



Biochemische Grundlagen zum Endocannabinoid-System



Cannabinoide Lehrgang
09-10.7.2021

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Institut ICANNA



vs



Eine Droge?



Genus?

Ein Medikament?



Gesundheit?



Fakten

~~Mythen~~

Hanf / Cannabis basics

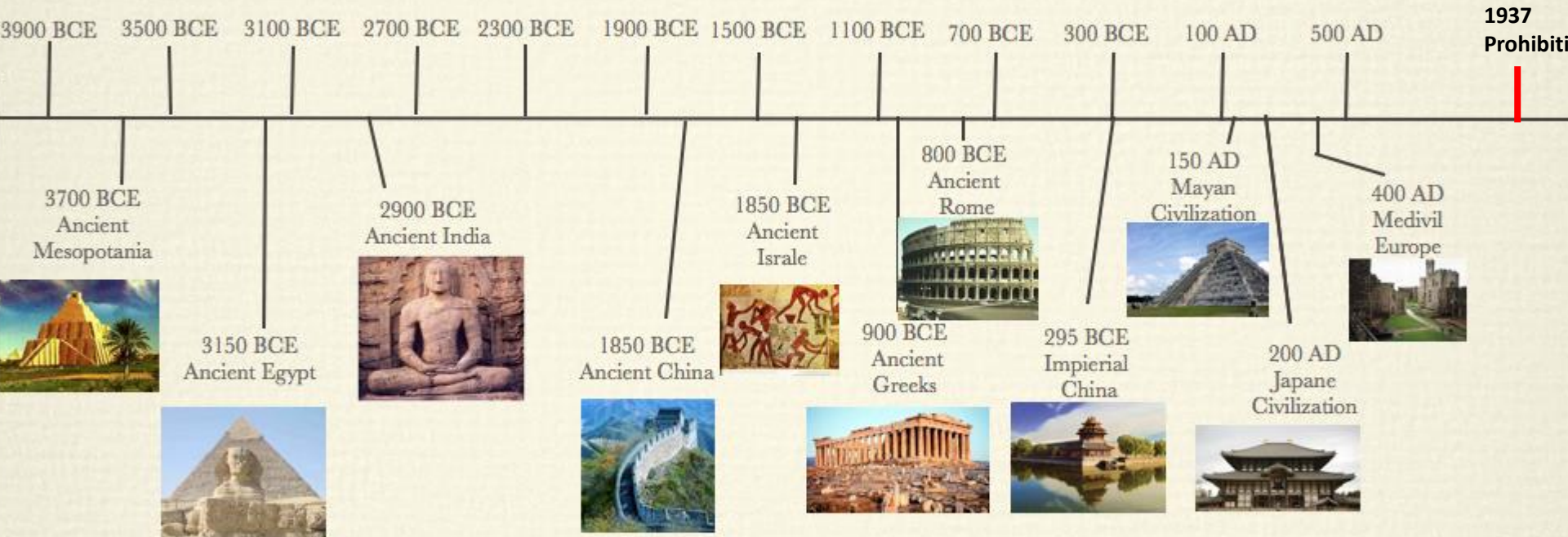


37 Millionen Jahre



OBDOBJE	DOBA (začetek pred milijoni let)	ŽIVLJENJSKO OKOLJE	RAZVOJ ŽIVLJENJA
kenozoik	kvartar	holocen pred 10.000 leti	konec zadnje ledene dobe, otoplitev
		pleistocen 2	ledena doba
		pliocen 5	nastanek gorovij, vulkanov, hladno podnebje
		miocen 25	oblikovanje gorovij, suho in hladno podnebje
	terciar	oligocen 38	nastanek Alp in Himalaje, vulkani, hladno in suho podnebje
		eocen 55	otoplitev
		paleocen 65	izginjanje jezer, blago do hladno in vlažno podnebje
mezozoik	kreda 144	ločitev kontinentov, nastanek hribov, veliko močvirij in jezer, toplo podnebje	prve cvetnice (magnolija), vrhunec razvoja orjaških plazilcev, ki mu je sledilo izumrtje , izumrtje praprtiča, prve sodobne ptice in mali sesalci
	jura 213	nastanek gorovij, jezer, blago podnebje	gozdovi iglavcev, obdobje plazilcev, razvoj praprtiča in vrečarjev
	trias 248	nastanek gorovij, širjenje puščav, suho in toplo podnebje	prevladujejo semenke, prvi iglavci, pogoste praproti, prvi orjaški plazilci, stokovci (sesalci, ki ležejo jajca)
paleozoik	perm 286	ledena doba , nastane Pangea, spremenljivo podnebje	raznolikost semenk, prvi sagovci, razvoj modernih oblik žuželk, plazilci podobni sesalcem, izumrtje mnogih nevretenčarjev
	karbon 360	ravna in močvirnata pokrajina, toplo in vlažno podnebje, proti koncu ohladiitev	gozdovi orjaških praproti, mahov, lisičjakovcev, semenk in jetrenjakov, prvi plazilci, mnogo dvoživk, žuželk in morskih psov
	devon 408	ledena doba , mnogo jezer	raznolikost rastlin, prvi gozdovi, prve semenke in mahovi, ribe pljučarice in resoplavutarice, prve dvoživke (ščitoglavci) in krilate žuželke, trilobiti
	silur 438	ravna pokrajina, poplave, toplo podnebje	alge, prve kopenske rastline (psilofiti), ribe oklepnice, prvi kopenski členonožci, koralni grebeni
	ordovicij 505	morje prekriva kontinente, toplo podnebje	morske alge in nevretenčarji, prvi vretenčarji (ostrakodermi), korale, trilobiti, začetek prehoda alg na kopno
	kambrij 570	blago in vlažno podnebje, najstarejše kamnine, v katerih so našli fosile	alge, bakterije, cianobakterije, glive, doba morskih nevretenčarjev, morski ježki, trilobiti, ramenonožci, spužve, graptoliti
	predkambrij 4000	prvi sledovi življenja (bakterije, alge), prvi evkarionti pred 2 milijardama let, prvi večcelični organizmi pred 900 milijoni let; dve ledeni dobi	

Timeline



Cannabis sativa L.

Die weibliche Blüte



Ženska roža
• Female flower

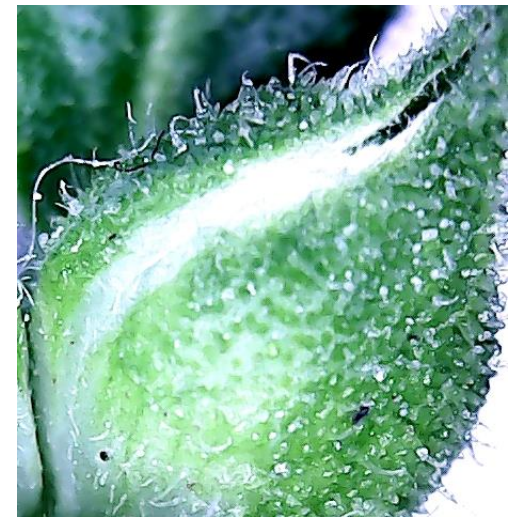
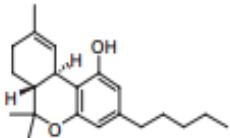


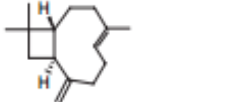

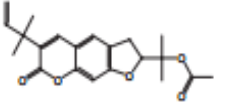
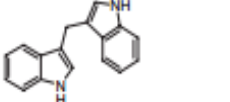


Foto and illustratioin source: Institut ICANNA

Trichomes – griechisch trikoma bedeutet “Haar”



Table 2 Plant natural products that have been shown to interact directly with cannabinoid (CB) receptors

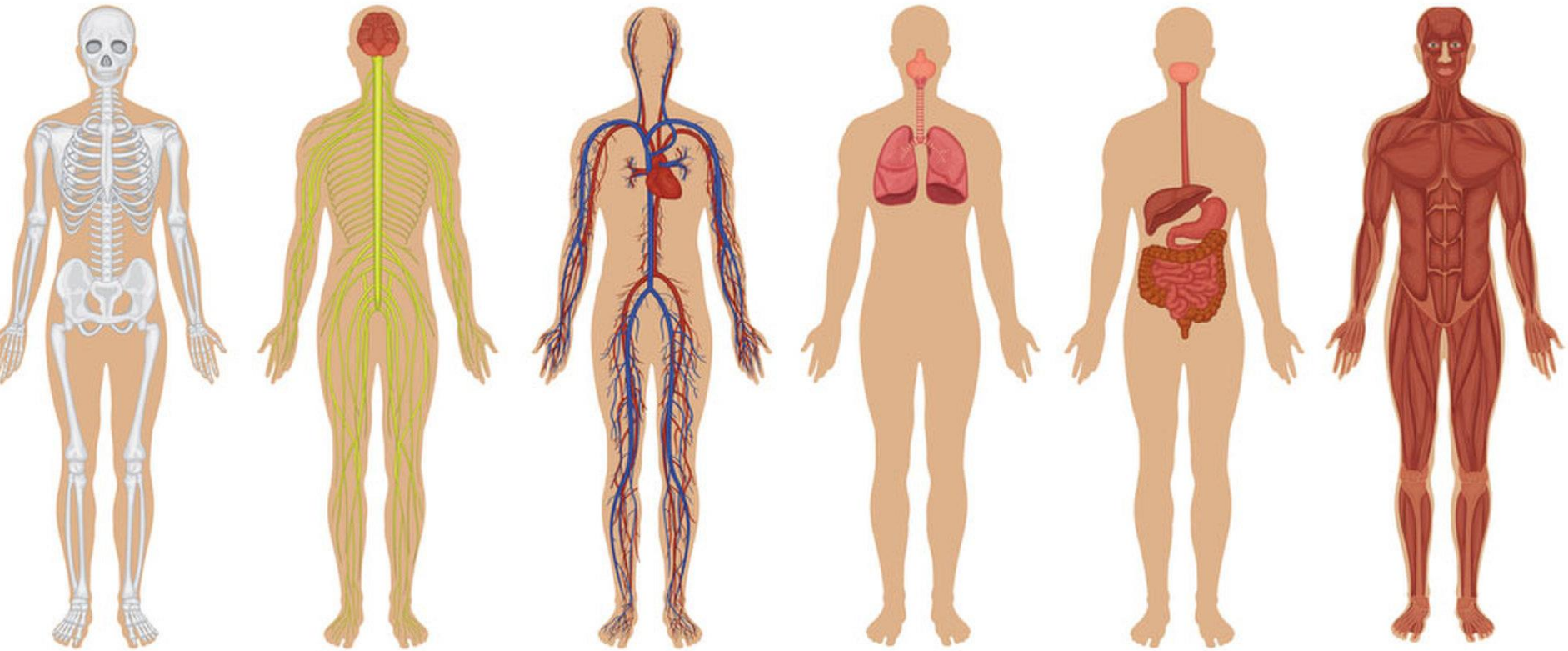
Structure	Name	Origin	CB receptor affinity	Function	In vivo efficacy	Other targets (ECS)	References
	Δ ⁹ -THC	<i>Cannabis sativa</i> L.	Non-selective CB ₁ and CB ₂ affinity (K _i values <50 nM) (human)	Partial agonist G _i /o Inhibition by SR141716 and SR144528	Validated in CB ₁ and CB ₂ KO mice	GPR55 PPARs Different ion channels	Mechoulam, 1986; Pertwee, 2006
	N-alkylamide	<i>Echinacea</i> spp.	Selective CB ₂ affinity (K _i value <100 nM) (human)	Partial agonist [Ca ²⁺] _i Inhibition by SR144528	No data	PPAR-γ Inhibition of AEA transport	Raduner <i>et al.</i> , 2006; Chicca <i>et al.</i> , 2009
	N-alkylamide	<i>Echinacea</i> spp.	Selective CB ₂ affinity (K _i value <100 nM) (human)	Partial agonist [Ca ²⁺] _i Inhibition by SR144528	No data	Partial FAAH inhibition PPAR-γ Inhibition of AEA transport Partial FAAH inhibition	Raduner <i>et al.</i> , 2006; Chicca <i>et al.</i> , 2009
	β-caryophyllene	Widespread in plants	Selective CB ₂ affinity (K _i value <200 nM) (human)	Full agonist G _i /o [Ca ²⁺] _i	Validated in CB ₂ KO mice	No data	Gertsch <i>et al.</i> , 2008
	Falcarinol	Relatively widespread in Apiaceae (e.g. <i>Daucus carota</i> L.)	Non-selective CB ₁ affinity (K _i value <1 μM) (human)	CB ₁ receptor-selective inverse (covalent) agonist Inhibition of AEA/WIN55212-2	No data	No data	Leonti <i>et al.</i> , 2010
	Rutamarin	<i>Ruta graveolens</i> L.	Selective CB ₂ affinity (K _i value <10 μM) (human)	No data	No data	No data	Rollinger <i>et al.</i> , 2009
	DIM 3,3'-diindolylmethane metabolite from indole-3-carbinol	Relatively widespread in the <i>Brassica</i> genus	Selective CB ₂ affinity (K _i value ≈1 μM) (human)	Partial agonist at CB ₂ receptor	No data	No data	Yin <i>et al.</i> , 2009

Δ⁹-THC is shown as the major phytocannabinoid from *Cannabis sativa* L. but there are several other structurally related cannabinoids that interact with CB receptors.

