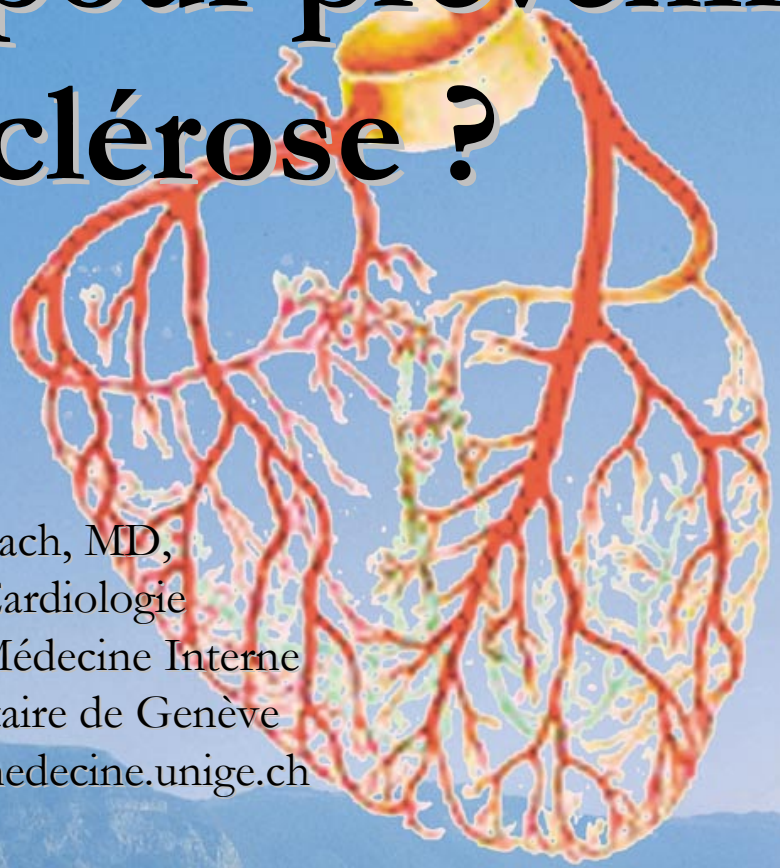
Le Cannabis pour prévenir l'athérosclérose ?



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Genève, le 26 juillet 2005

Pathophysiology of atherosclerosis

REVIEW ARTICLE

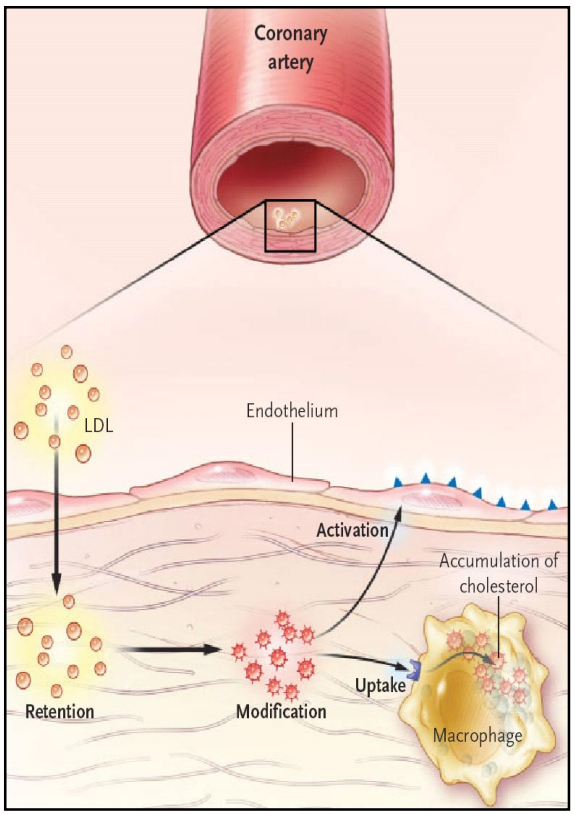
MECHANISMS OF DISEASE

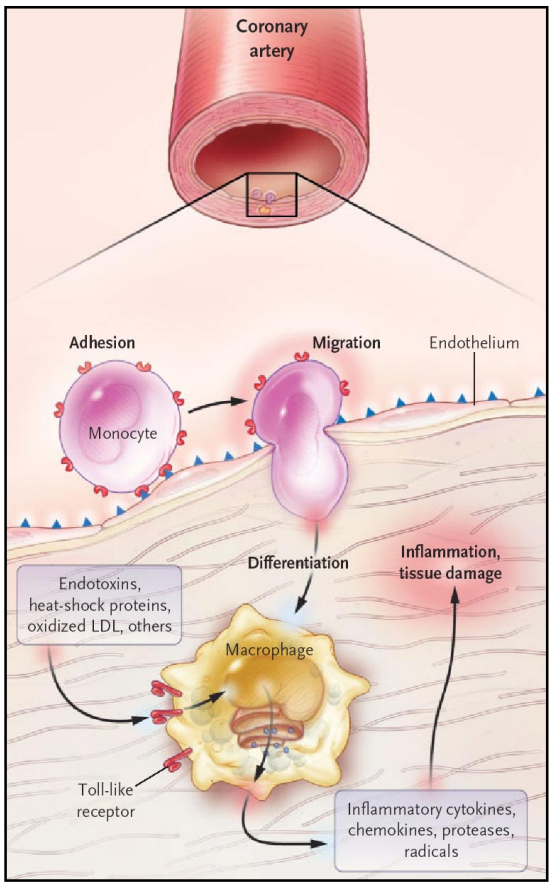
Inflammation, Atherosclerosis, and Coronary Artery Disease

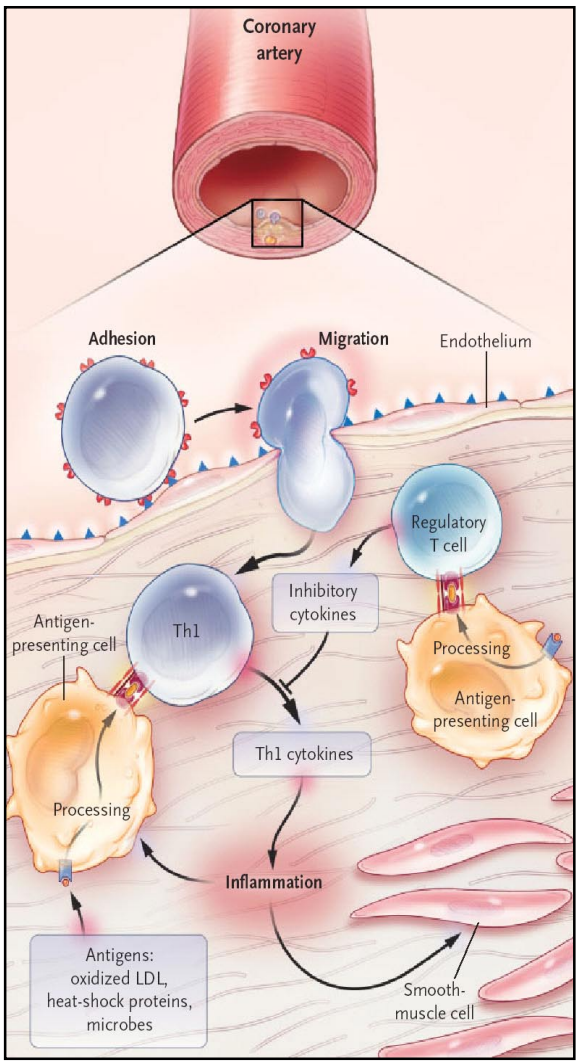
Göran K. Hansson, M.D., Ph.D.

