

AMWC 2022  
AESTHETIC & ANTI-AGING  
MEDICINE WORLD CONGRESS

CELEBRATING THE  
20<sup>th</sup> EDITION OF  
AMWC MONACO  
March 31 - April 1-2  
IN-PERSON *Live-Stream*



# ANTI-INFLAMMATORY ARSENAL 2022



Patrizia A d'Alessio, MD PhD

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Pr Dr University Paris Sud-11 and Genopole d'EVRY

# What ?

There is something out there called “aging”.

*Think about a more youthful  
lifestyle*





# Why ?

*Since mankind emerged, we have always thought it possible to smoothen the effects of « aging » yet different approaches are possible*



*with the help of nature*

# How ?

*Slowing down seems the  
most difficult anti-aging  
strategy to achieve*

*Yet it may quietly  
embellish the skin.*

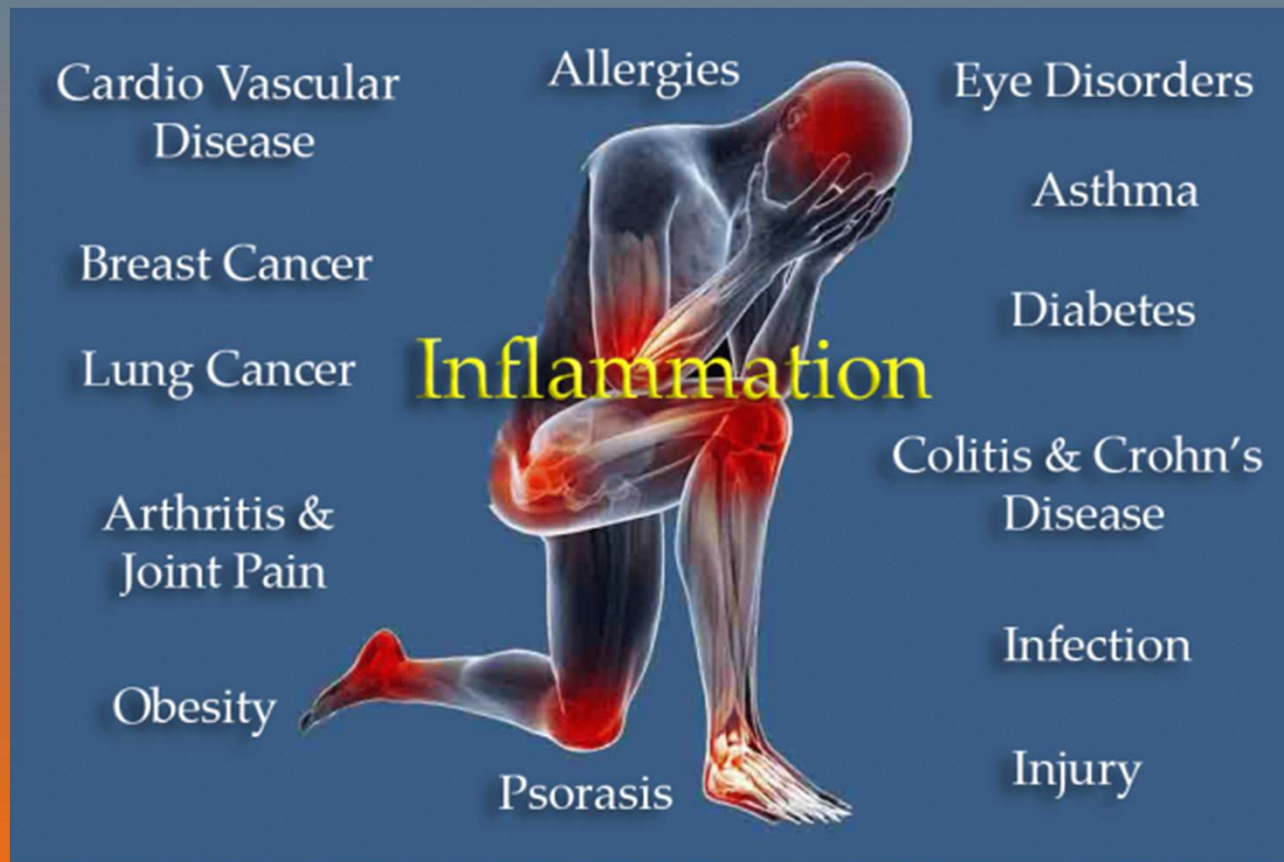




# Aging and inflammation?



# Inflammation **that we ache about**



# Inflammation **that we are not aware of**



is at the base of chronic disease,  
cancer and neurodegeneration

But also digestive disorders,  
depression and insomnia, decrease  
of ***beauty and fitness***

In both cases...



Control of immune responses was lost  
at some point...



# A short history of anti-inflammatory drugs

Mid XIXth : **salicylates**



Mid XXth : **corticosteroids**

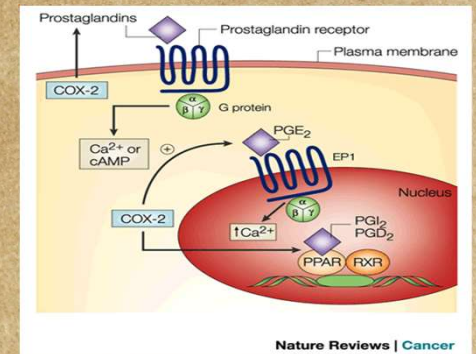


Further on :

Non steroid anti inflammatory drugs (**NSAID**) : organic acids

## Prostaglandin inhibitors ('70)

- Aspirin
- Indomethacin
- Phenylbutazone



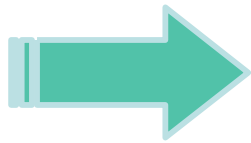
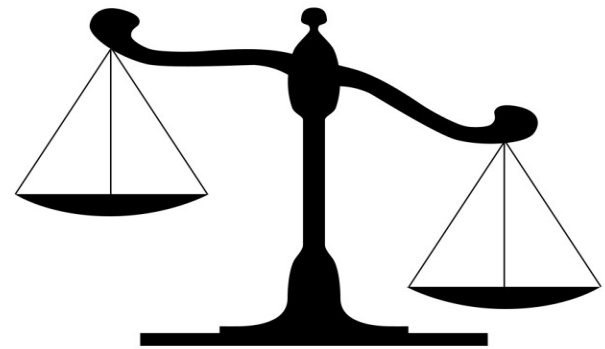
# The pioneers

## Physiology and Medecine Nobel Prize 1989

- Se K. Bergström,
- Bengt I. Samuelsson,
- **John R. Vane**



- Anti-inflammatory drugs are efficient but on a fraction of the population



Only 25% responders !