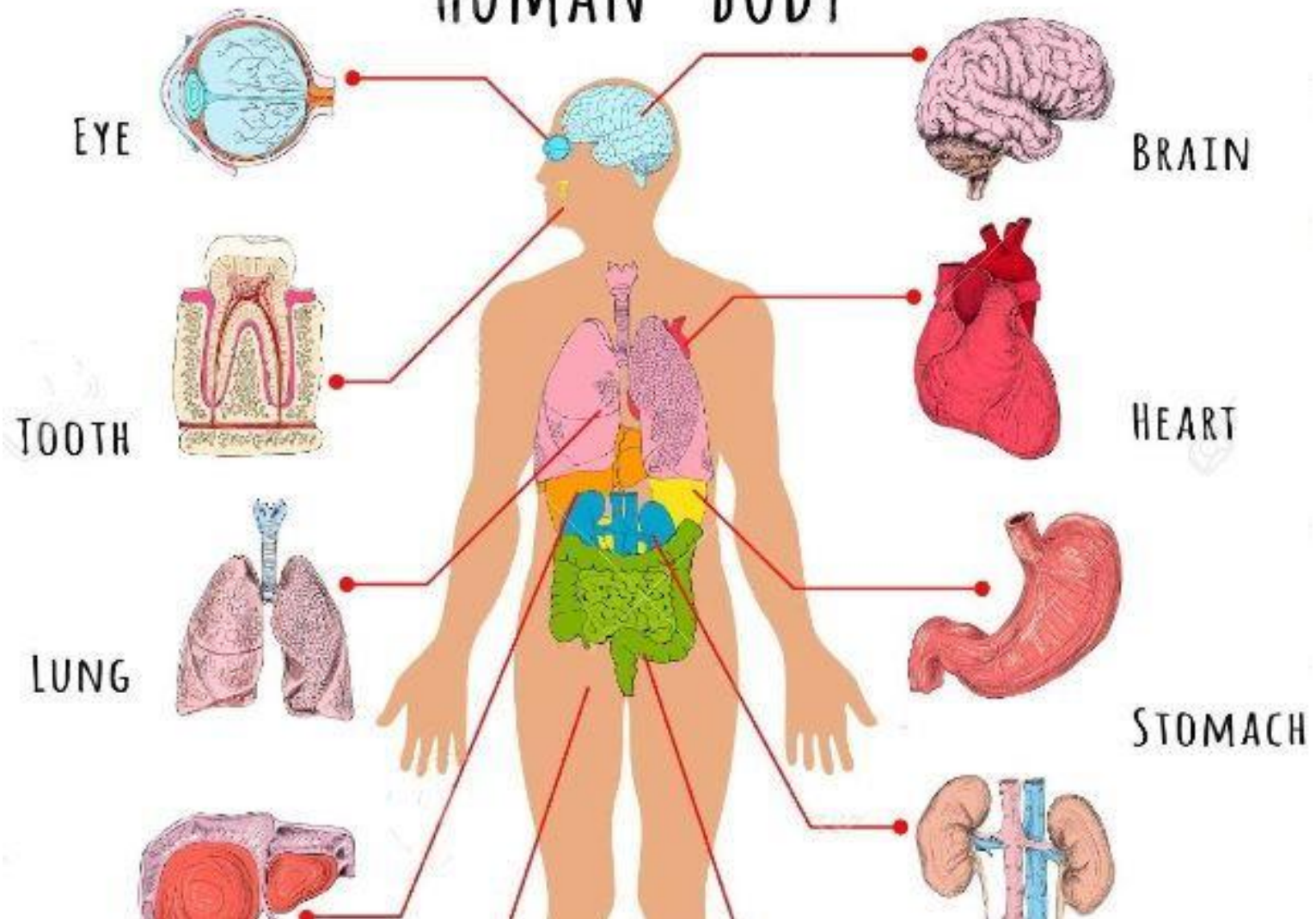
Δ⁹-THC, Δ⁹-tetrahydrocannabinol; DIM, 3,3'-diindolylmethane; ECS, endocannabinoid system; FAAH, fatty acid amide hydrolase; PPAR, peroxisome proliferator-activated protein.

Gertsch J, Pertwee RG, Di Marzo V. Phytocannabinoids beyond the Cannabis plant - do they exist? Br J Pharmacol. 2010 Jun;160(3):523-9. doi: 10.1111/j.1476-5381.2010.00745.x.

~ 35 Milliarden (10^{12}) Zellen

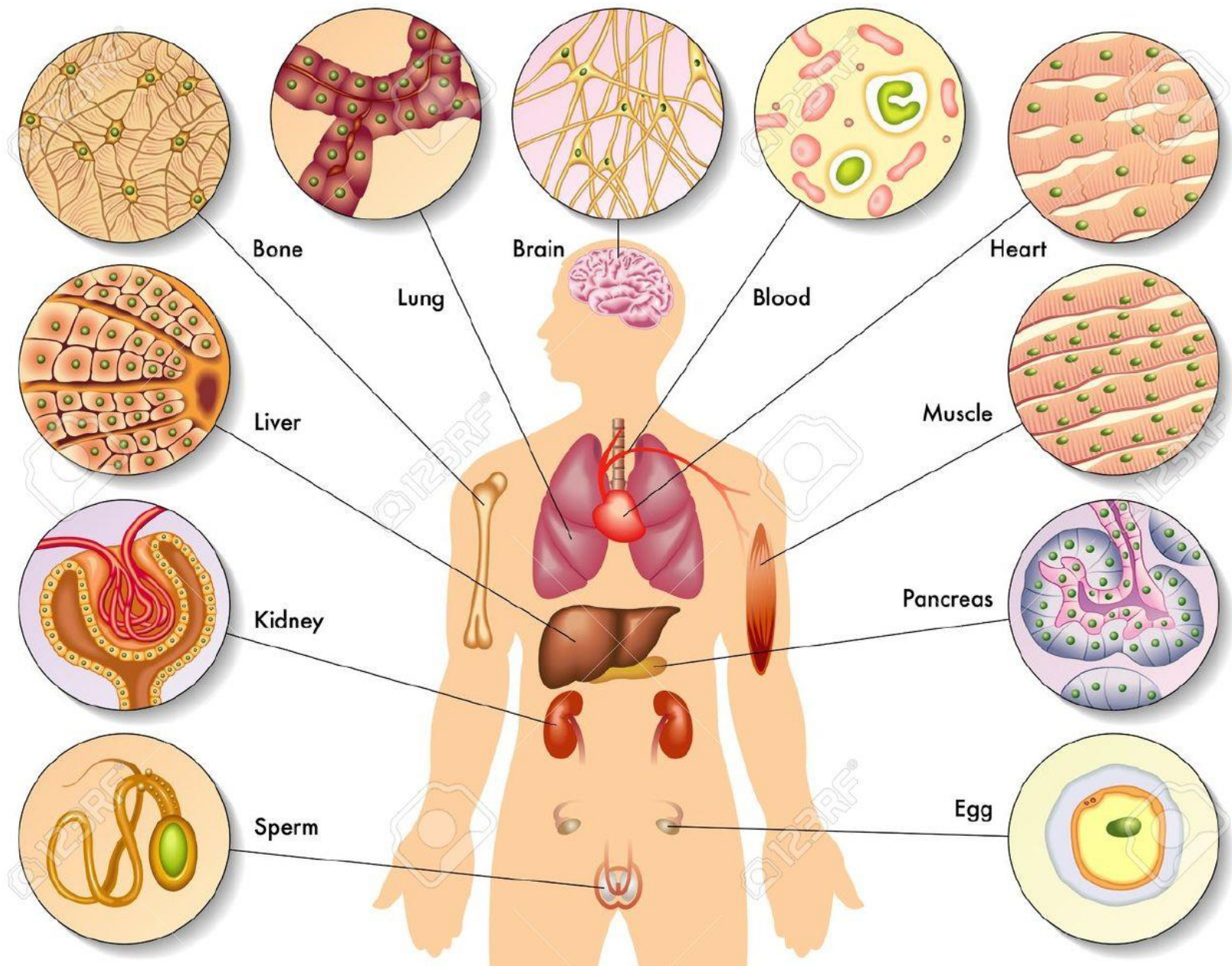


HUMAN BODY



www.institut-icanna.com

Source: <https://www.tes.com/teaching-resource/human-body-organs-11366454>

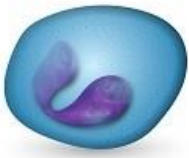


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Source: https://www.123rf.com/photo_14776744_human-body-cells.html



Neutrophil



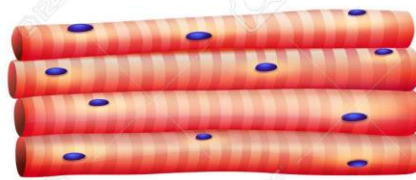
Eosinophil



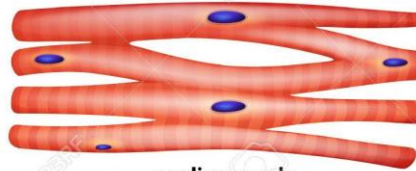
Basophil



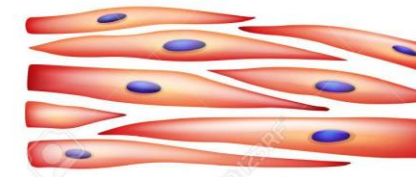
Monocyte



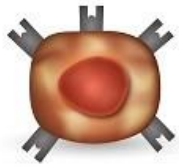
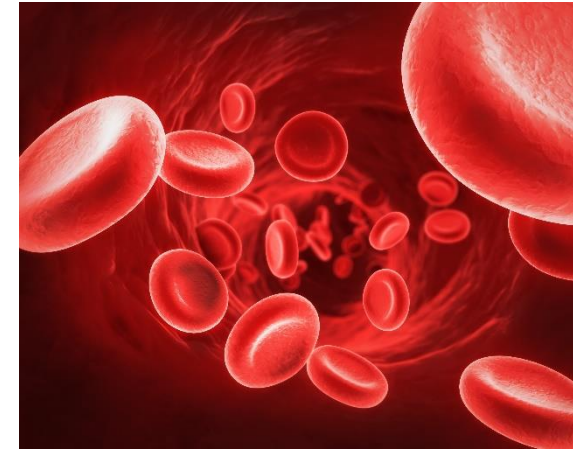
skeletal muscle



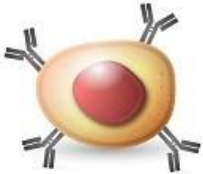
cardiac muscle



smooth muscle



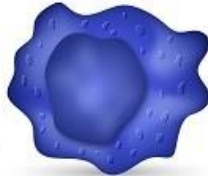
T Cell



B Cell



Natural killer



Macrophage



Human body \approx 35 trillion (10^{12}) cells



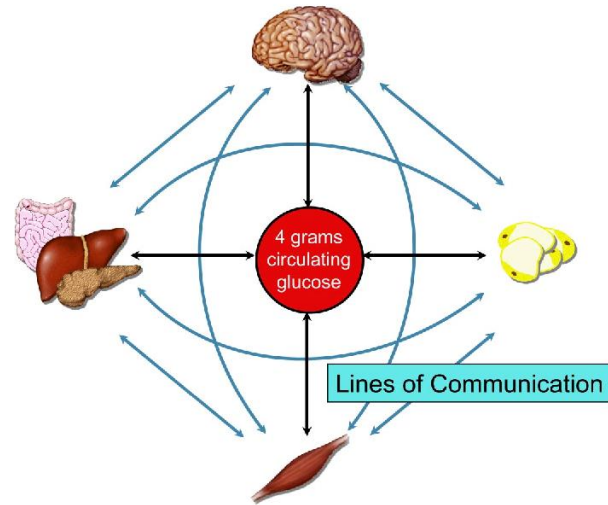
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Human Cells

