tant de maux. Il relate leurs efforts pour lutter contre les infections, proposer l'hygiène, offrir les traitements antiseptiques ou antibiotiques, et prévenir les maladies infectieuses à l'aide des vaccins. Il met en parallèle de surprenantes analogies entre des événements historiques et des événements associés à la pandémie de COVID-19, devenue le fil rouge de ce récit : les liens incestueux entre certains scientifiques et la presse scientifique, les querelles entre doctes docteurs, entre contagionnistes et anticontagionnistes, entre rassuristes et alarmistes... Il rappelle l'usage des masques initié au XVI^e siècle, l'extraordinaire sagesse de la vaccination accompagnée de la concomitante réticence face aux vaccins. Autant d'événements témoins de la guerre déclarée aux microbes et de la guerre des égos. Sur son chemin, il croise ses héros favoris, Metchnikoff et Semmelweis, déniche des génies oubliés, et n'hésite pas à égratigner l'image d'Épinal de Louis Pasteur, entretenue par ses hagiographes.

Jean-Marc Cavaillon est professeur honoraire de l'Institut Pasteur, où il a été directeur d'une unité de recherche et du département « Infection et épidémiologie ». Il est récipiendaire de deux sociétés savantes : « International Endotoxin and Innate Immunity Society » et « European Shock Society ».

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