N Engl J Med April 21 2005;352:1685

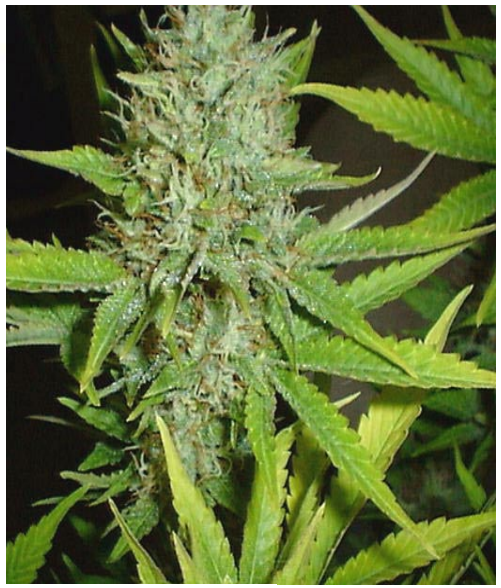
Pathophysiology of atherosclerosis

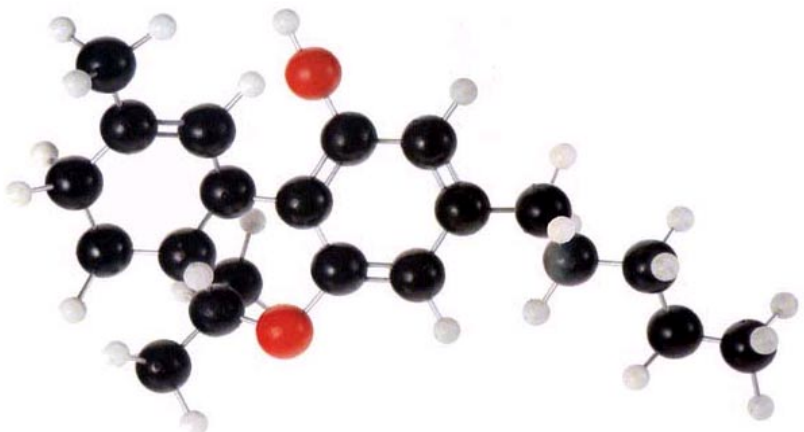






N Engl J Med 2005;352:1685

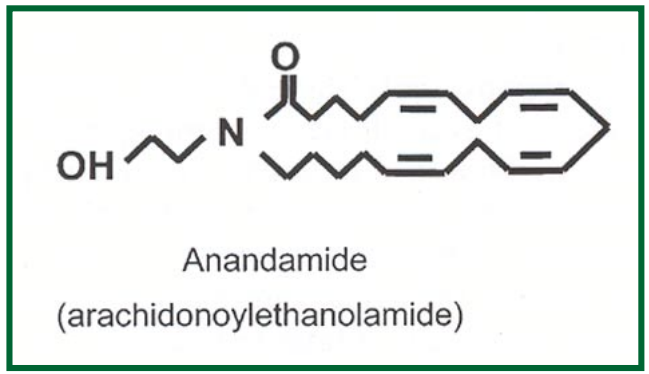




$\triangle^9$-tetrahydrocannabinol (THC)

The endocannabinoid system

⇒ 2 cannabinoid receptors + endogenous ligands

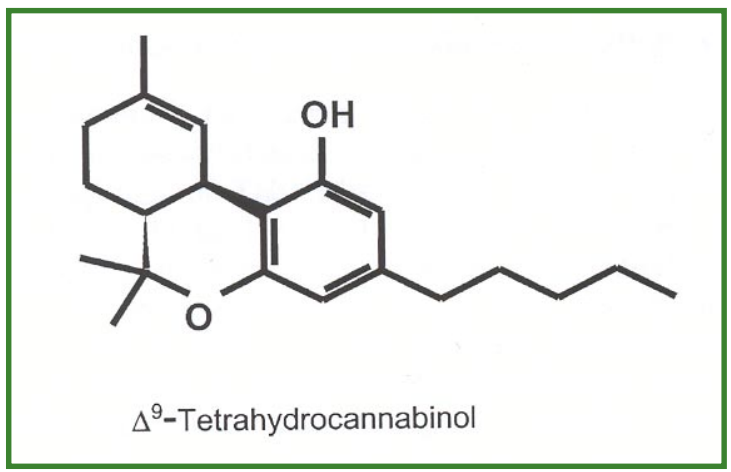


Anandamide
(arachidonoylethanolamide)