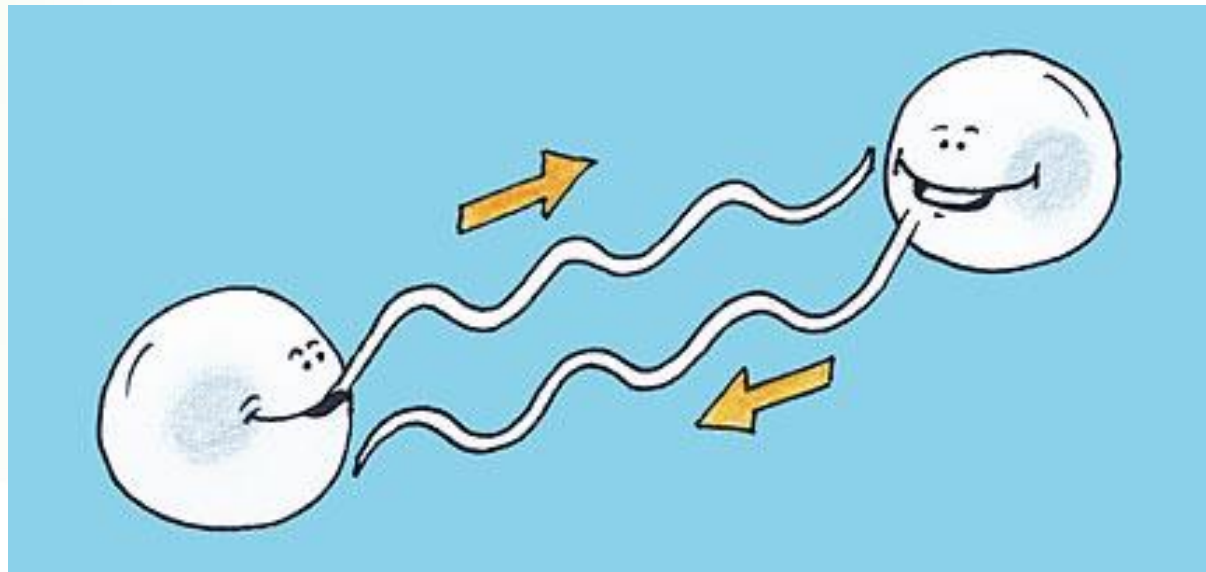
Communication in dem Körper



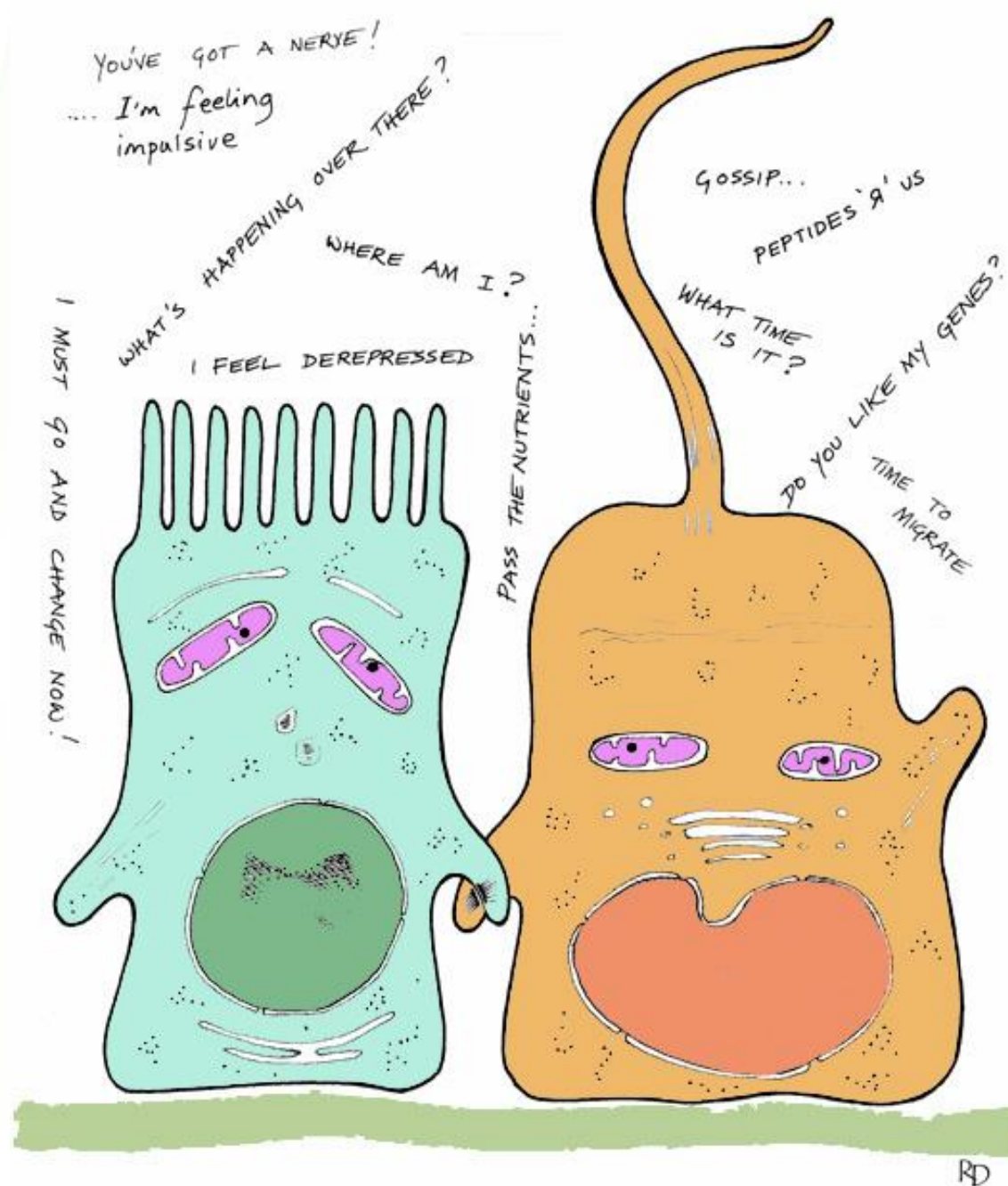
<https://maryhartley.com/>



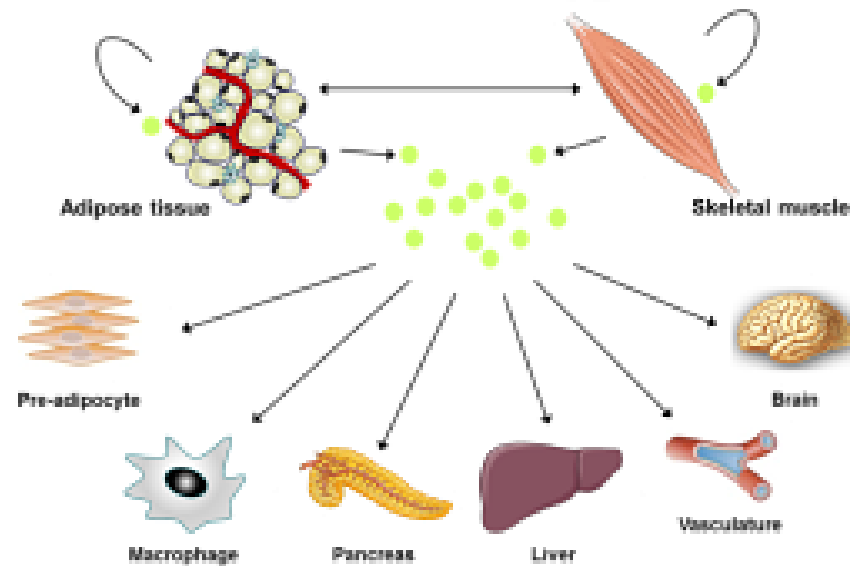
<https://totalhuman.wordpress.com/2014/03/>



<http://www.saferadiotherapy.com/cells-talk-to-their-neighbors-before-making-a-move/>