**AND SIDE EFFECTS!!**



# STOP !!!!

In **2004**, **rofecoxib** usage is reported to induce important secondary **cardiovascular** side effects (heart attack)

Alternatives :

- platelet aggregation inhibitors
- **leucocyte recruitment inhibitors**
- **endothelial protectors**

# 2022 anti-inflammatory arsenal

Steroids

NSAIDs & « *biologics* »

Fluvoxamine

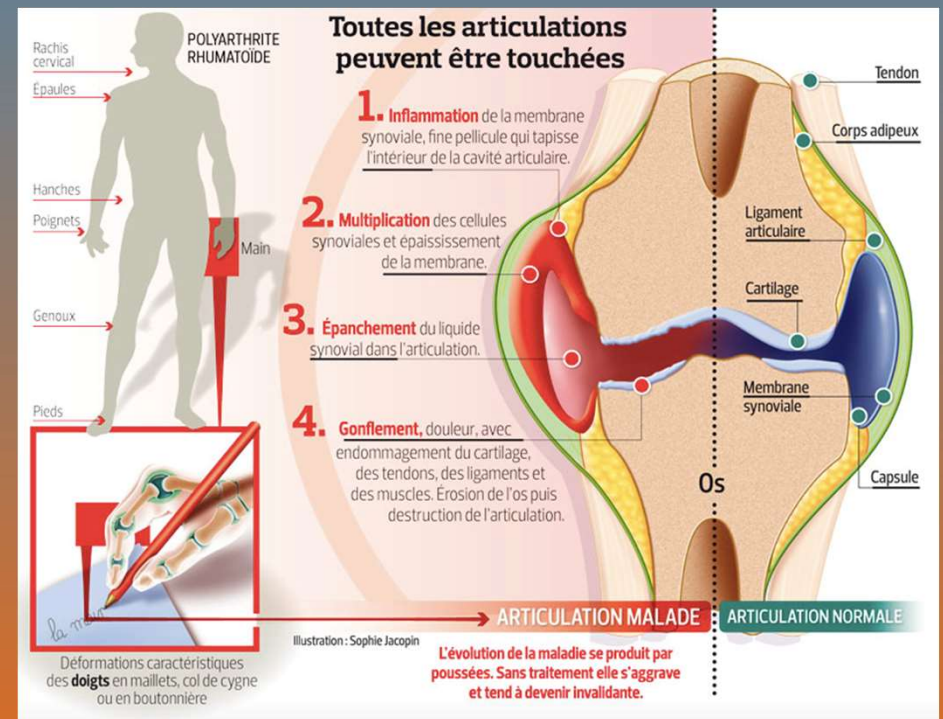
New approaches

# Targeting auto-immunity?

**Infliximab** (remicade) MoAb **anti-TNF- $\alpha$**   
indications : RA, spondylarthritis, Crohn

**Etanercept** (enbrel) chimeric TNF-R2 / IgGFc;  
indications : RA and spondylarthropathies

**Adalimumab** (humira) **humanised** anti TNF  
MoAb, indications : RA





# NEW approaches

- Fluvoxamine (PROZAC) fighting both inflammation and depression

## Effect of early treatment with fluvoxamine on risk of emergency care and hospitalisation among patients with COVID-19: the TOGETHER randomised, platform clinical trial

Gilmar Reis, Eduardo Augusto dos Santos Moreira-Silva, Daniela Carla Medeiros Silva, Lehana Thabane, Aline Cruz Milagres, Thiago Santiago Ferreira, Castilho Vitor Quirino dos Santos, Vitoria Helena de Souza Campos, Ana Maria Ribeiro Nogueira, Ana Paula Figueiredo Guimaraes de Almeida, Eduardo Diniz Callegari, Adhemar Dias de Figueiredo Neto, Leonardo Cançado Monteiro Savassi, Maria Izabel Campos Simplicio, Luciene Barra Ribeiro, Rosemary Oliveira, Ofir Harari, Jamie I Forrest, Hinda Ruton, Sheila Sprague, Paula McKay, Alla V Glushchenko, Craig R Rayner, Eric J Lenze, Angela M Reiersen, Gordon H Guyatt, Edward J Mills, for the TOGETHER investigators\*

### Summary

**Background** Recent evidence indicates a potential therapeutic role of fluvoxamine for COVID-19. In the TOGETHER trial for acutely symptomatic patients with COVID-19, we aimed to assess the efficacy of fluvoxamine versus placebo in preventing hospitalisation defined as either retention in a COVID-19 emergency setting or transfer to a tertiary hospital due to COVID-19.



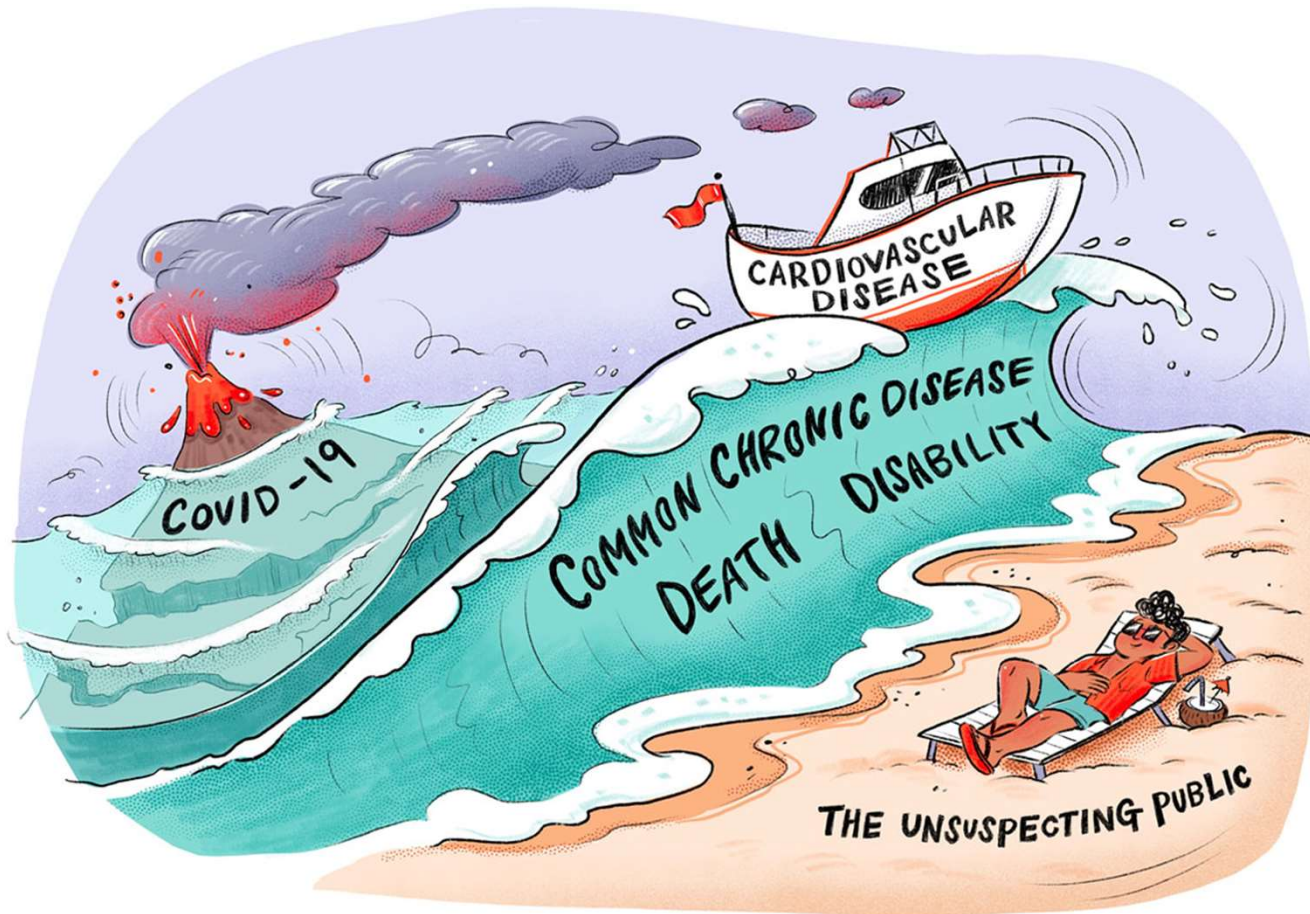
*Lancet Glob Health* 2021  
Published Online  
October 27, 2021  
[https://doi.org/10.1016/S2214-109X\(21\)00448-4](https://doi.org/10.1016/S2214-109X(21)00448-4)

# NEW approches

## Associating anti-inflammatory / anti-viral effects

- ◆ **Opaganib**, inhibitor of sphingosine-kinase-2 (SK-2 ) with
  - ◆ anti-inflammatory activity in auto-immune diseases ;
  - ◆ anti-viral effects





# Circulation

**Avoiding the Coming Tsunami of Common, Chronic Disease**

**What the Lessons of the COVID-19 Pandemic Can Teach Us**

Robert M. Califf 

Originally published 6 Apr 2021 |  
<https://doi.org/10.1161/CIRCULATIONAHA.121.053461> |  
Circulation. 2021;143:1831–1834



## « Cytokine storm »

“The fact is that the real morbidity and mortality of this disease is probably driven by **this out-of-proportion inflammatory response** to the virus...”