<u>Receptors:</u>

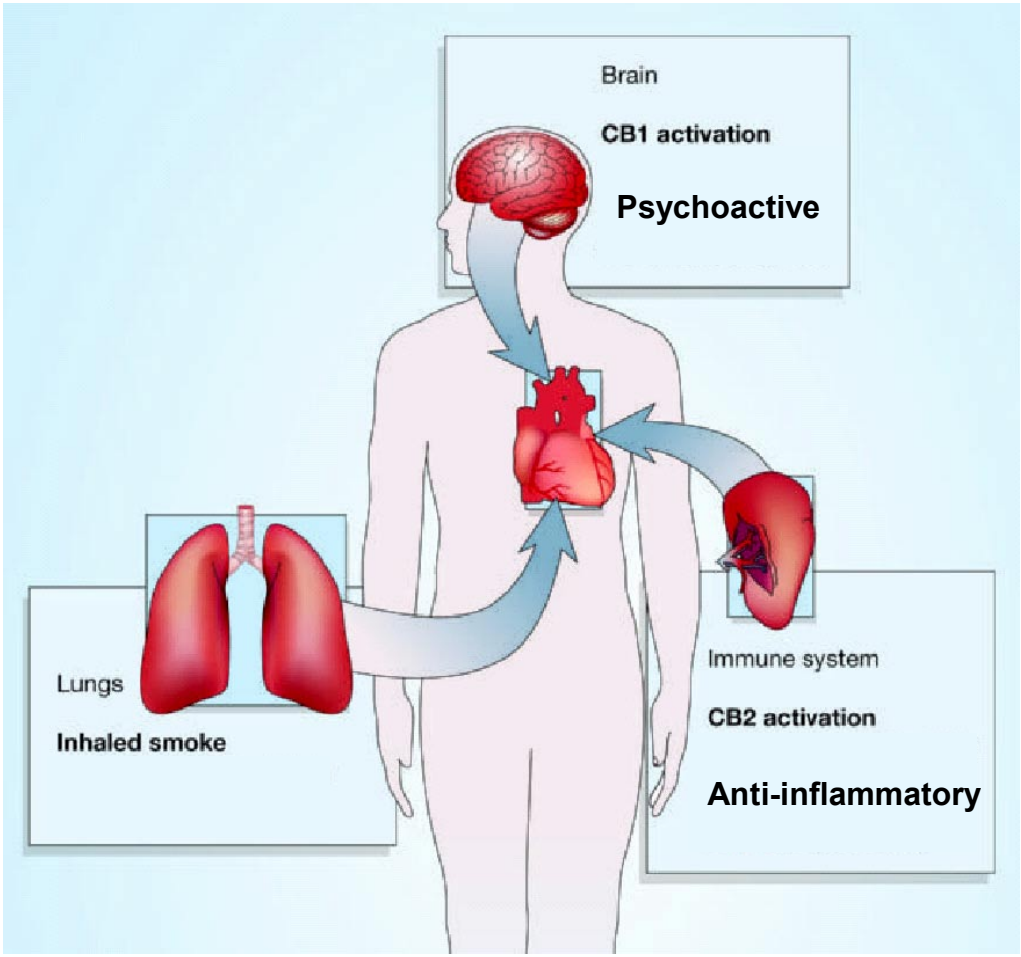
CB1: central and peripheral nervous system

CB2: on immune cells



Δ^9-Tetrahydrocannabinol

The endocannabinoid system

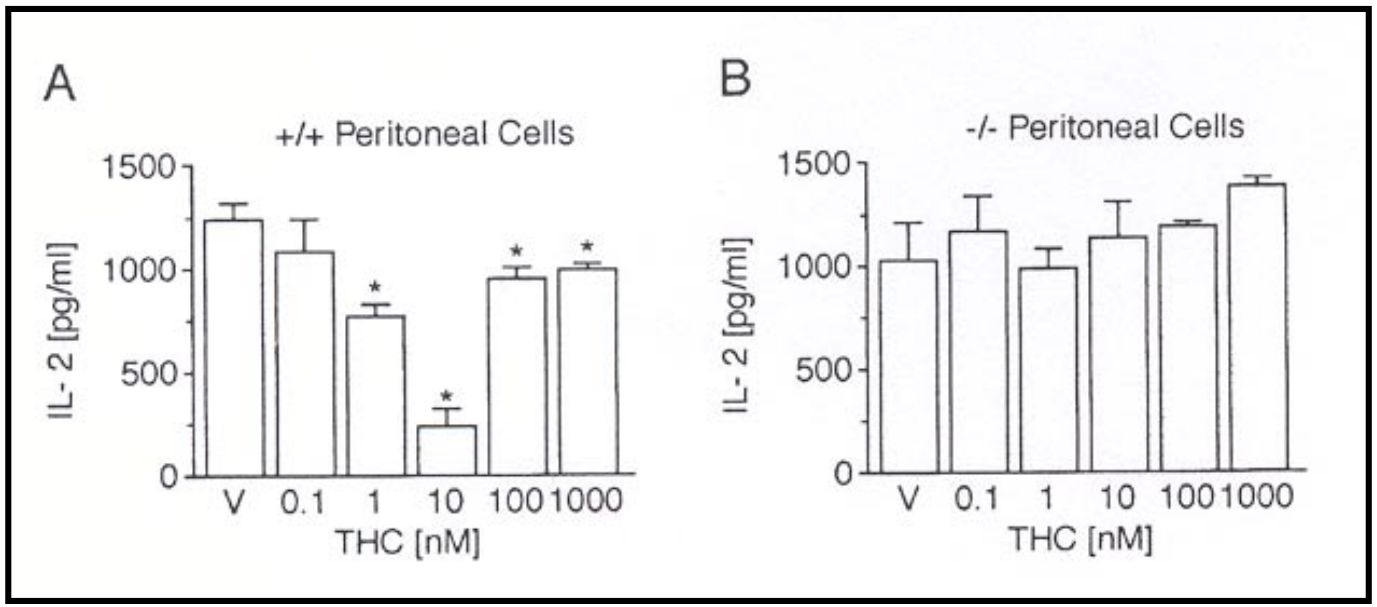


Cannabis has a treatment for

- **Anorexia**
- **Vomitting**

Nature 2005;434:708

Immunomodulation by cannabinoids is absent in mice deficient for the cannabinoid CB2 receptor



T cell co-stimulation assay with peritoneal macrophages from wildtype$^{+/+}$ or CB2$^{-/-}$ mice

Eur J Pharmacol 2000;396,141

Cannabinoids as therapeutic agents ?

Rheumatoid arthritis:

The nonpsychoactive cannabis constituent cannabidiol is an oral anti-arthritic therapeutic in murine collagen-induced arthritis

Malfait AM et al. *PNAS* 2000;97:9561

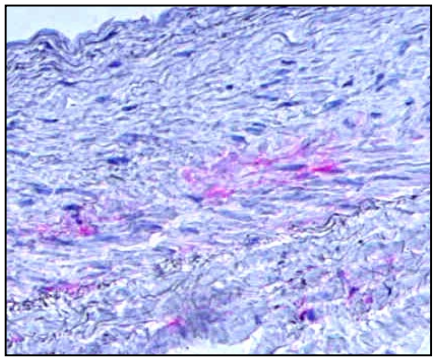
Multiple sclerosis:

Delta 9-tetrahydrocannabinol: a novel treatment for experimental autoimmune encephalomyelitis

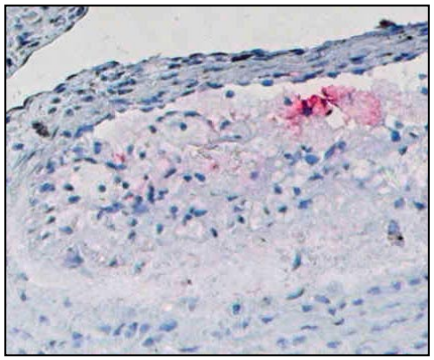
Lyman WD et al. *J Neuroimmunol* 1989;23:73

Does THC treatment have anti-atherosclerotic effects ?