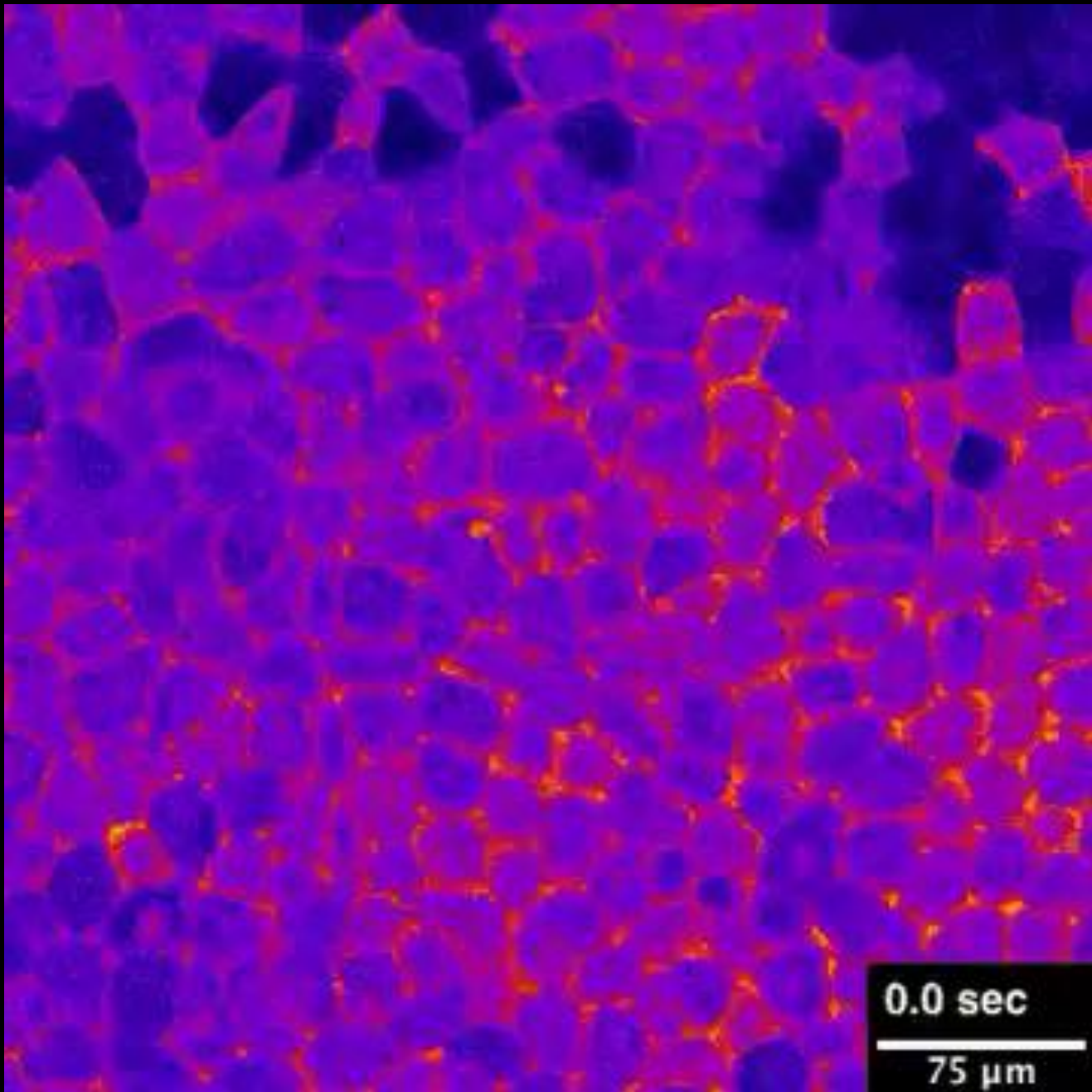


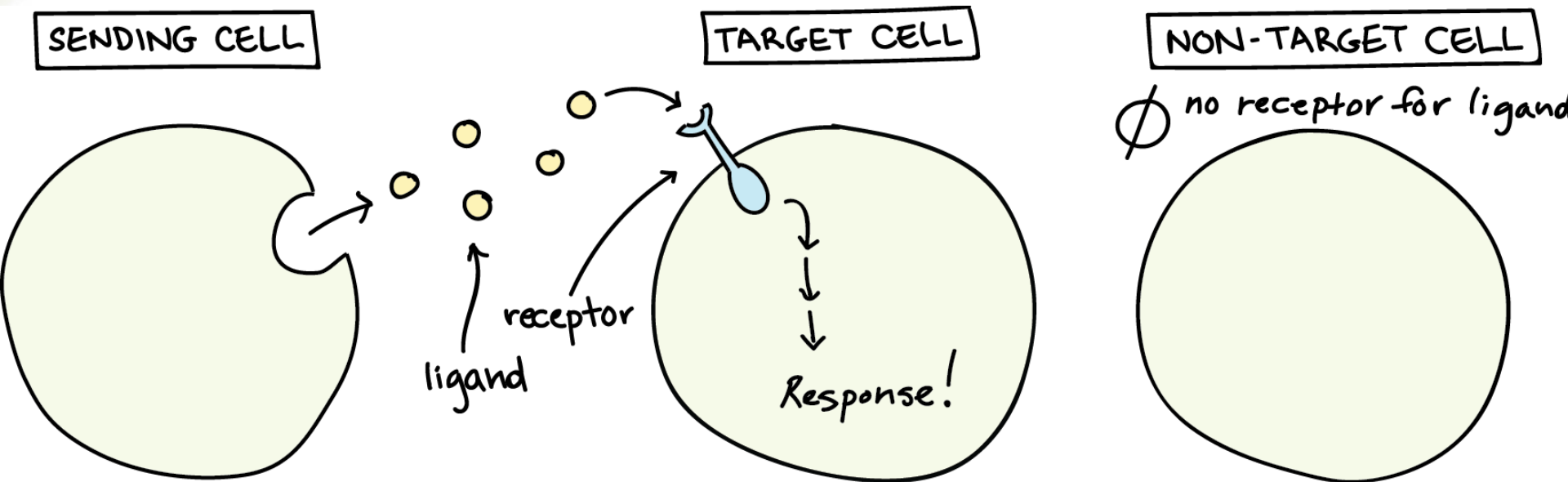
Signall Molekülen

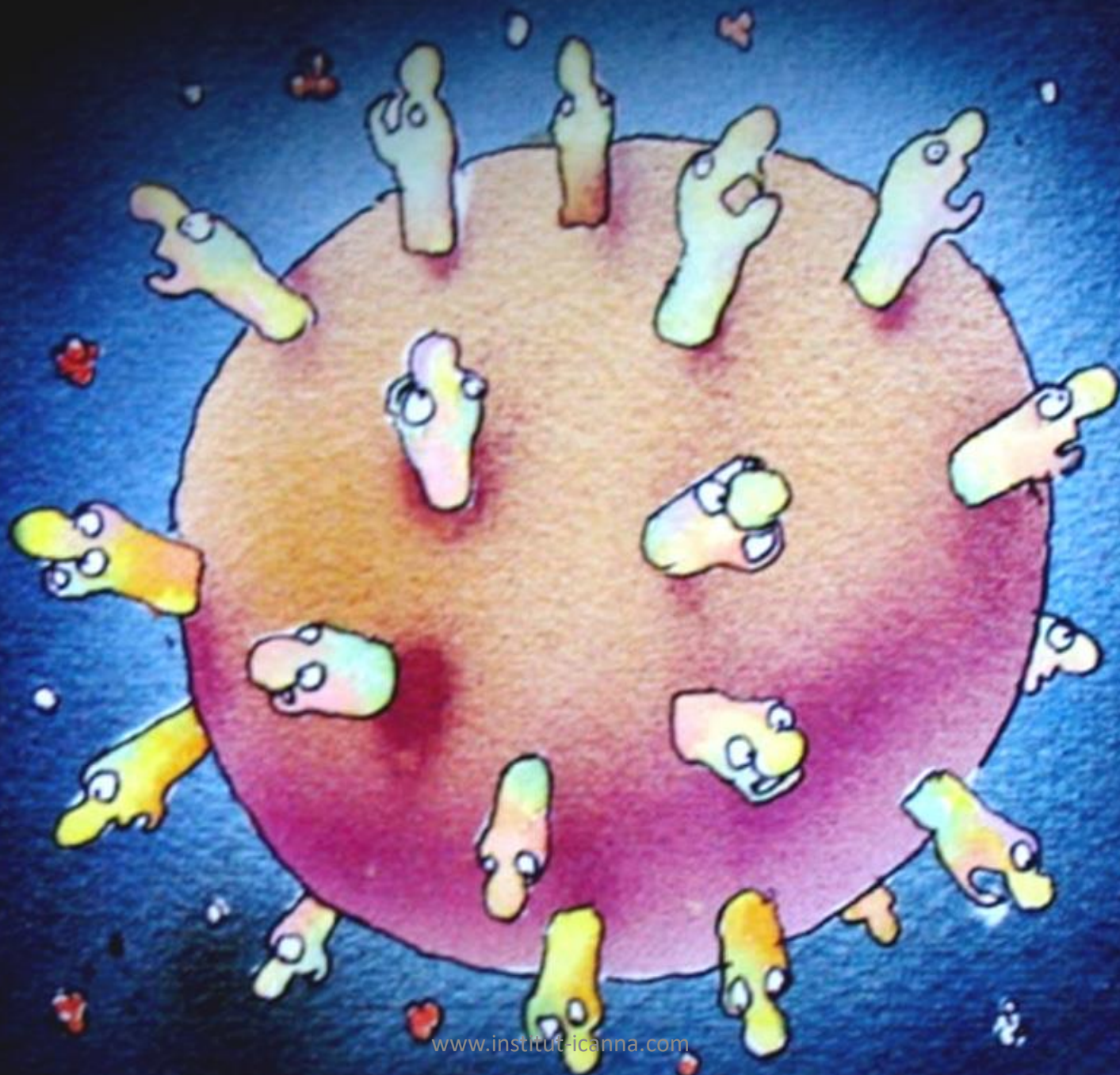


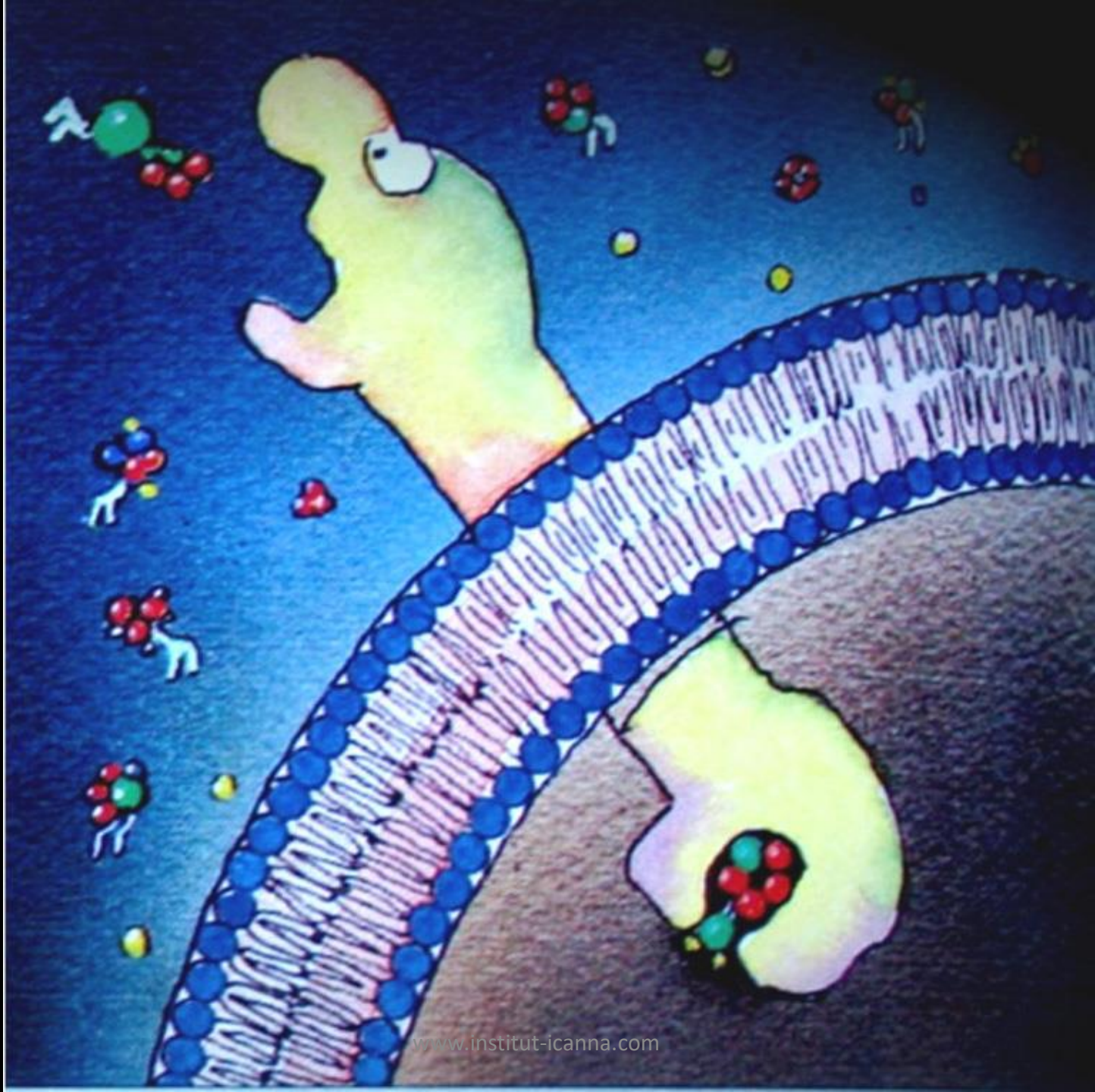
<https://aging-matters.com/ampk-a-complicated-metabolic-signalling-pathway/>

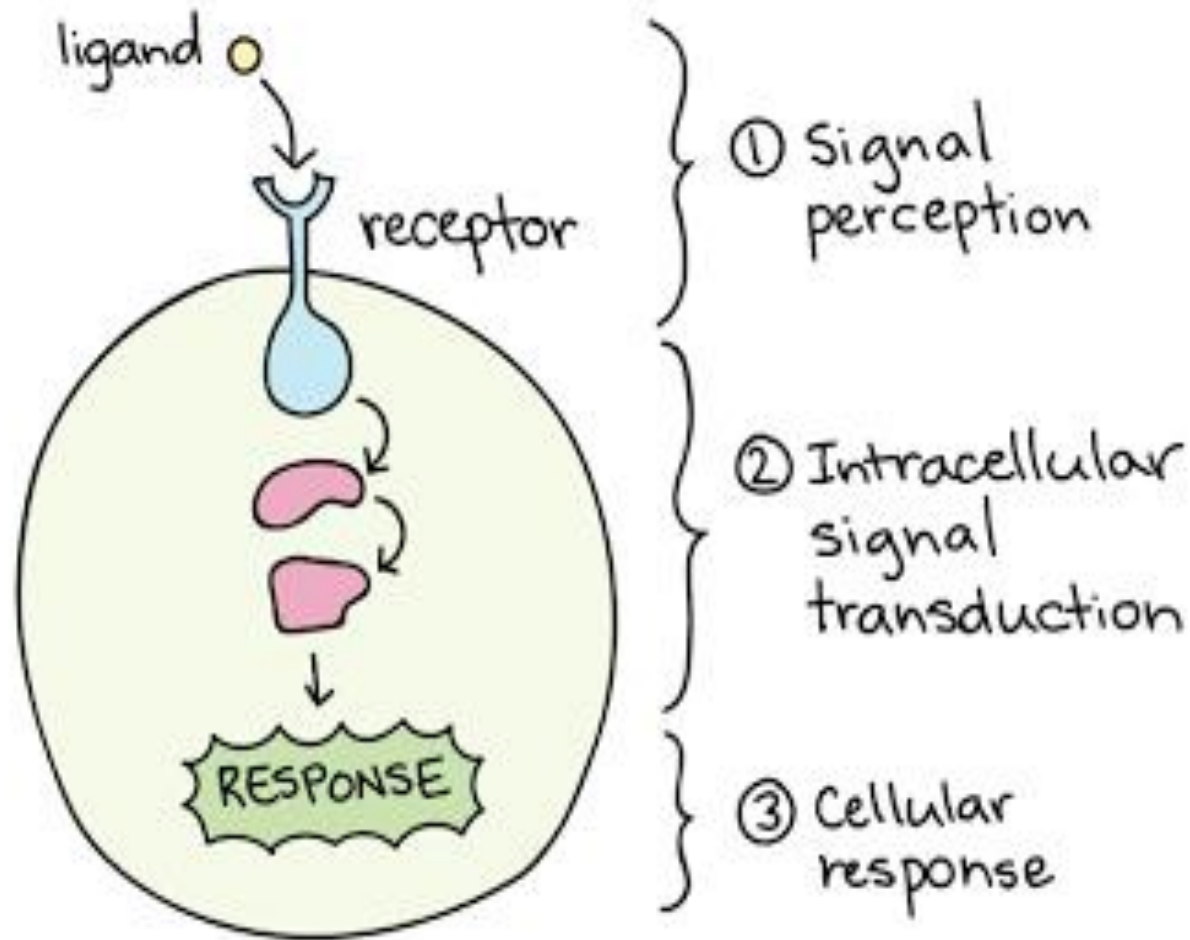
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A close-up, vertical photograph of a green, textured, leaf-like structure, possibly a succulent or a small plant, set against a bright, blurred background of green and white. The structure is dark green with a bumpy, scale-like texture. The background features soft, out-of-focus green and white shapes, suggesting a natural, light-filled environment.