Dr. Jamie Garfield,  
Temple University Hospital

# NEW approches

- Anti-inflammatory botanicals – before check-point inhibitors



◆ Pierre Potier

TABLE 3: Botanicals Used to Fight Inflammation

Botanical	Source	Effect
<b>Chalcones</b>		
Butein	Heartwood of <i>Dalbergia odorifera</i>	Inhibit activation of pro-inflammatory factors
Xanthohumol	The hop plant	Inhibit IL-12 production
<b>Flavonoids</b>		
Fisetin	Smoke tree ( <i>Cotinus coggygria</i> )	Inhibition of wide range of biomarkers
Morin	Mulberry figs and other Chinese herbs	Chemoprevention via inhibition of inflammatory factors
<b>Alkaloids</b>		
Berberine	<i>Rhizoma coptidis</i>	Enhance insulin sensitivity & reduce blood sugar
Sanguinarine	<i>Sanguinaria canadensis</i> and poppy <i>Fumaria</i> species	Anti-tumor via inhibition of transcription factor
<b>Xanthones</b>		
γ-Mangostin	<i>Garcinia mangostana</i>	To control GI problems, wound infections and chronic ulcers
Gambogic acid	<i>Garcinia morella</i> and <i>Garcinia hurburyi</i>	Anti-cancer
<b>Triterpenoids</b>		
Ursolic acid	Rosemary, apple, cranberry, beefsteak, pear, plum, basil, and jamun	Anti-cancer
Acetyl-11-keto-β-boswellic acid	Derivative of boswellic acid	Anti-cancer and anti-osteoarthritis
<b>Quinones</b>		
Thymoquinone	Black seed oil ( <i>Nigella sativa</i> )	Against lung disease, arthritis and hypercholesterolemia
Capsaicin	Red chili pepper <i>Capsicum</i>	Against neuropathic pain, itching and numerous cancer types
<b>Polyphenols</b>		
Curcumin	Turmeric ( <i>Curcuma longa</i> )	Against stomach upset, dysentery, ulcers, jaundice, arthritis, sprains, wounds, acne and skin and eye infections
Tocotrienol	Vitamin E	Diabetes, cardiovascular, Parkinson's and cancer
Contignasterol	Polyoxygenated steroid from the marine sponge <i>Petrosia contignata</i> in Papua New Guinea	Potential candidate in the treatment of asthma and other inflammatory diseases

Source: Journal of Agriculture and Food Chemistry, 2012.

# 2022 : what else?

Steroids  
NSAIDs & « *biologics* »  
Fluvoxamine  
New approaches

Mobilisation therapies  
Physical activity





# Mobilisation therapies and « body awareness »

Kinesiology  
Osteopathy  
Fasciatherapy  
Balneotherapy  
Feldenkrais....



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# Moderate movement inhibits age-related inflammation



This information is current as of March 27, 2022.

## **Moderate Exercise Inhibits Age-Related Inflammation, Liver Steatosis, Senescence, and Tumorigenesis**

Arianna Bianchi, Letizia Marchetti, Zoe Hall, Henrique Lemos, Michele Vacca, Hannah Paish, Kile Green, Bronte Elliott, Dina Tiniakos, João F. Passos, Diana Jurk, Derek A. Mann and Caroline L. Wilson

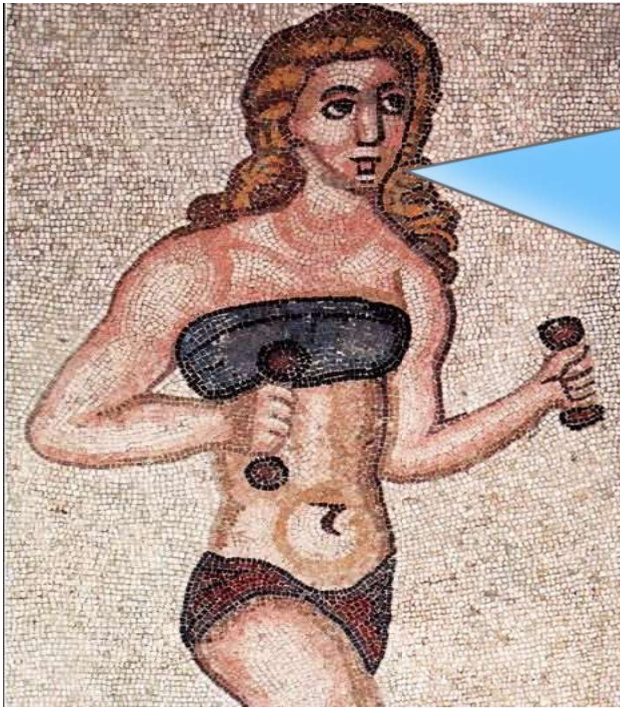
*J Immunol* 2021; 206:904-916; Prepublished online 13 January 2021;

doi: 10.4049/jimmunol.2001022

<http://www.jimmunol.org/content/206/4/904>



# L'EXERCISE : de-toxyfying effect



◆ *Fascias* are pressed like a sponge and rehydrated

◆ « **bulk water** » will be replaced by « **bound water** »

# 2022 : what else?

Steroids  
NSAIDs & « *biologics* »  
Fluvoxamine  
New approaches

Mobilisation therapies  
Physical activity

Nutrition  
Fasting  
CR



# Here too we have pioneers

## Fasting



BUCH/NGER  
W/LHELM

Dr Otto **Buchinger** starts fasting to treat a severe RA, on base of war trauma.

**Body & soul** harmony will remain at the base of his anti-inflammatory approach.



# Modern version of fasting is TRE

## Time Restriction Eating

- Pr Pamela M Peek's, new method :
- Eat **10-12 hours / day** ;
- privileging fat, low carbs and glucose;
- **re-enabling a perturbed (erratic eating) metabolic circadian rhythm**;
- nutrients regulate autonomic nervous and endocrine systems;
- endpoints : **loose 10 kg in 2 months**, stabilise your FBG\*

■\* fasting blood glucose

Peek et al. *Nutrition and Diabetes* (2021) 11:6  
<https://doi.org/10.1038/s41387-021-00149-0>

Nutrition & Diabetes

ARTICLE

Open Access

Effect of time restricted eating on body weight and fasting glucose in participants with obesity: results of a randomized, controlled, virtual clinical trial

Pamela M. Peek<sup>1</sup>, Frank L. Greenway<sup>2</sup>, Sonja K. Billes<sup>3</sup>, Dachuan Zhang<sup>2</sup> and Ken Fujioka<sup>4</sup>