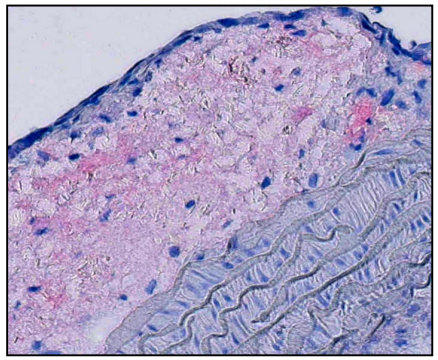
The cannabinoid receptor CB2 is expressed within human and mouse atherosclerotic plaques



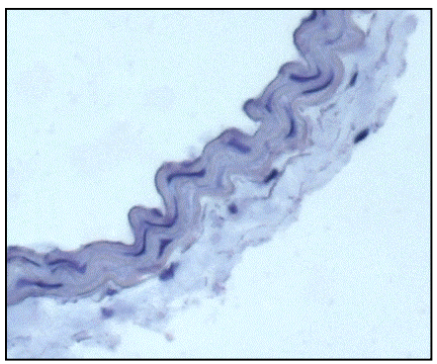
human coronary plaque



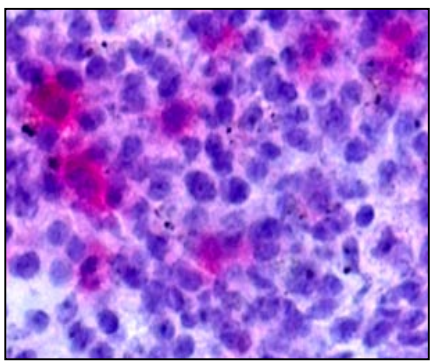
mouse aortic root plaque



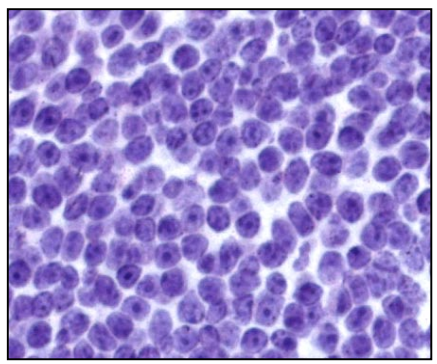
mouse aortic arch plaque



mouse normal carotid artery

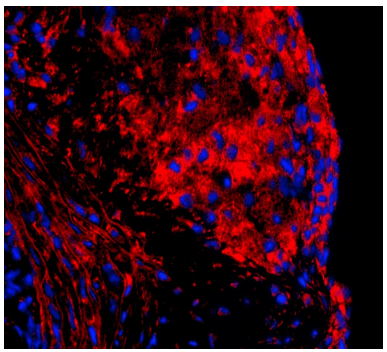


mouse spleen

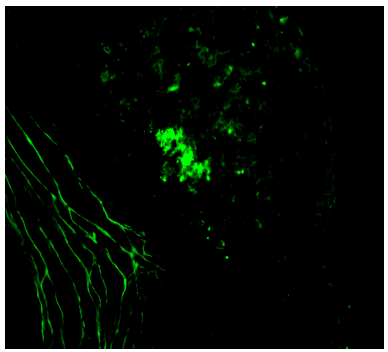


CB $2^{-/-}$ mouse spleen

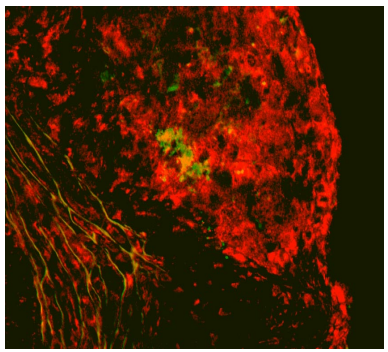
The cannabinoid receptor CB2 is expressed on macrophages and T lymphocytes within mouse atherosclerotic plaques