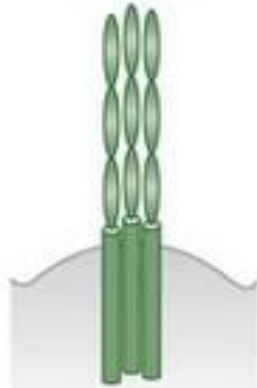
Transcription

Type I/II
cytokine receptor



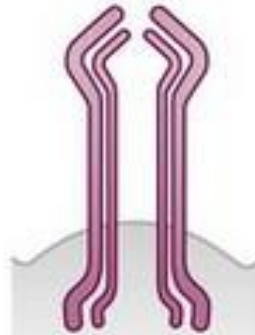
Heterodimeric or
homodimeric
receptors

TNF
receptor



Trimeric proteins
usually associated
with cell surface

TGF- β
receptor



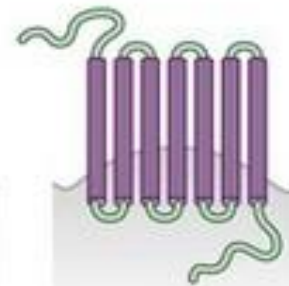
Receptor serine/
threonine kinase

Toll/IL-1
receptor



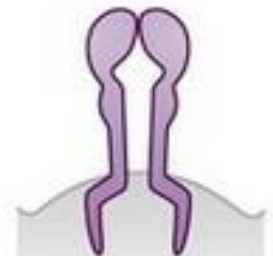
Single-pass
membrane
receptors with
Toll-IL-1
receptor domains

Chemokine
receptor



G protein-
coupled receptor
family

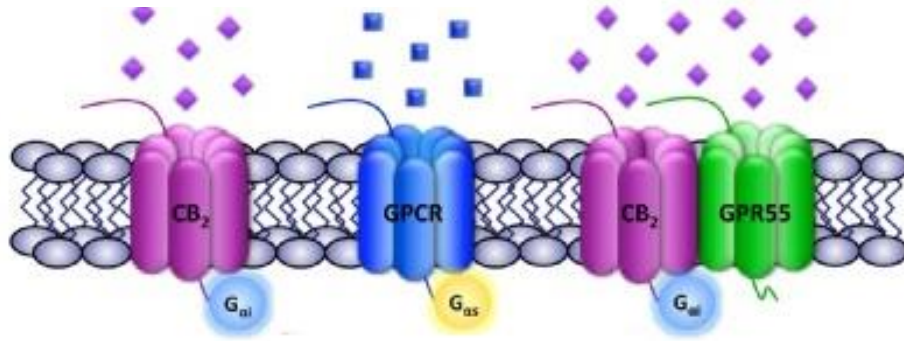
Receptor
tyrosine
kinase



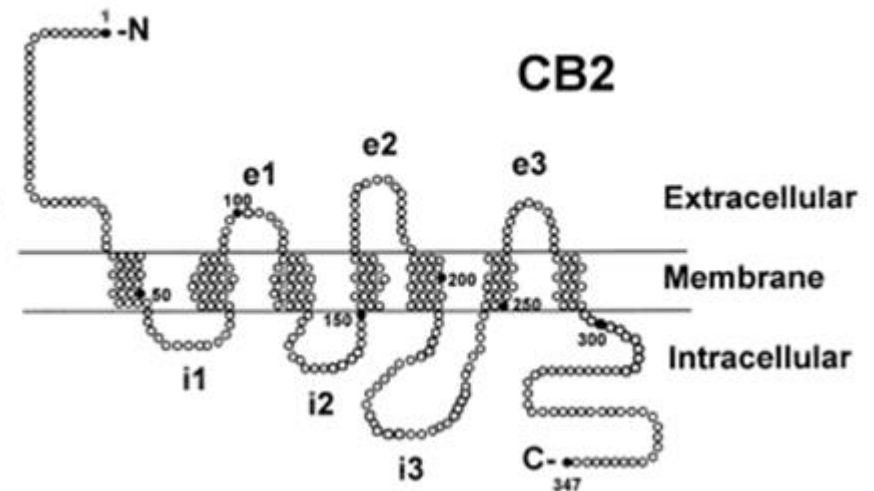
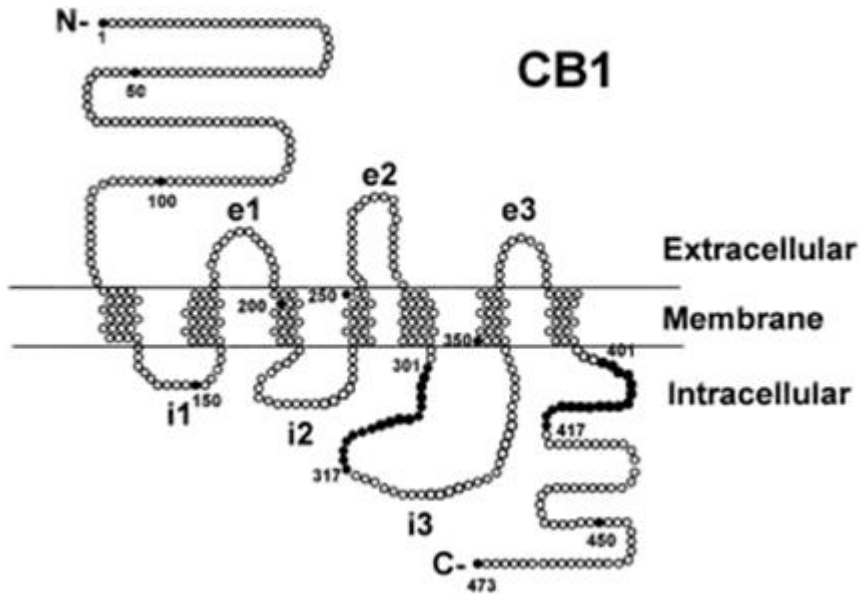
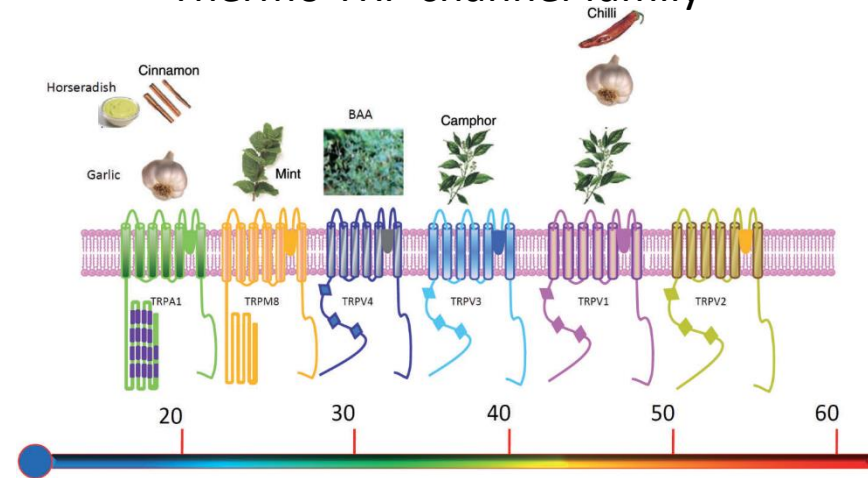
Enzyme-linked
receptors that
phosphorylate
tyrosine residues


The novel cannabinoid receptor GPR55
mediates anxiolytic-like effects in the
medial orbital cortex of mice
with acute stress

Qin-shi^{1*}, Liu-kun Yang^{1*}, Wen-long Shi², Lu Wang¹, Shi-meng Zhou¹, Shao-yu Guan¹, Ming-gao Zhao¹
and Qi Yang^{1,3*}



Thermo TRP channel family

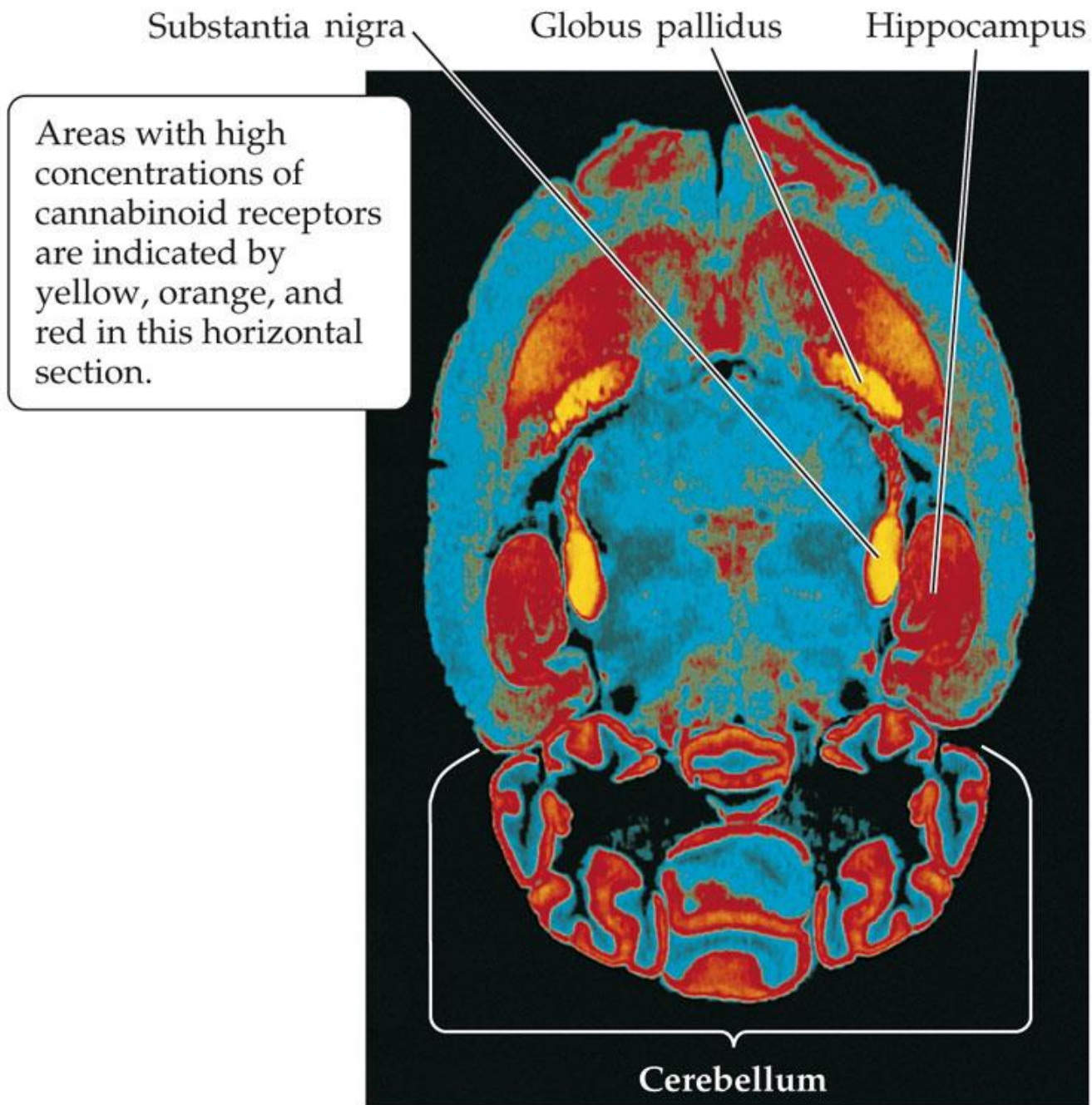


A glowing blue brain is shown inside a human head silhouette, set against a dark blue background. The brain is depicted with intricate, glowing neural pathways and a bright blue color scheme.

CB1 is found mostly in the brain.

A glowing blue immune system diagram is shown, featuring a human silhouette with various cells and receptors. The diagram is set against a dark blue background and includes several glowing blue cells and receptors, with a bright blue color scheme.

CB2 receptors are mostly found within the immune system.