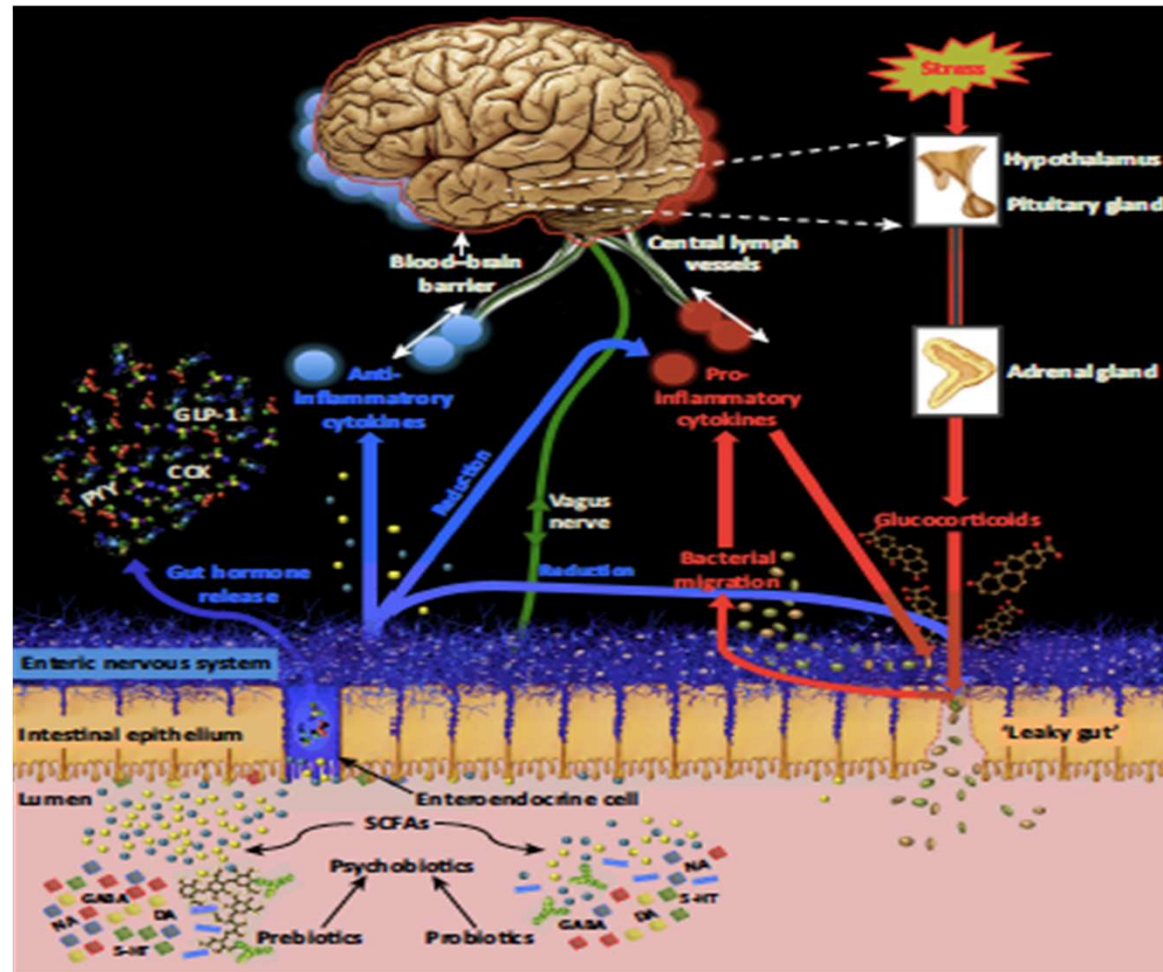
# Stress and Food alike regulate us

## Pre-biotics

Non digestibles  
fibres

## Pro-biotics

Live  
microorganisms

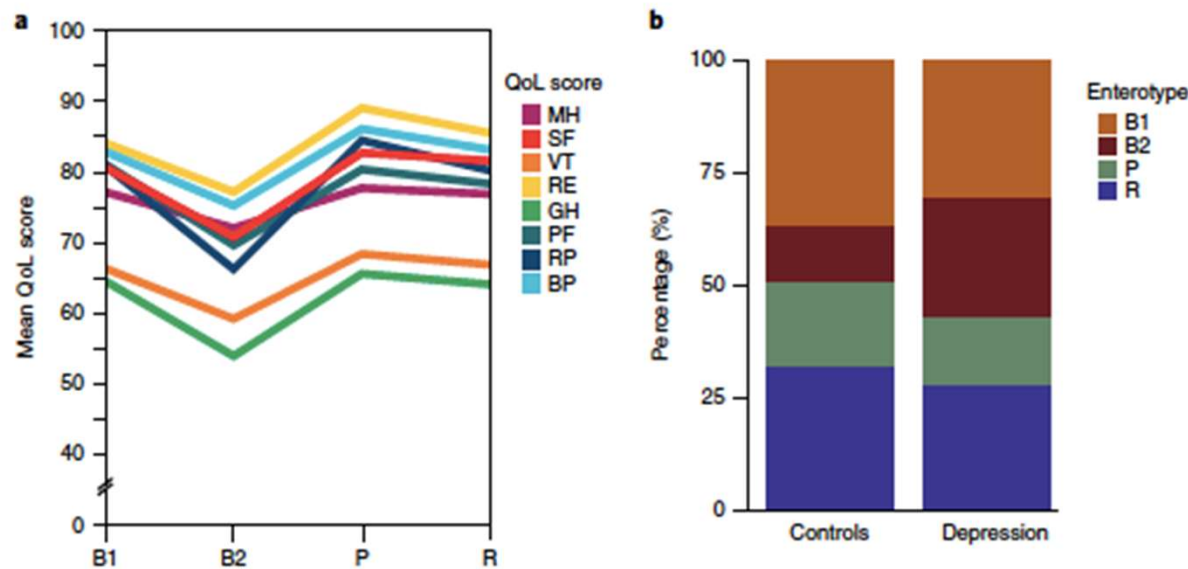


A. Sarkar et al Trends in Neurosciences Cell Press 11 : 763-781, 2016.



# Potent anti-inflammatory effect of food due to the **neuroactive potential** of microbiota

*Faecalibacterium* et *Coprococcus* are at the base of our well-being

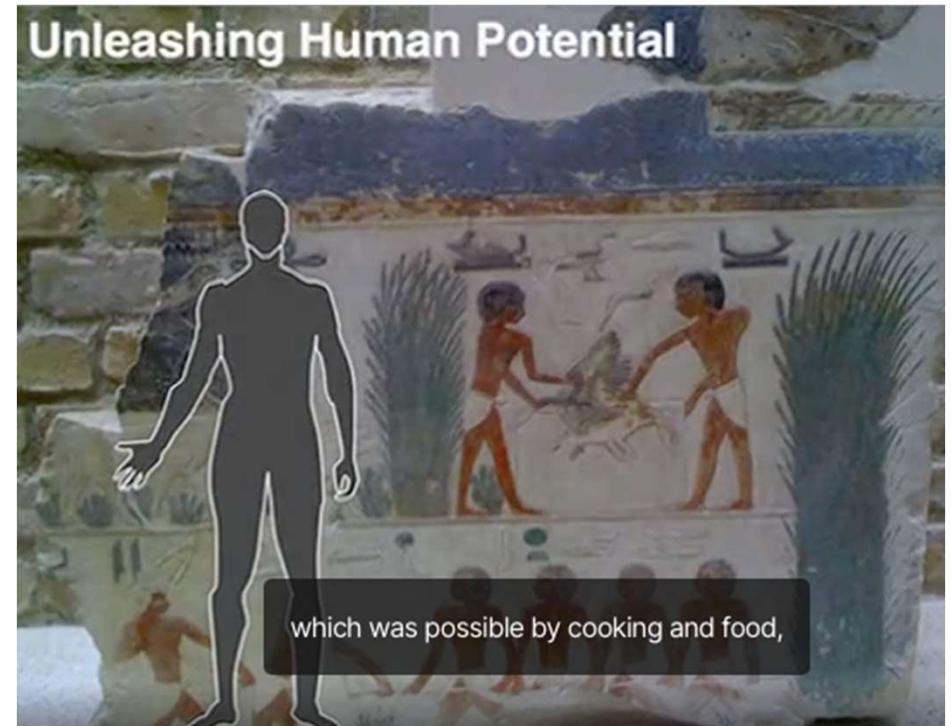


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# Cooking, vector of positive psychology