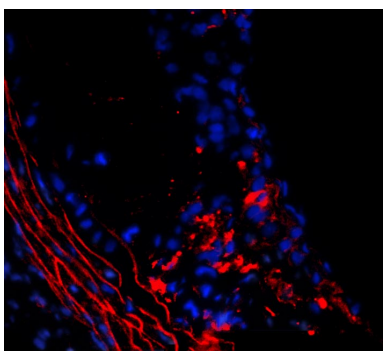
MΦ/DAPI



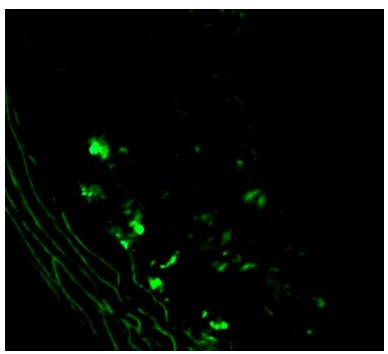
CB2



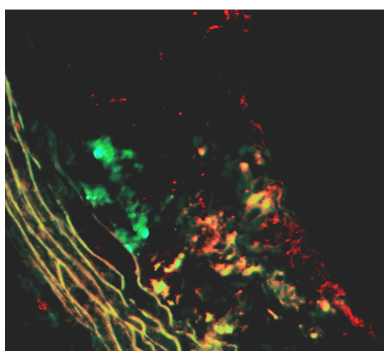
MΦ/CB2



CD4/DAPI

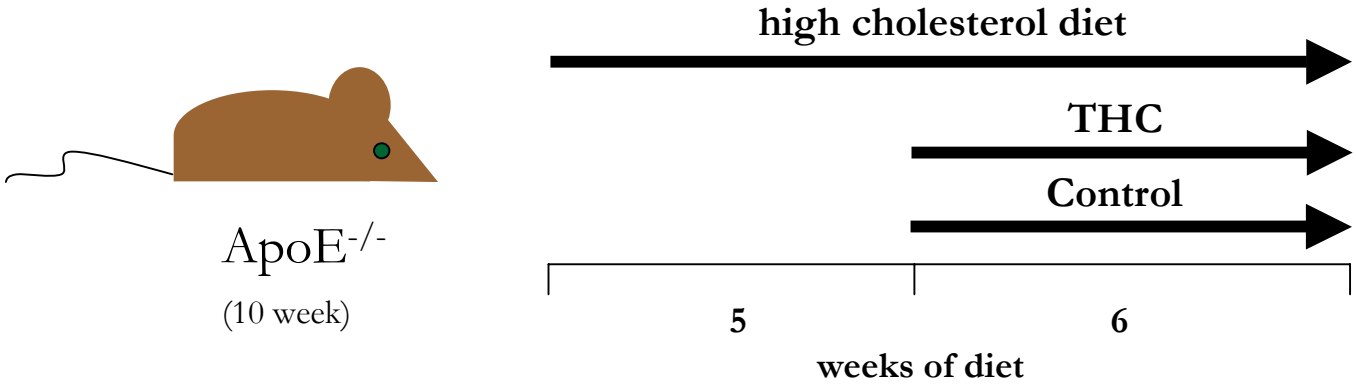


CB2



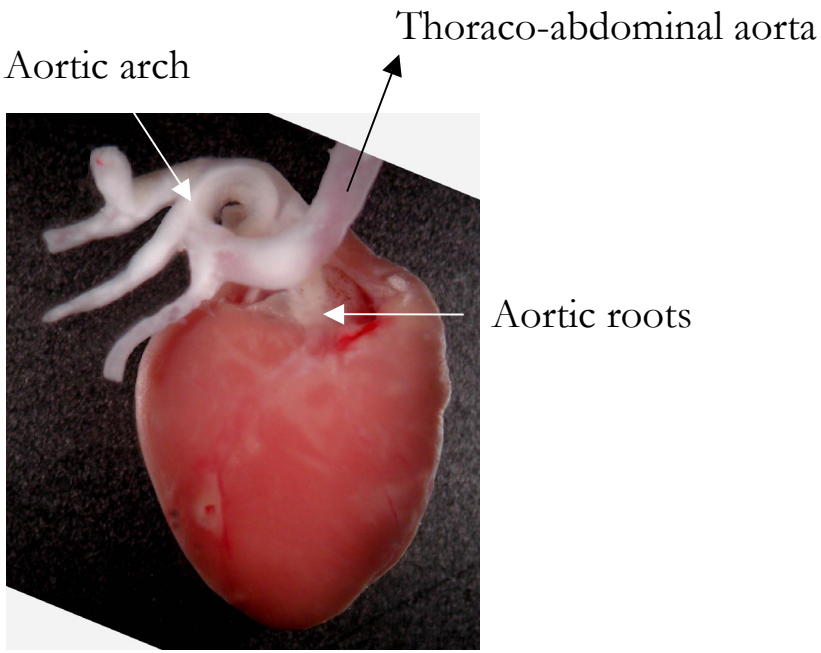
CD4/CB2

Experimental protocol

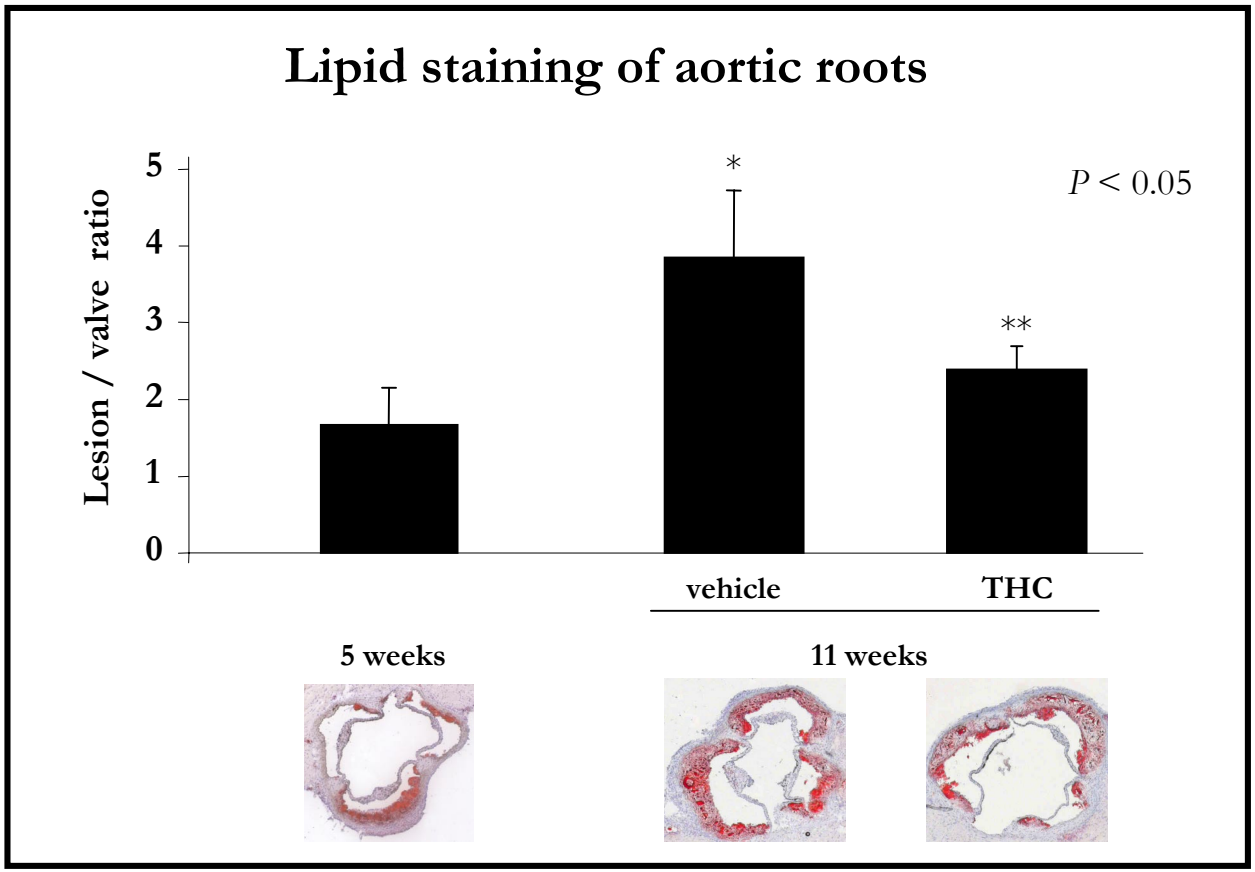


> delta-9-Tetrahydrocannabinol (**THC**)