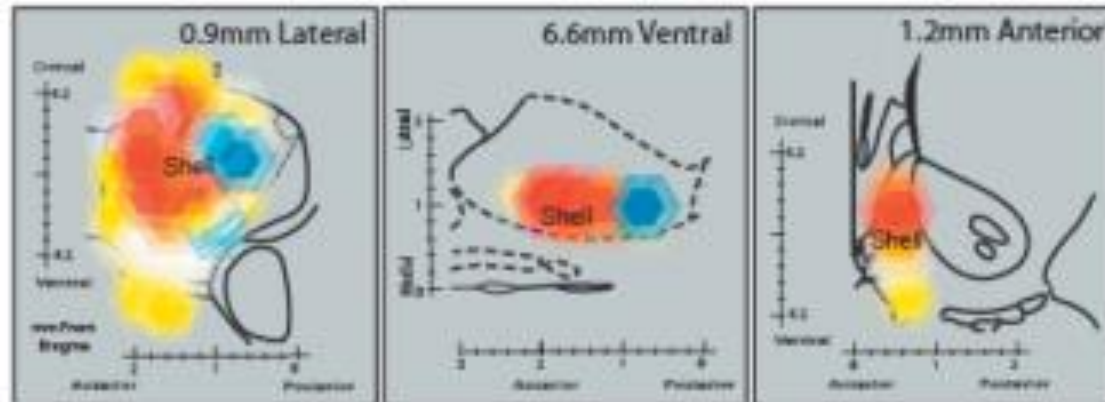
THE MIND'S MACHINE 2e, Figure 4.12

Hedonic brain hot spots

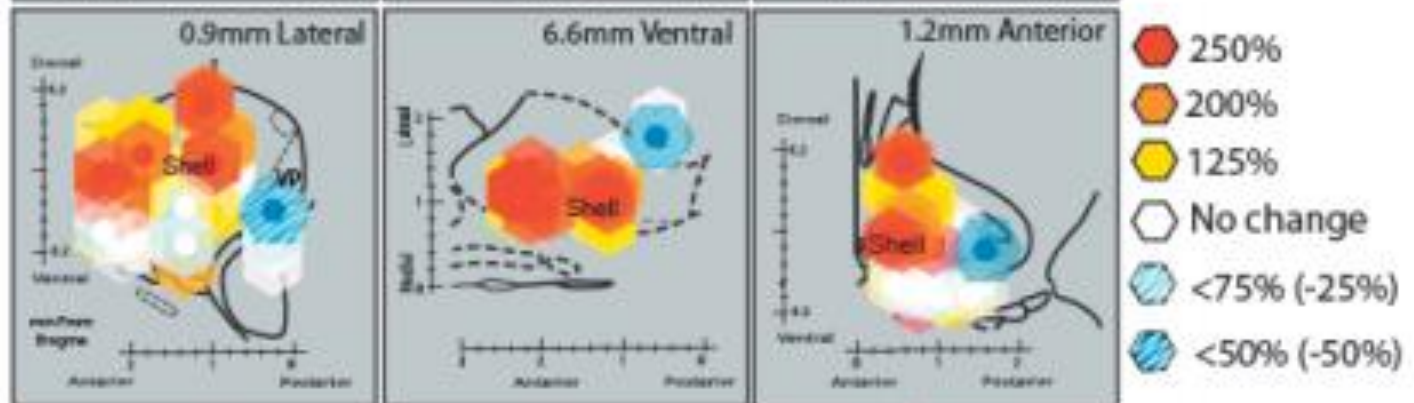
Nucleus Accumbens Hedonic Hotspots



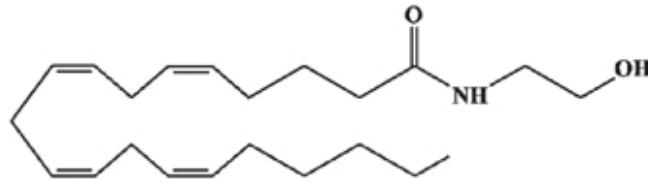
Opioid
Hotspot



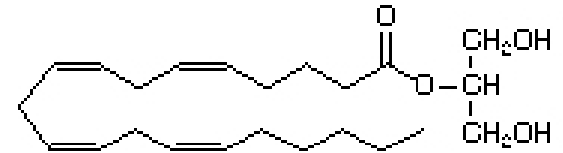
Endocannabinoid
Hotspot



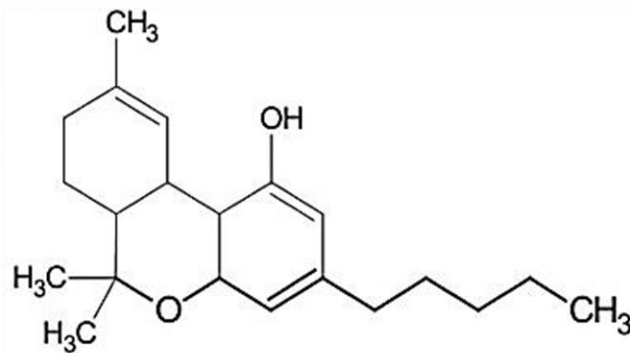
(endo) cannabinoide



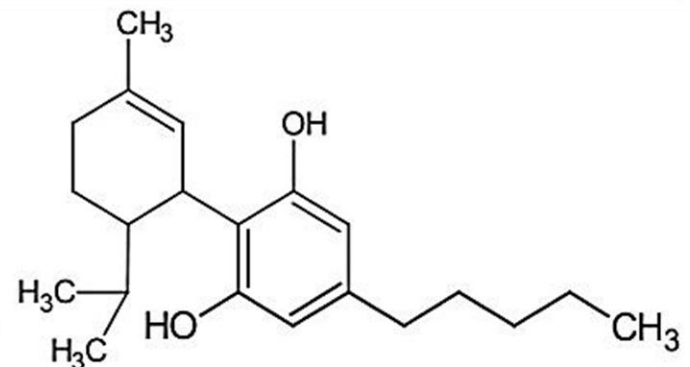
ANANDAMIDE



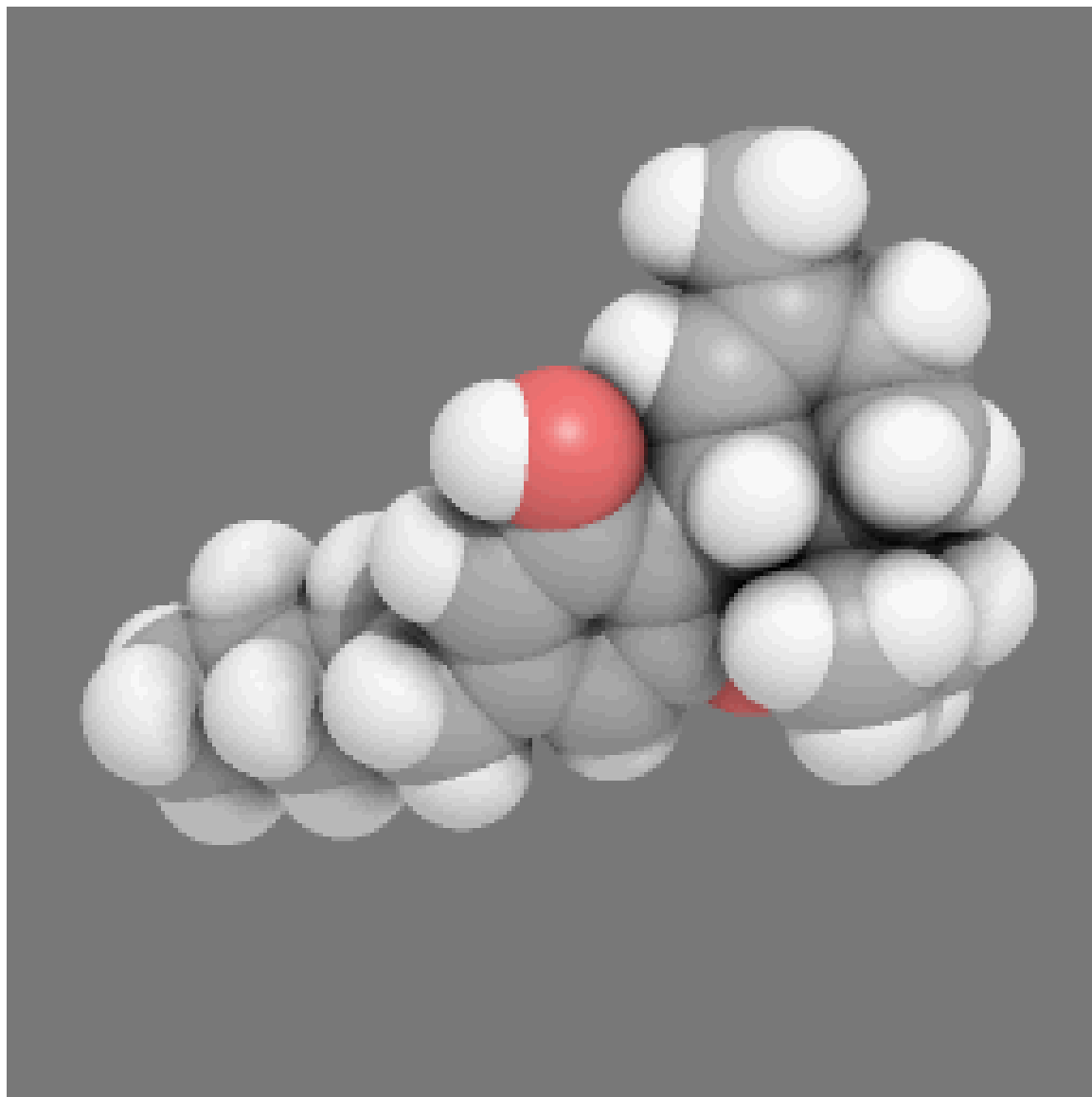
2-ARACHIDONOYL- GLYCEROL



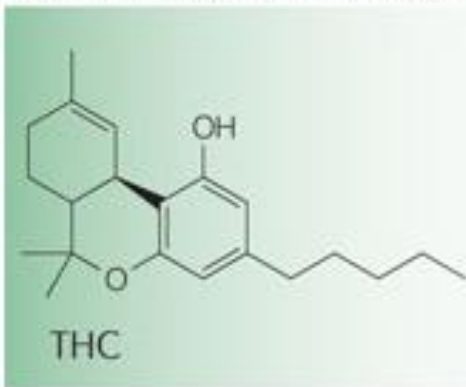
Tetrahydrocannabinol (THC)



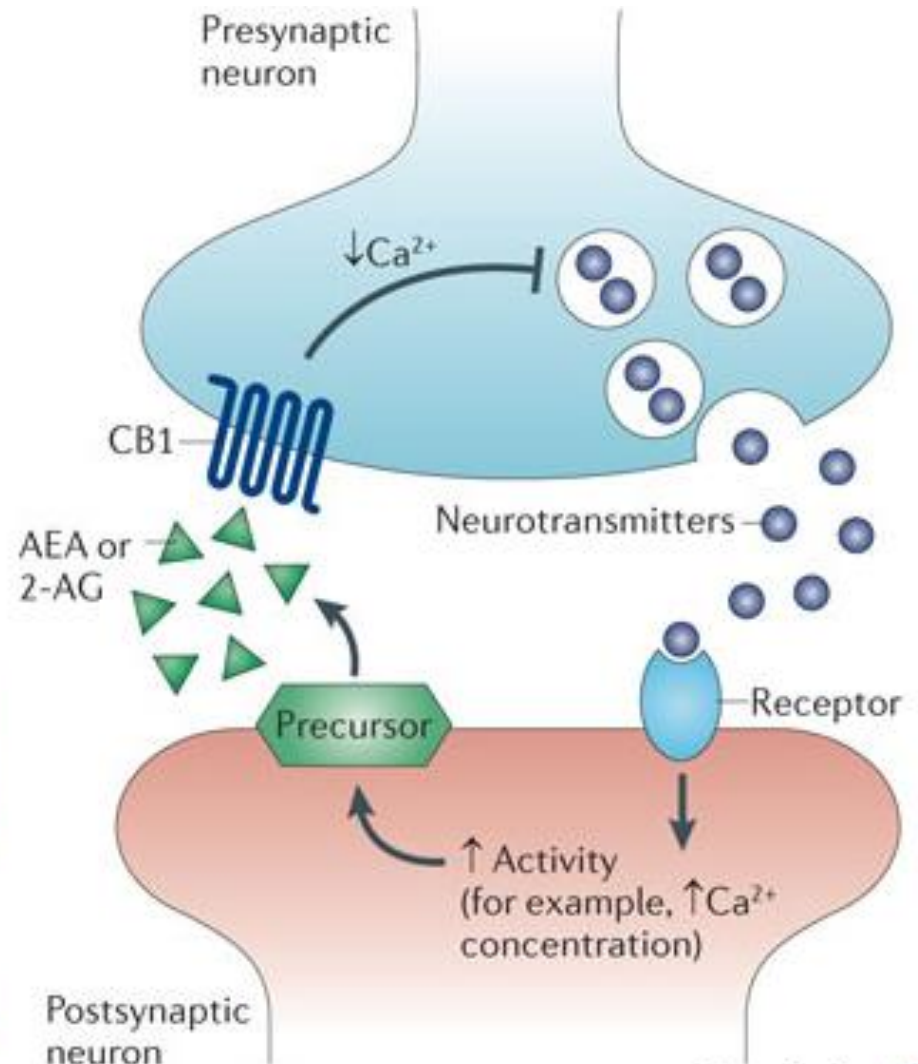
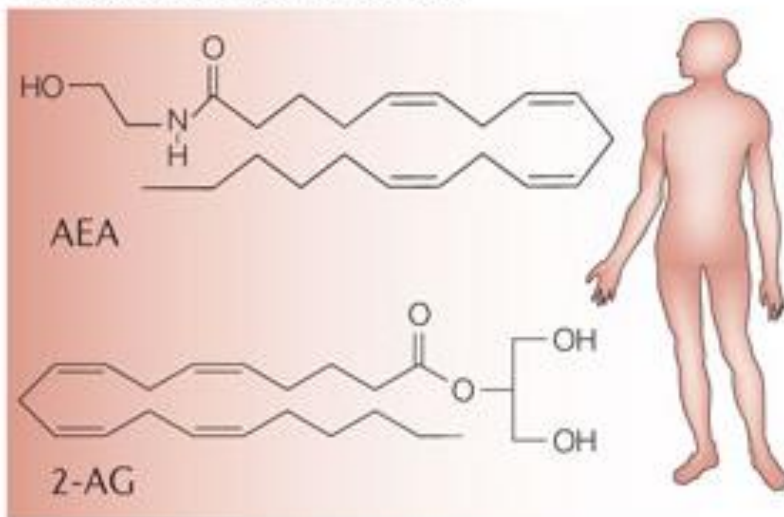
Cannabidiol (CBD)