- Cooking has allowed us to become **migrants**, transformation of undigestible nutrients developing the knowledge about spices and thus **drugs**



TEDGlobal 2010 • July 2010 | 1.8M views

## The brain in your gut

Heribert Watzke

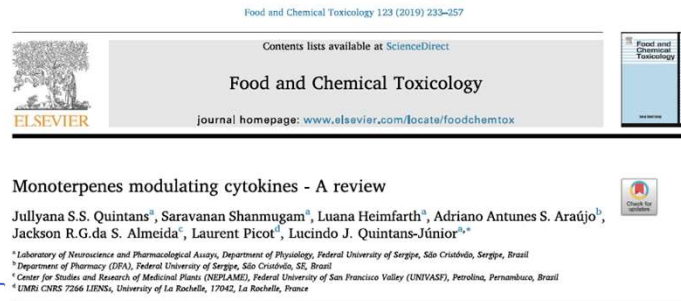
# Arsenal 2022 : what else?

Steroids  
NSAIDs & « biologics »  
Fluvoxamine  
New approaches

Natural substances

Mobilisation therapies  
Physical activity

Nutrition  
Fasting  
CR  
TRE



antioxidants

Review

## Terpenoids as Potential Geroprotectors

Ekaterina Proshkina<sup>1</sup>, Sergey Plyusnin<sup>1,2</sup>, Tatyana Babak<sup>1</sup>, Ekaterina Lashmanova<sup>1</sup>, Faniya Maganova<sup>3</sup>, Liubov Koval<sup>1,2</sup>, Elena Platonova<sup>1,2</sup>, Mikhail Shaposhnikov<sup>1</sup> and Alexey Moskalev<sup>1,2,\*</sup>





# Monoterpenes address the brain-gut axis



- ◆ Monoterpenes protect and repair the gut barrier, stopping inflammation to go generalised;
- ◆ Inhibiting inflammatory cytokines;
- ◆ Enhancing mood;
- ◆ Contributing in slowing down aging.

« The Gut-brain axis is relevant to skin aging ». d'Alessio PA PRIME July 2020, Vol 10 Issue 4, 36-42

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2003-2006 Fudan University Shanghai



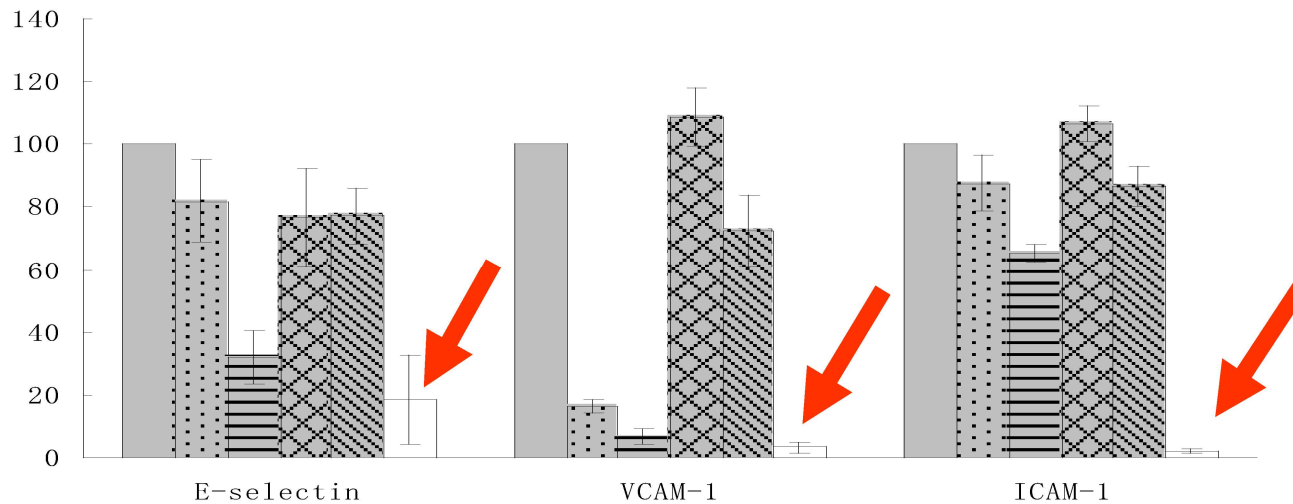
Lei Gong Teng



**“Tripterine, inhibits the expression of adhesion molecules in activated endothelial cells”**

Deng-hai Zhang, Anthony Marconi, Li-Min Xu, Chun-xin Yang, Guo-wu Sun, Xiao-ling Feng, Shu-min Xu, Chang-quan Ling, Wan-zhang Qin, Georges Uzan, and **Patrizia d'Alessio**. J Leuk Biol, 80: 309-319, **2006**.

# Tripterine vs panel anti-inflammatory



Tripterine inhibits the expression of adhesion molecules in activated endothelial cells

Deng-hai Zhang,<sup>\*,†</sup> Anthony Marconi,<sup>\*</sup> Li-min Xu,<sup>†</sup> Chun-xin Yang,<sup>‡</sup> Guo-wu Sun,<sup>†</sup> Xiao-ling Feng,<sup>†</sup> Chang-quan Ling,<sup>§</sup> Wan-zhang Qin,<sup>‡</sup> Georges Uzan,<sup>\*</sup> and Patrizia d'Alessio<sup>\*,1</sup>

<sup>\*</sup>INSERM U602, Hôpital Paul Brousse, Villejuif, France; <sup>†</sup>Shanghai Pudong Gongli Hospital, Ruijin Hospital Group, Jiao Tong University, China; <sup>‡</sup>Zhongshan Hospital, Fudan University, Shanghai, China; and <sup>§</sup>Changhai Hospital, Shanghai Second Military Medical University, China

2006.

**Key Words:** inflammation · ICAM-1 · VCAM-1 · NSAID · Chinese medicinal plant

0741-5400/06/0080-309 © Society for Leukocyte Biology

<sup>1</sup> Correspondence: INSERM U602, Hôpital Paul Brousse, 12 avenue Paul Vaillant Couturier, 94807, Villejuif, France. E-mail: dalessio@vjf.inserm.fr

Received October 26, 2005; revised April 8, 2006; accepted April 10, 2006; doi: 10.1189/jlb.1005611.