> daily oral administration of 1 mg per kg THC in high fat milk

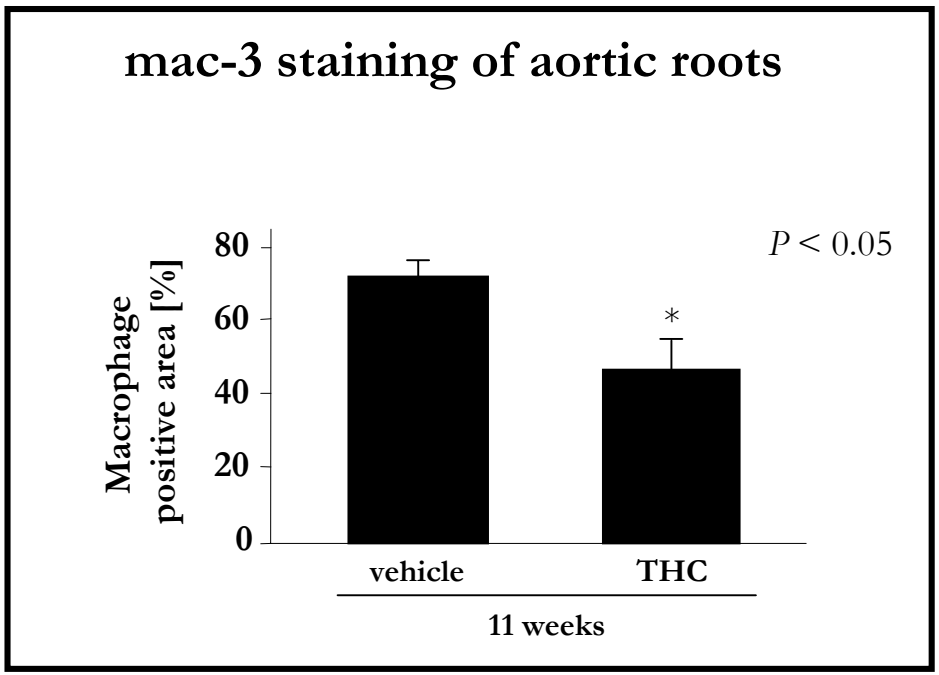


THC treatment reduces atherosclerotic plaque development



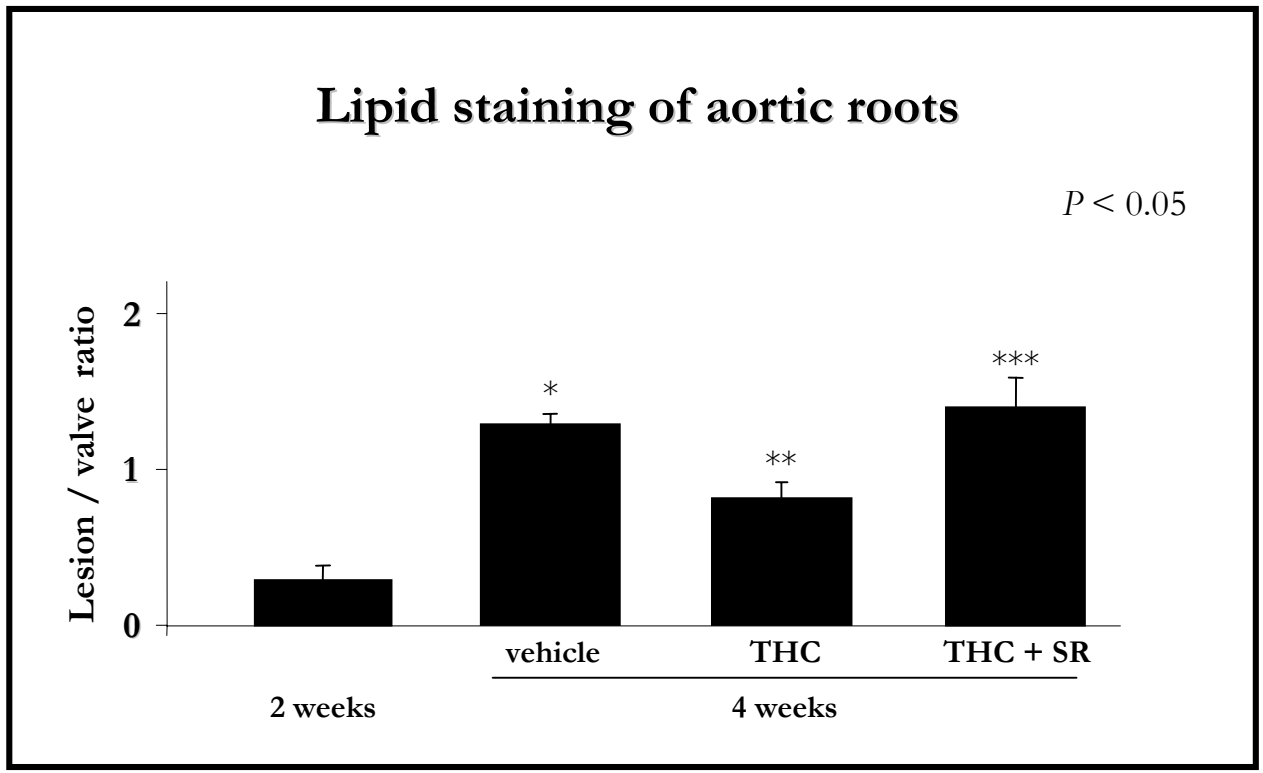
Oral administration of 1 mg kg^{-1} THC (daily dose)

Reduced relative macrophage content in THC-treated mice



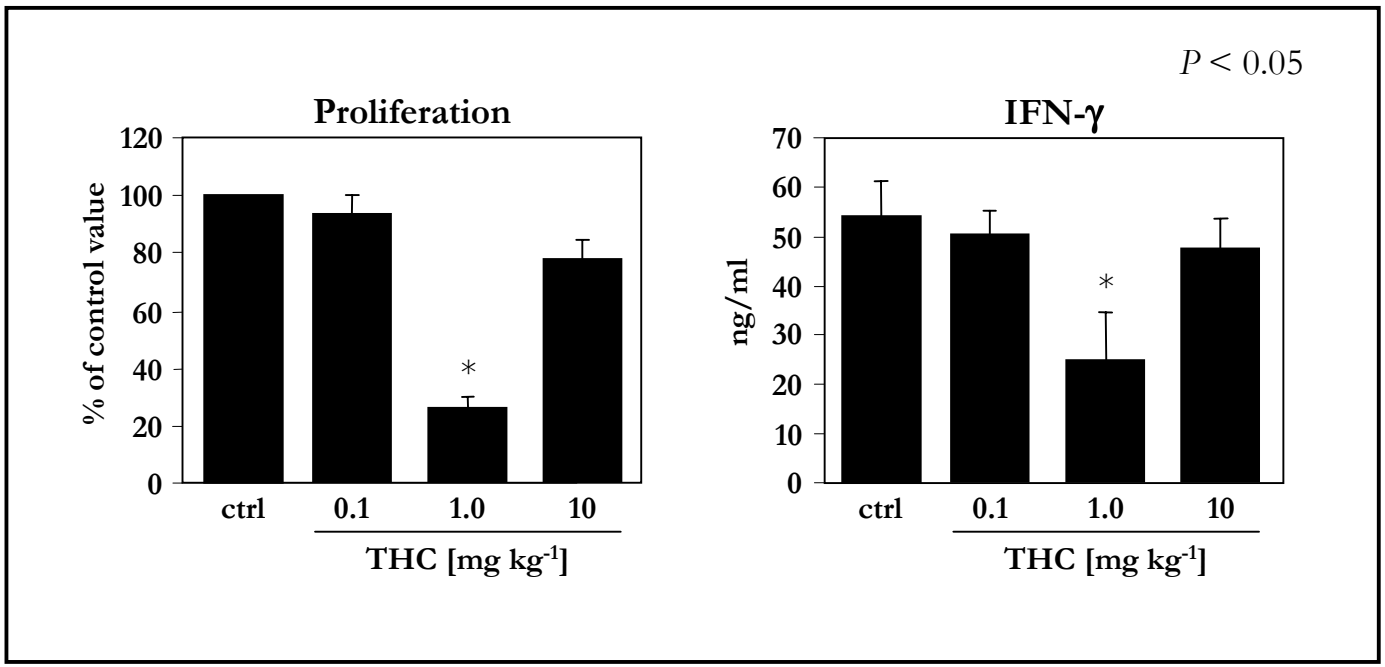
Oral administration of 1 mg kg^{-1} THC (daily dose)