Plant-derived cannabinoid

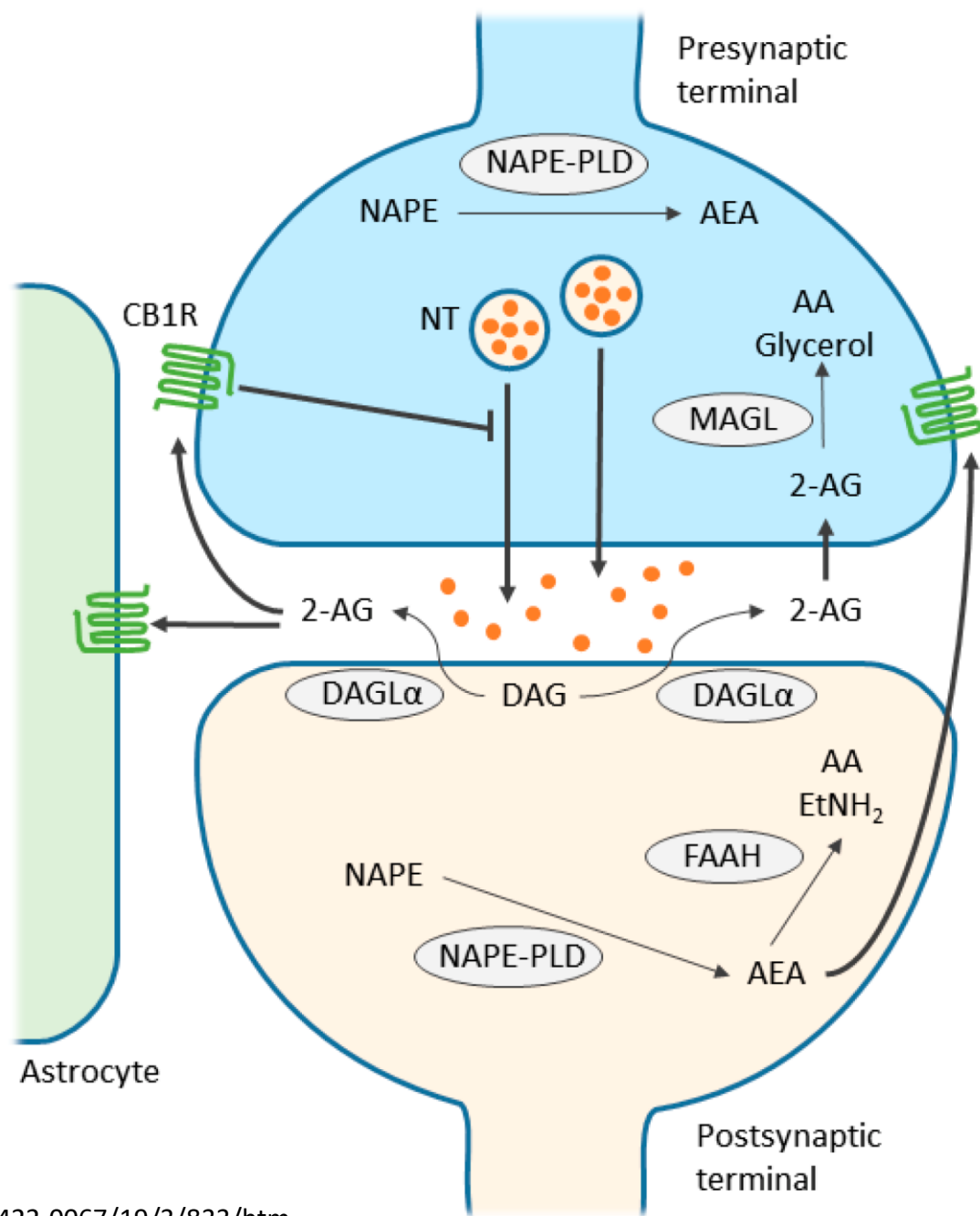


Endogenous cannabinoids

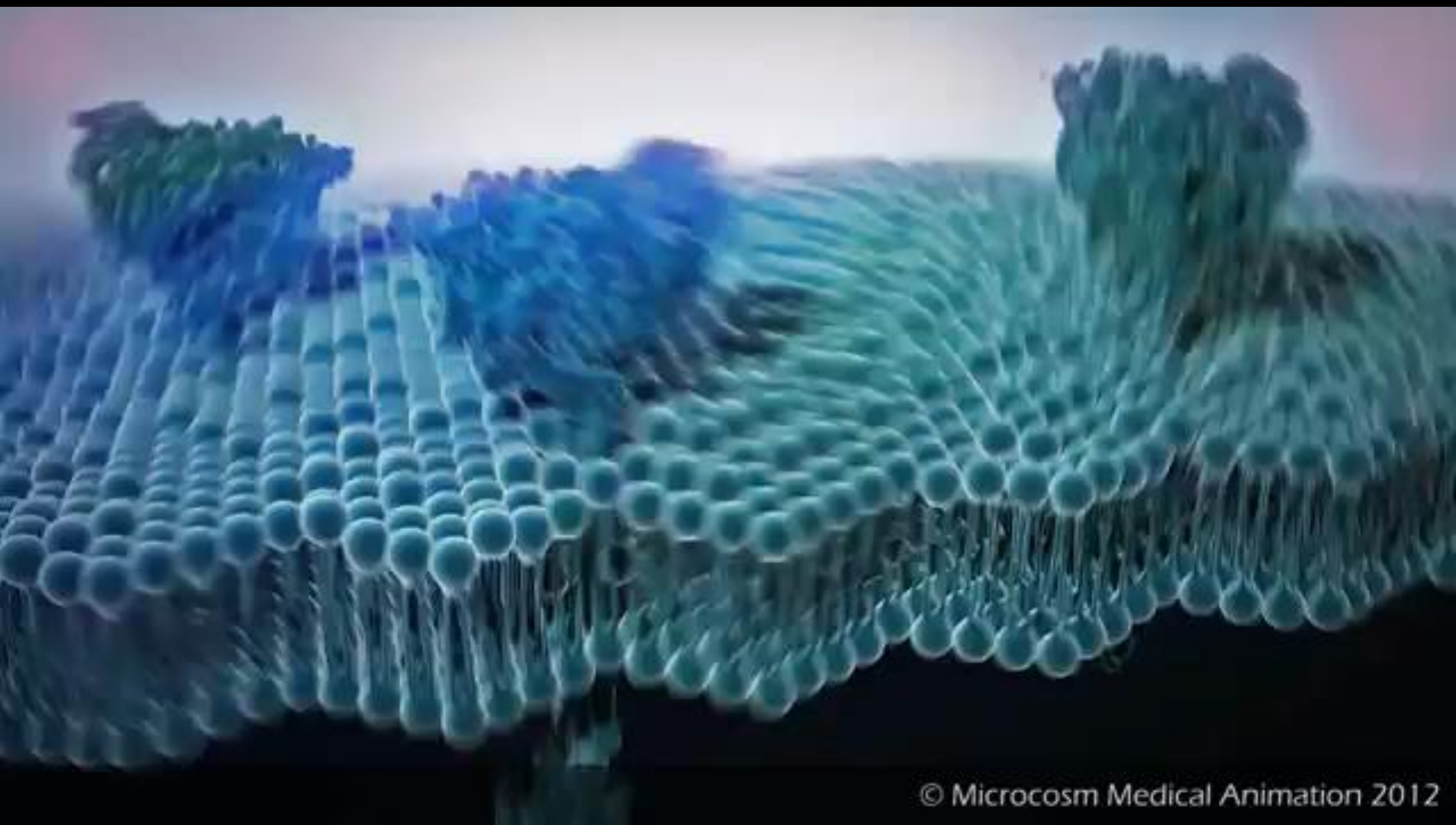


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<https://www.nature.com/articles/nrc3247>



- retrograd
- schnell degradiert
- lokale Wirkung

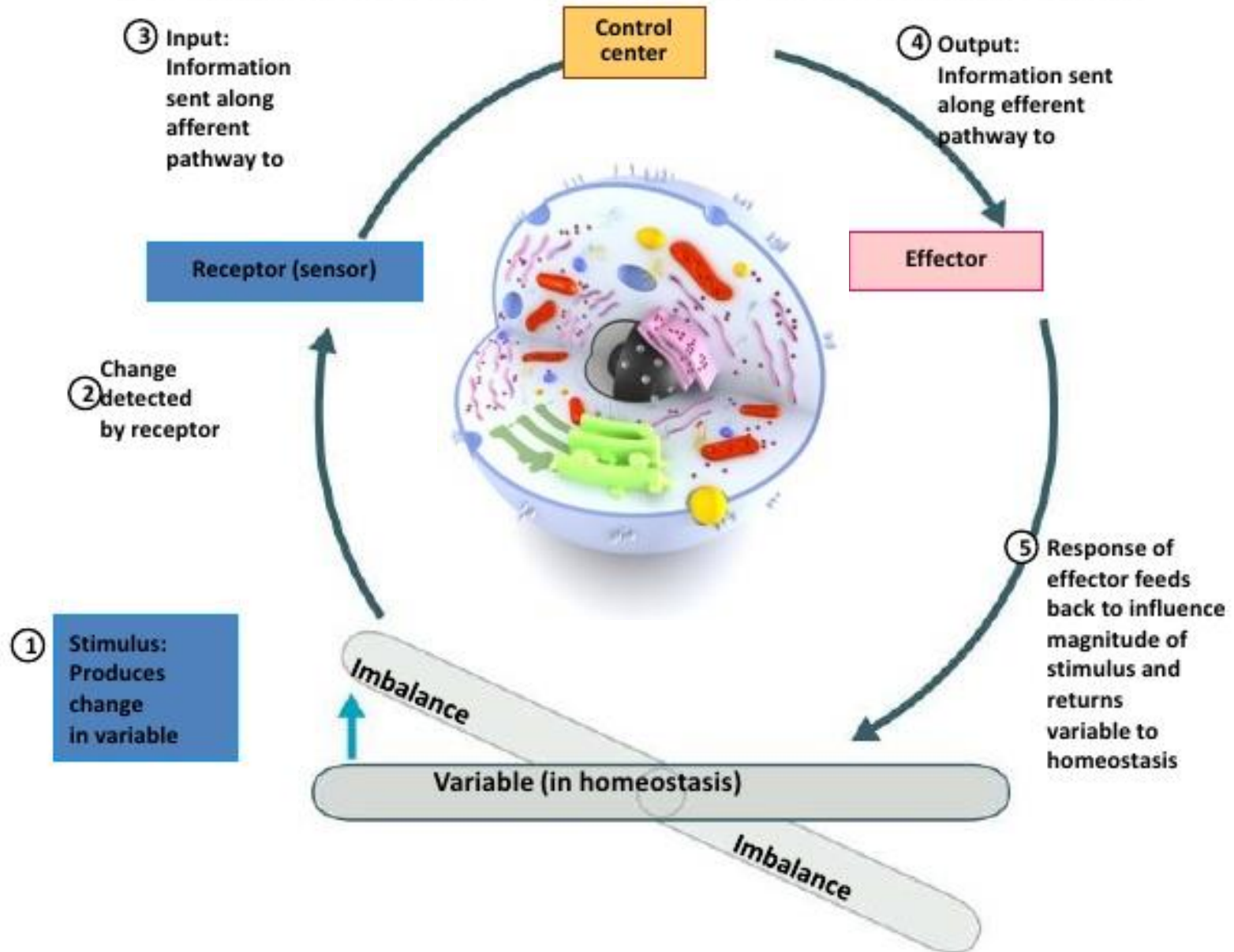


© Microcosm Medical Animation 2012

the ensemble of endocannabinoids, endocannabinoid-like mediators, and their several receptors and metabolic



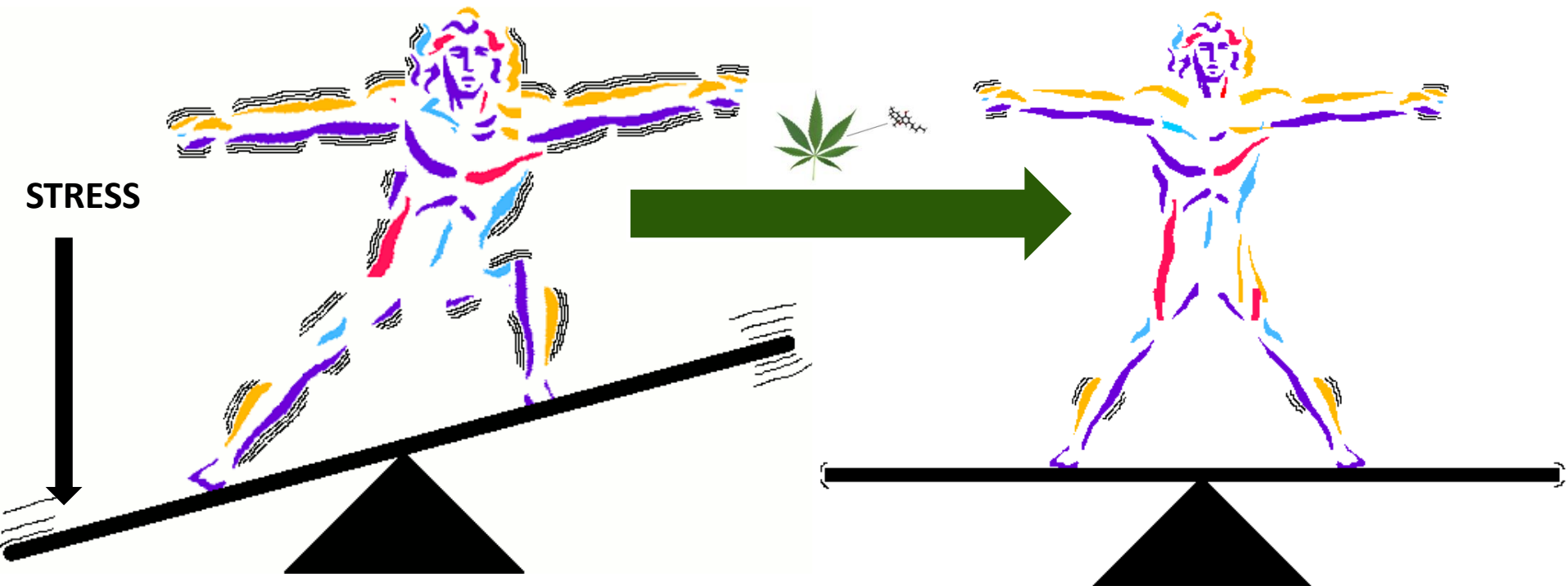
Homeostatic Control Mechanisms



Homeostasis

the tendency of organisms to auto-regulate and maintain their internal environment in a stable state

**Zellen, Gewebe, Organe, Körper, Emotionen,
Leben**



The endocannabinoid system is essential to life and it relates messages that affect how we eat, sleep, relax, forget and protect.