Journal of Leukocyte Biology Volume 80, August 2006 309

TNF-α

Dexamethasone 1 mM

Ibuprofen 1 mM

Methotrexate 1 mM

ProbucoI 1 mM

Tripterine 200 nM



# Quid of our AI Arsenal 2022 ?

Nutraceuticals are an option



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J Med Foods 2014 « **Nutraceuticals of anti-inflammatory activity as complementary therapy for rheumatoid arthritis** » [Sahar Y Al-Okbi](#)

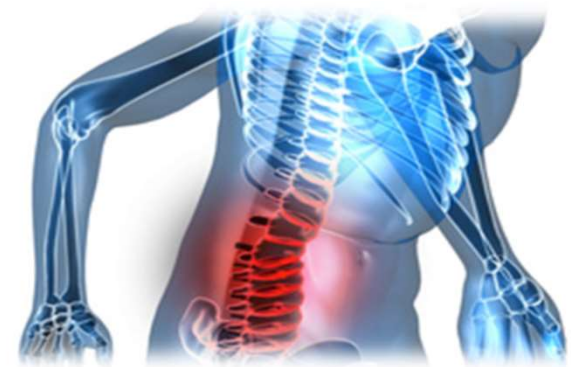
## INTERMEDIATE PSORIASIS

PSORIASIS study : 9 patients open label - 45 days



D0

D45



Global Journal of Dermatology & Venereology, 2015, 3, 1-4

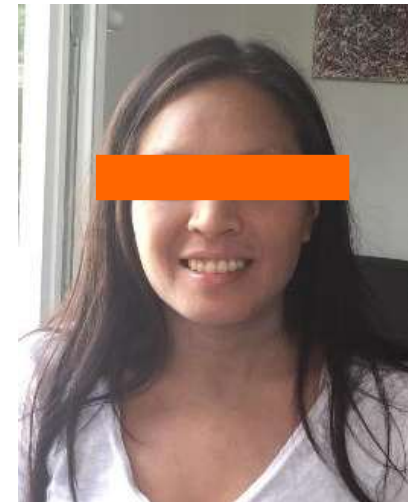
# Med-cosmetics is the new trend

## Nutraceuticals & Cosmeceuticals can ameliorate skin conditons

Day 0

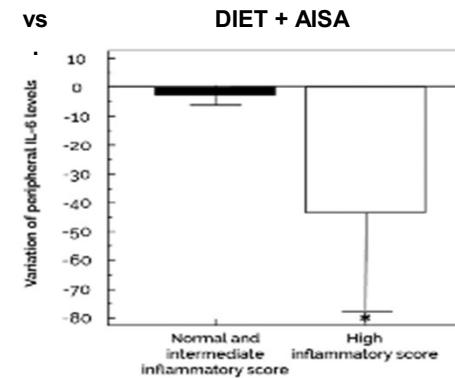
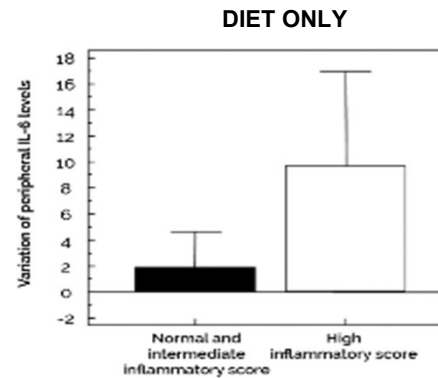
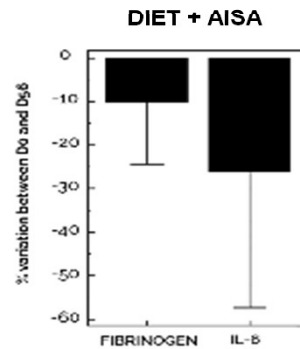


Day 56



# FP7 EU Projet “RISTOMED” on 140 patients

## Inflammation markers



Significant modifications of inflammation markers (fibrinogen and IL-6) were observed in individuals with baseline moderate inflammation (**RISTOMED diet + AISA**) between D0 and D56.



Clinical Nutrition 2016;35:812-818

# Anti-inflammatory Arsenal 2022

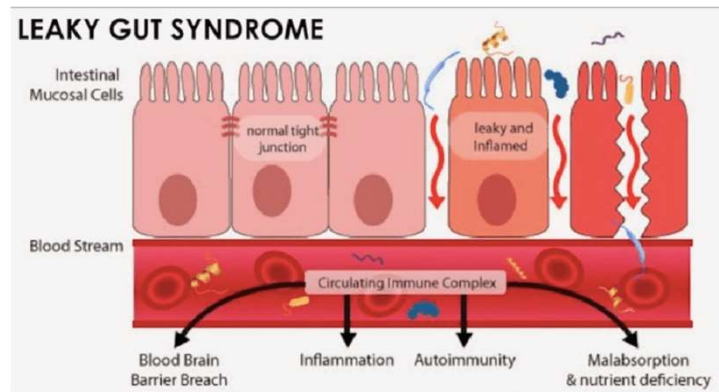
- Conventional drugs, potent, toxic & not selective