The CB2 receptor antagonist SR144528 abolishes the anti-atherosclerotic effect of THC

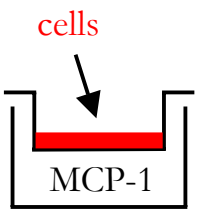


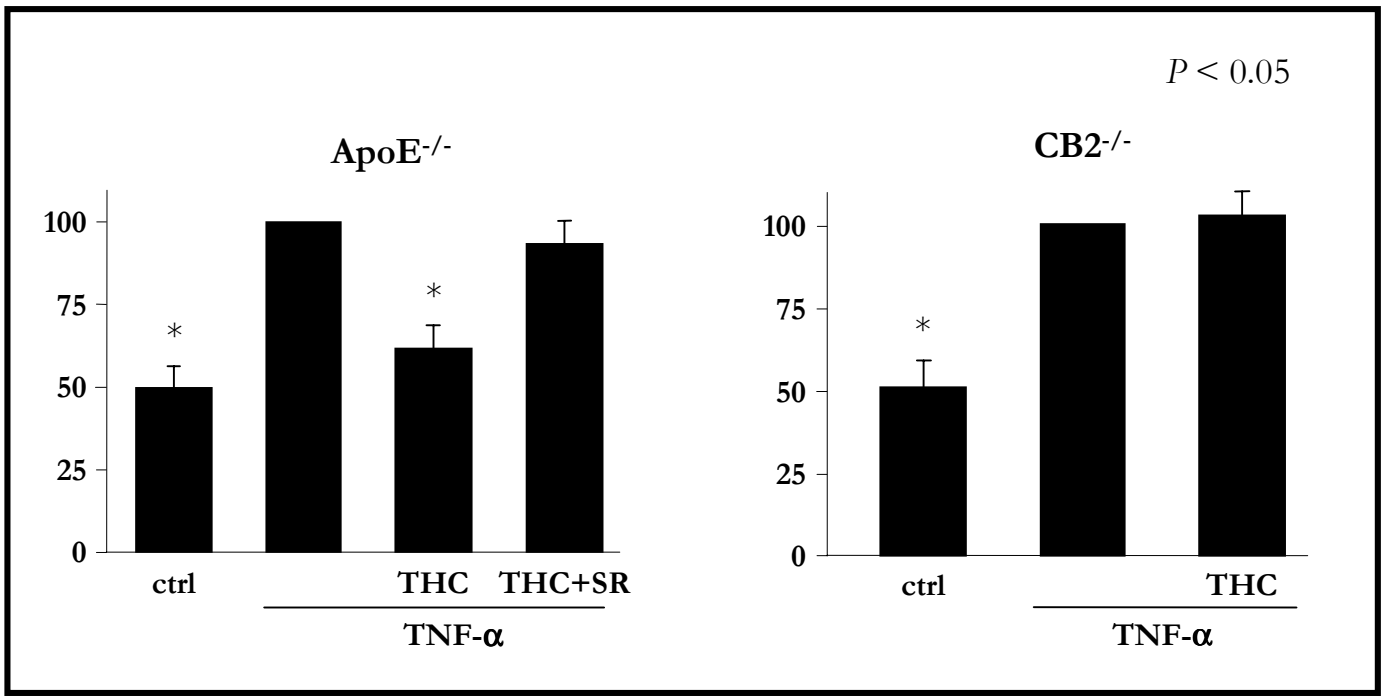
Oral administration of 1 mg kg^{-1} THC (daily dose)