- Nutrition,
- CR & TRE

- natural substances, terpenoids,

- Mobilisation & slow movement

- Vagus tone activation



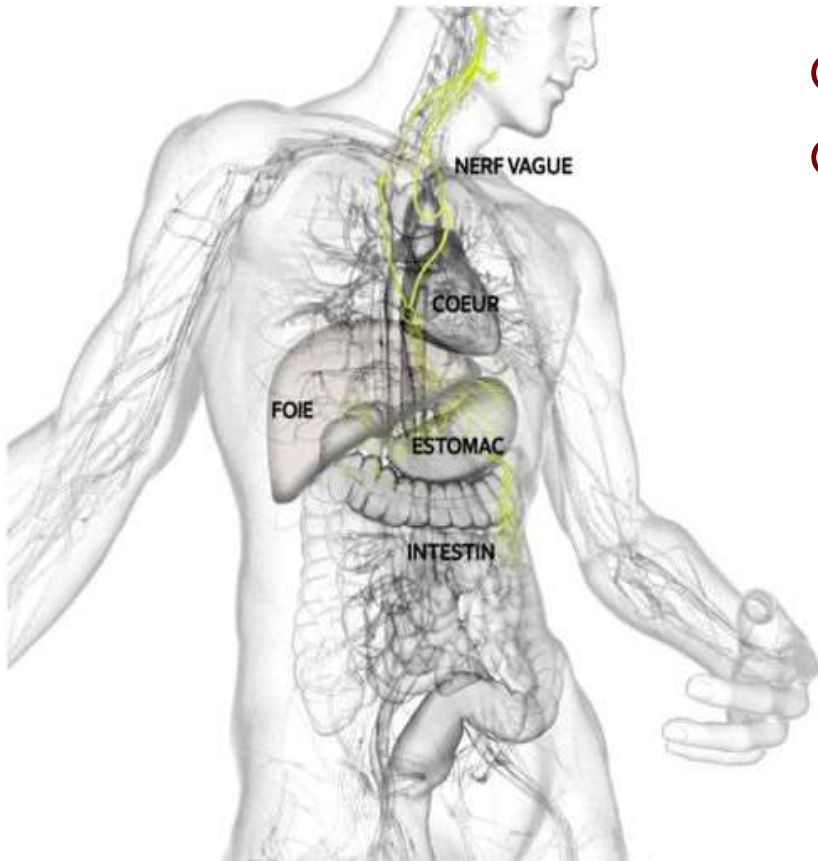
■ **Bio-objects !**

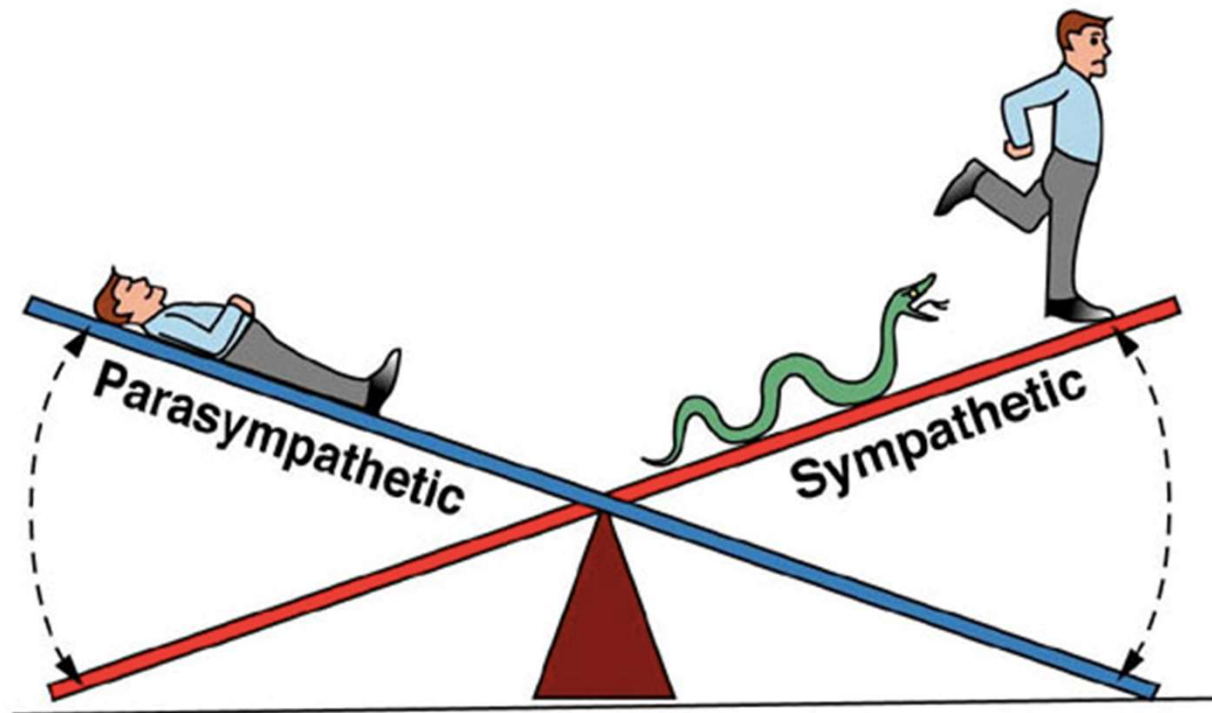




# Vagus activation,

our most potent endogenous  
anti-inflammatory partner





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# The ammunitions of SAM

« Sympathetic Adrenal Medullary axis »

	Orthosympathique	Parasympathique
Fonctions activées	Pression sanguine, glycémie, chaleur	Digestion, élimination, système immunitaire
Effets psychologiques	Peur, culpabilité, tristesse, colère, velléité, agressivité	Calme, satisfaction, relaxation
Facteurs d'activation	Stress, peur, colère, soucis, rumination, activité physique excessive	Repos, sommeil, méditation, relaxation, sensation de sécurité et de protection
Rôle	Défense de l'organisme	Guérison, régénération, alimentation du corps
Effets	Catabolisme	Anabolisme
Organes activés	Cerveau, muscles, pancréas endocrine (insuline), thyroïde, surrénales	Foie, reins, pancréas exocrine (amylase), rate, estomac, intestin grêle, côlon
Hormones et substances impliquées	Insuline, cortisol, hormones thyroïdiennes	Parathormone, enzymes pancréatiques, bile, enzymes digestives

Ortho Sympathic system :

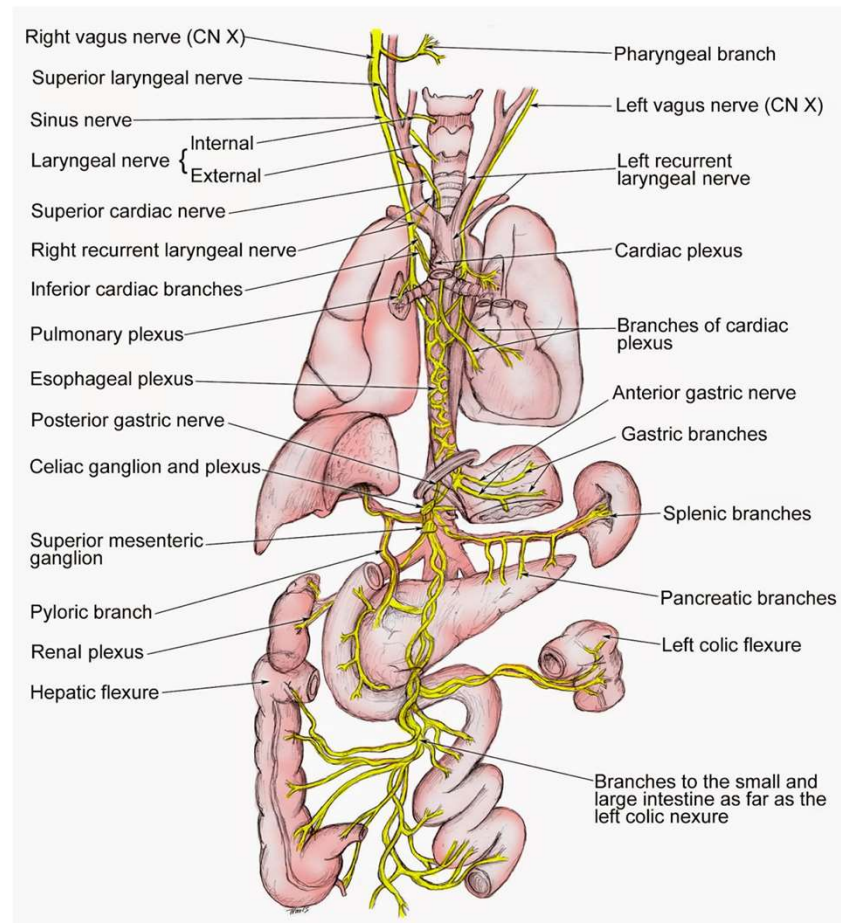
**Adrenaline** fight or flee

Para-sympathic system :

**Cholinergic** mechanism reducing systemic inflammation

# Anti-inflammatory cholinergic paths

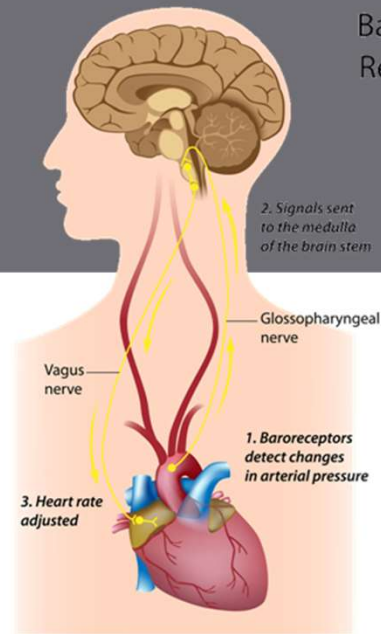
**Robert Dantzer,**  
stimulation of the  
efferent vagus  
**diminishes**  
production of  
inflammatory **cytokines**





# Perfume inhalation, sylvotherapy

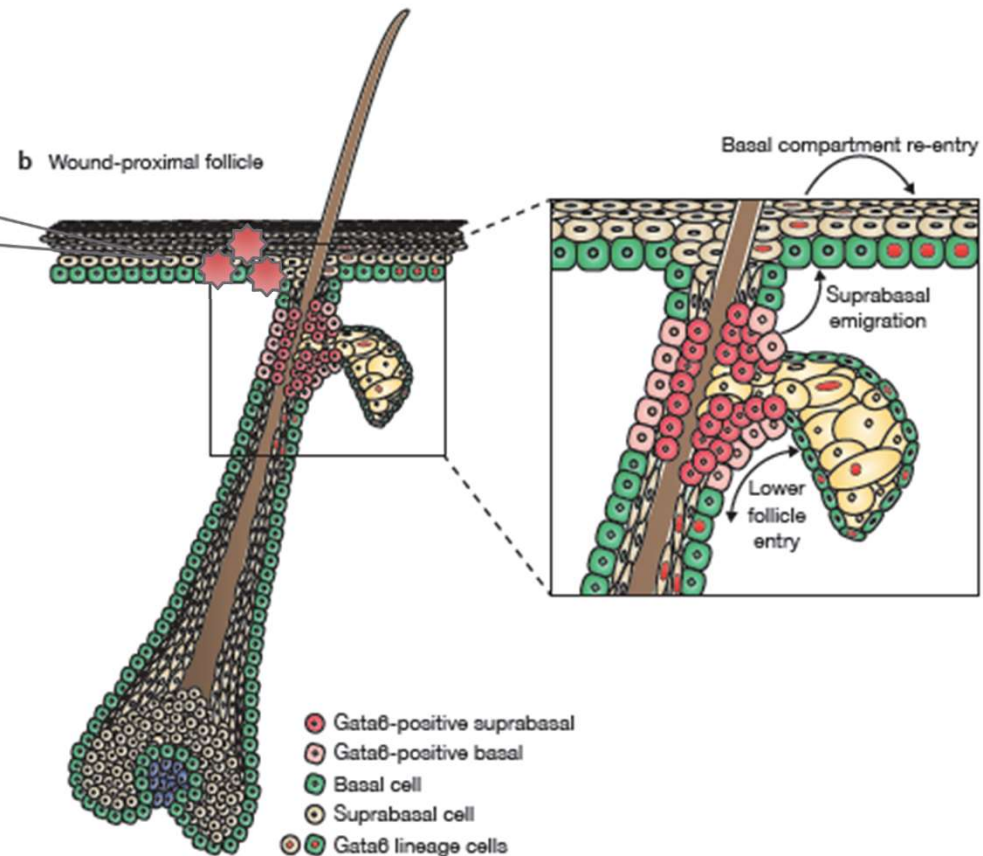
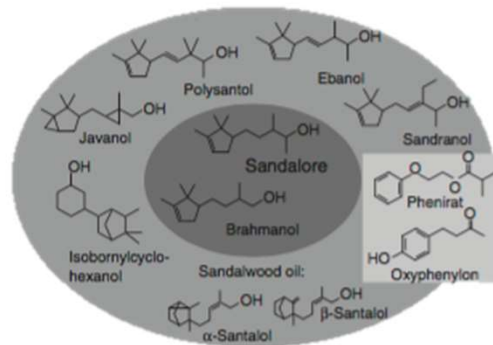
Deeply active  
vagal system;  
inducing relaxation  
and repair;  
diminishing all  
inflammation  
markers



Baroreceptor  
Reflex



# Small smelling molecules for skin repair



## A Synthetic Sandalwood Odorant Induces Wound-Healing Processes in Human Keratinocytes via the Olfactory Receptor OR2AT4

Daniela Busse<sup>1</sup>, Philipp Kudella<sup>1</sup>, Nana-Maria Grüning<sup>1,7</sup>, Günter Gisselmann<sup>1</sup>, Sonja Ständer<sup>2</sup>, Thomas Luger<sup>3</sup>, Frank Jacobsen<sup>4</sup>, Lars Steinsträßer<sup>4,8</sup>, Ralf Paus<sup>5</sup>, Paraskevi Gkogkolou<sup>6</sup>, Markus Böhm<sup>6</sup>, Hanns Hatt<sup>1</sup> and Heike Benecke<sup>1,9</sup>

Journal of Investigative Dermatology (2014), Volume 134

# Vagus stimulation by touch



- ◆ Social grooming and microbiota



- ◆ Emma Thompson & Greg Wise

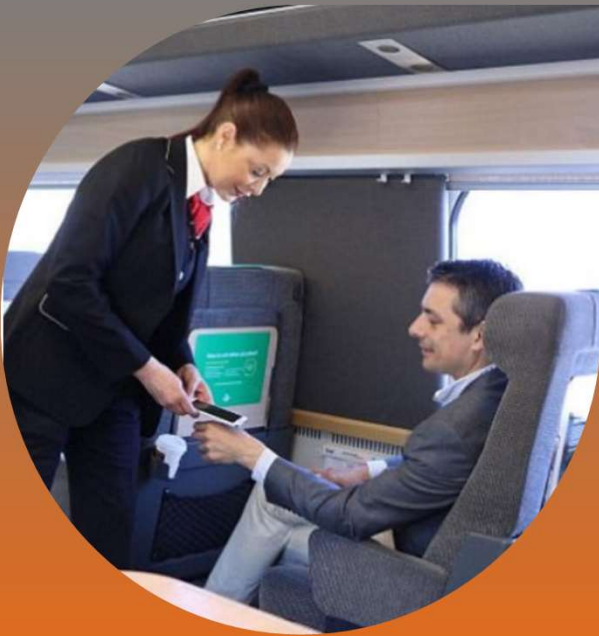
**Vagus** stimulation allows to exploit electron reservoir of the body



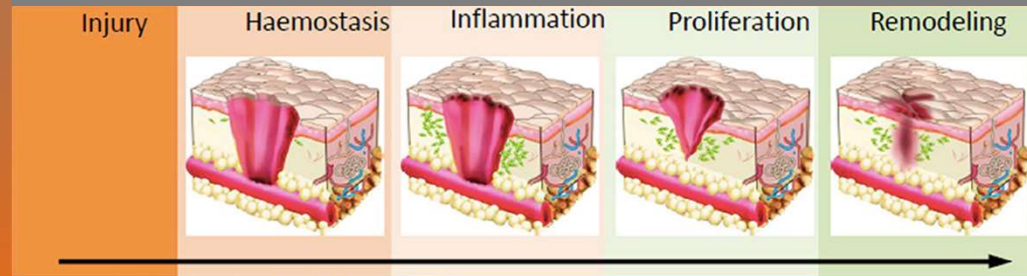


# The future?

## Bio-objets & « REMODELING »



- Soon sub-epidermal electronic implants matched to cellular elements
- will be activated to influence immune processes, ex gr. tissue repair



Lin et al. (2018). Copyright 2018, MDPI.

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# Quid of our AI Arsenal 2022 ?

- ◆ Drugs, conventional &
- ◆ Natural substances
- ◆ Mouvement therapies
- ◆ Nutrition & TRE
- ◆ Bio-objects integrating
  - ◆ Cell biology & AI
- ◆ Vagus activation

- ◆ Promise ?
  - ◆ Potent treatment
  - ◆ Amplification of the therapeutic effect



# TAKE HOME MESSAGE



**All you need to keep on the sunny side**

Protect / repair gut barrier  
Stop inflammation  
Enhance mood\*

\*Nutrients **2020**;12,800

Clinical Nutrition **2016**;35:812-818

Life Sciences **2013**;92:1151-1156

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# THANK YOU FOR YOUR ATTENTION



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European Innovation  
Partnership on Active  
and Healthy Ageing

REFERENCE SITE

[aisa-tx.com](http://aisa-tx.com)