THC reduces proliferative responses and inhibits TH1 polarization

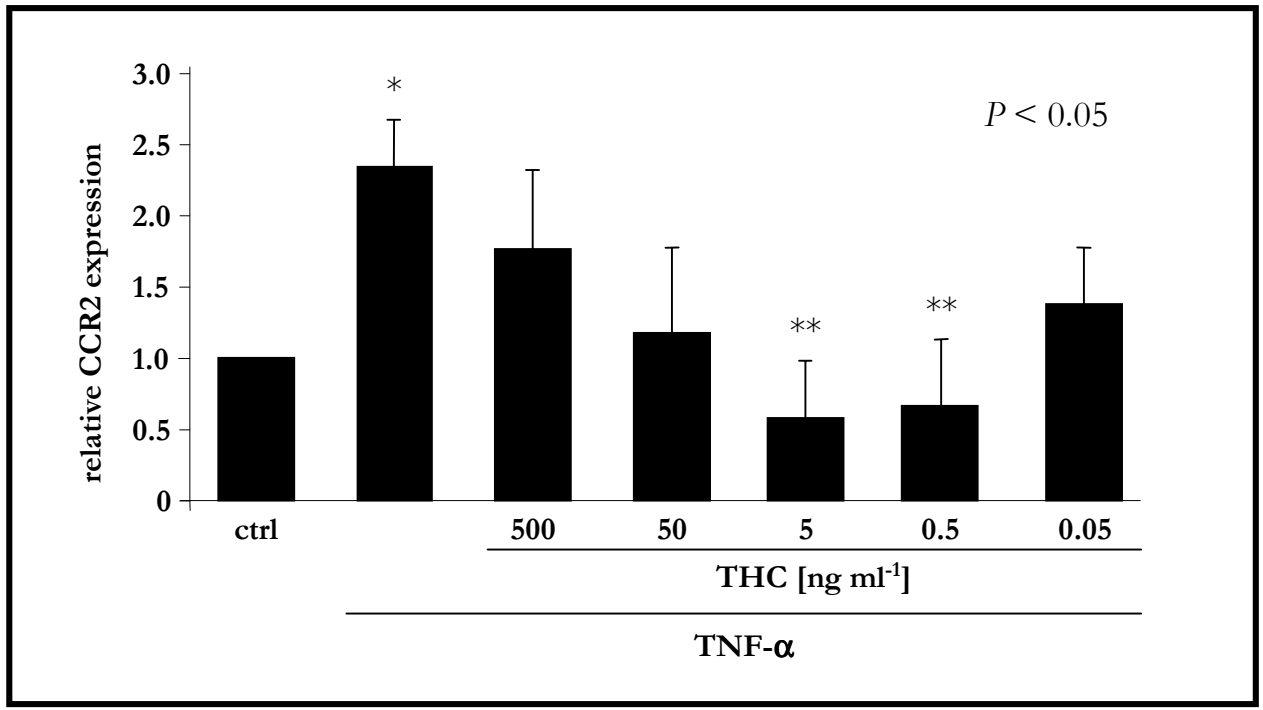


THC reduces migration capacity of peritoneal macrophages in vitro





THC reduces CCR2 expression on splenocytes in vitro



Real Time PCR analysis of stimulated splenocytes from ApoE-/- mice

Cannabinoids as therapeutic agents ?

letters to nature

Low dose oral cannabinoid therapy reduces progression of atherosclerosis in mice

Sabine Steffens[1], Niels R. Veillard[1]*, Claire Arnaud[1]*, Graziano Pelli[1], Fabienne Burger[1], Christian Staub[3], Andreas Zimmer[4], Jean-Louis Frossard[2] & François Mach[1]

[1]*Division of Cardiology, Department of Medicine, Foundation for Medical Research,*
[2]*Division of Gastroenterology and* [3]*Institute of Legal Medicine, University Hospital, Faculty of Medicine, 1211 Geneva, Switzerland*
[4]*Laboratory for Molecular Neurobiology, Department of Psychiatry, University of Bonn, 53105 Bonn, Germany*

* These authors contributed equally to this work

Nature April 7, 2005;434:782

Cannabinoids as therapeutic agents ?

news and views

Pharmacology

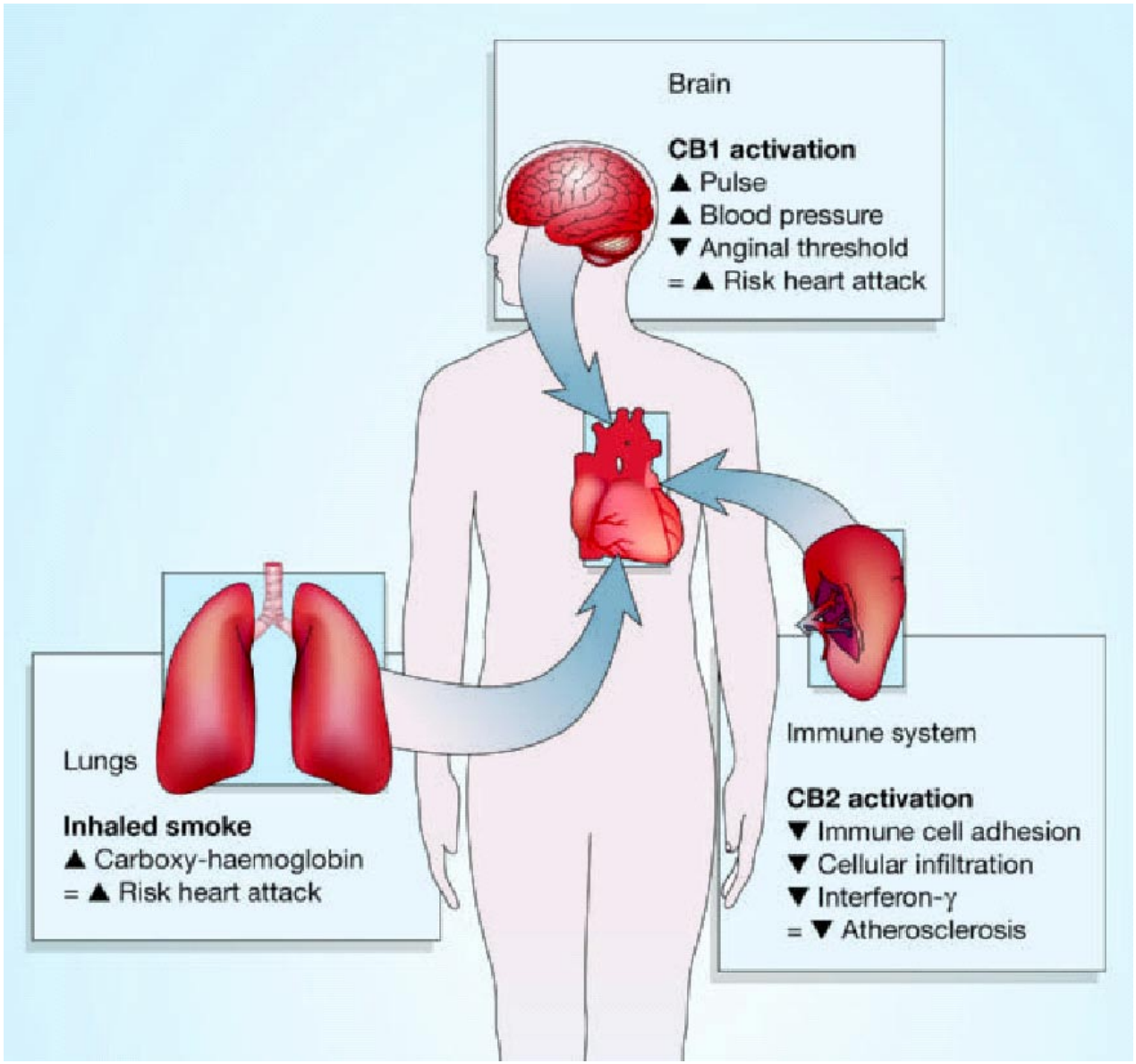
Marijuana and your heart

Michael D. Roth

Marijuana smoke can have harmful effects on the heart. But one of its active components may ease inflammation and slow the progression of coronary artery disease.

Nature 2005;434:708

Cannabinoids as therapeutic agents ?



Nature 2005;434:708

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Geneva University

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European Vascular Genomics Network

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