VINCENZO DI MARZO, Ph.D
RAPHAEL MECHOULAM, Ph.D



Schlüsselrolle bei der Bindung von
Blastozysten in der Gebärmutterschleimhaut



„Runners high“



Schlüsselrolle von
ECS vor und nach der Geburt



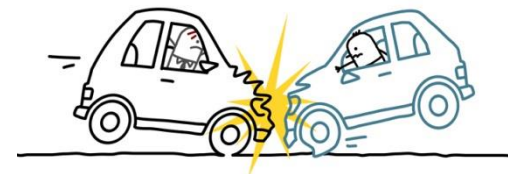
Partieller Gedächtnisverlust bei
traumatischen Ereignissen



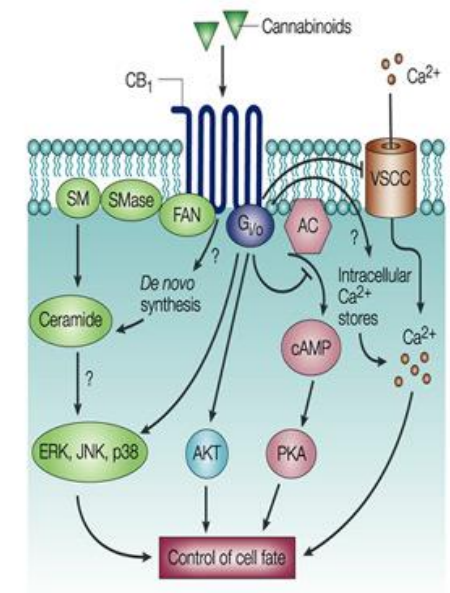
Cannabinoide in der
Muttermilch



Schmerzmodulation bei Verletzungen

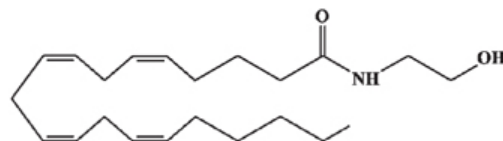


ECS system = SOS System

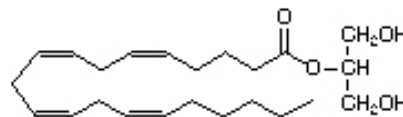


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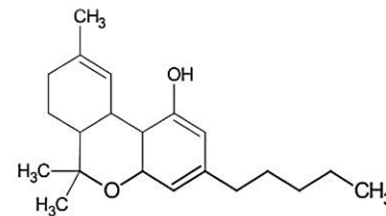
Cannabinoide = Schutz Molekülen



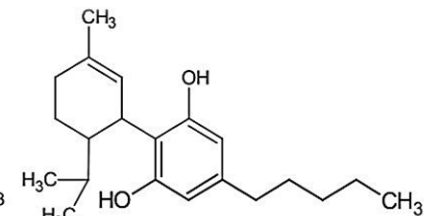
ANANDAMIDE



2-ARACHIDONOYL- GLYCEROL



Tetrahydrocannabinol (THC)



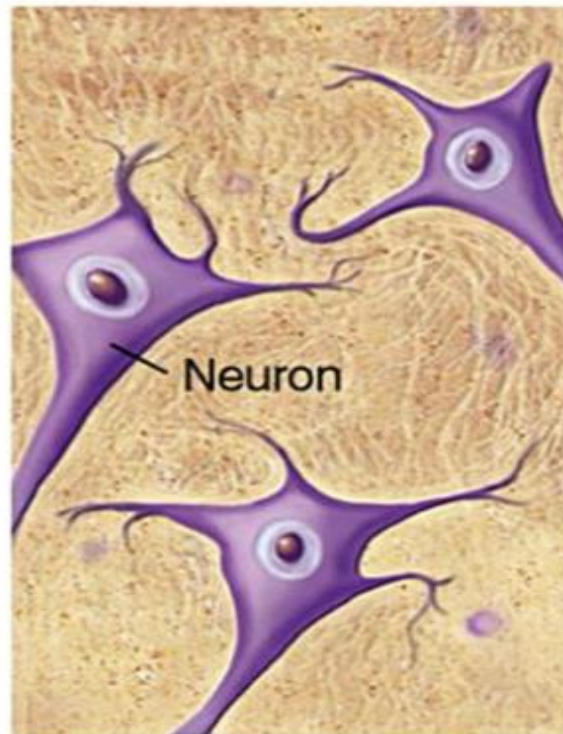
Cannabidiol (CBD)

Schutz Molekuele

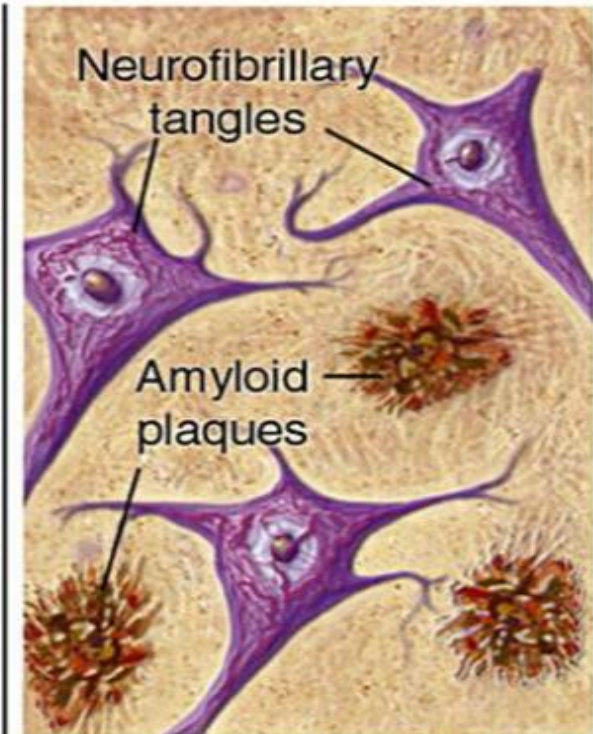
Das GEHIRN

Normal vs. Alzheimer's Diseased Brain

Normal

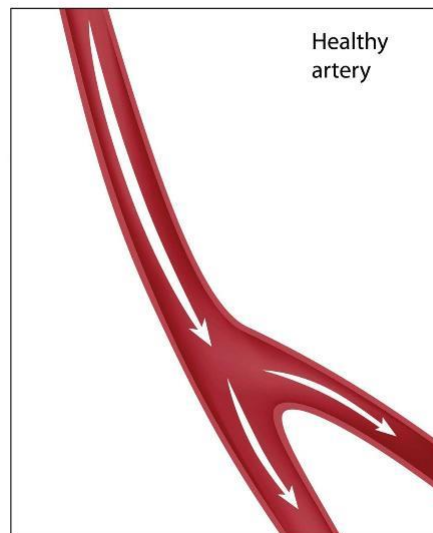
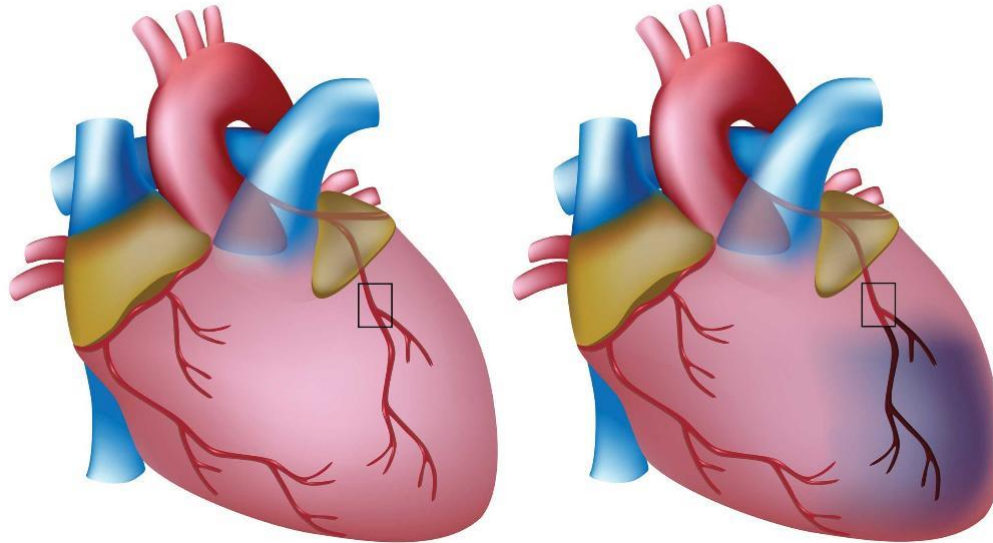


Alzheimer's

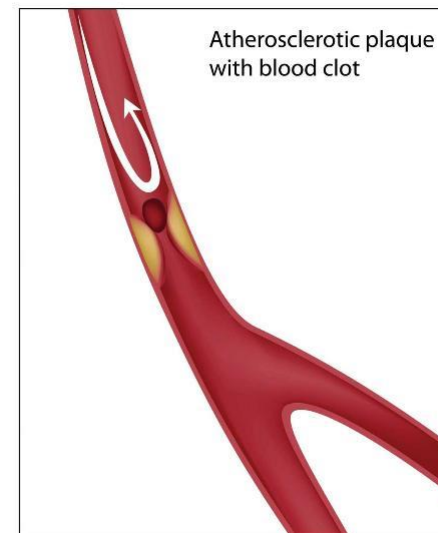


Schutz Molekuele

Das HERTZ



Healthy
artery



Atherosclerotic plaque
with blood clot

<https://www.dreamstime.com/stock-photos-anatomy-heart-attack-image19443513>

Schutz Molekuele

Der DARM

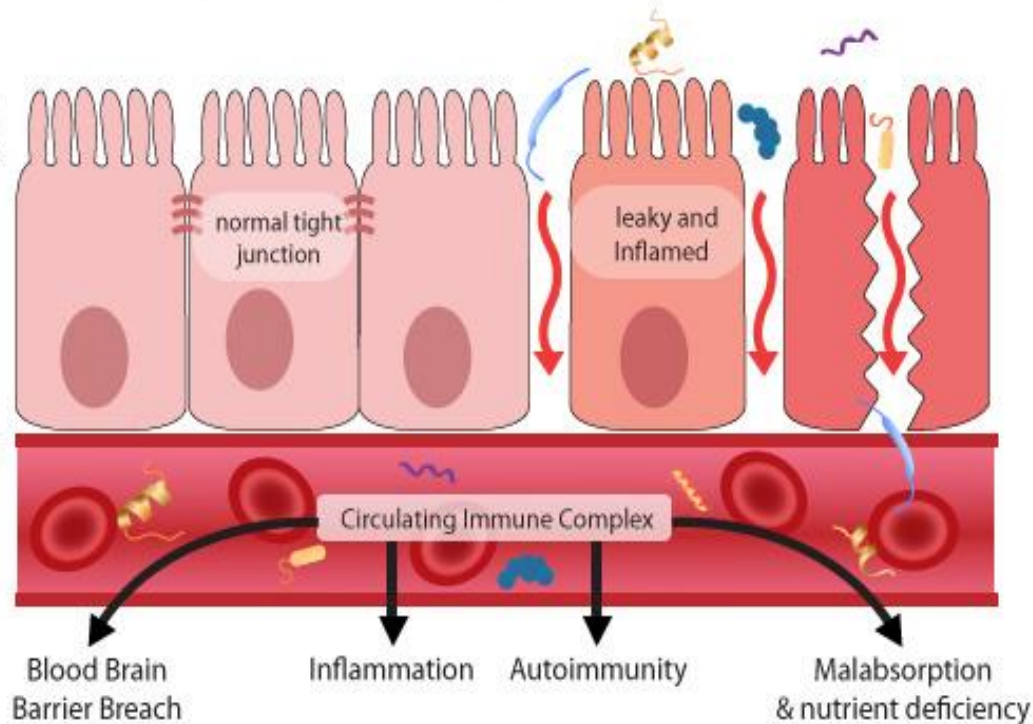
Leaky Gut Syndrome

Triggers Causing
Inestinal Damage

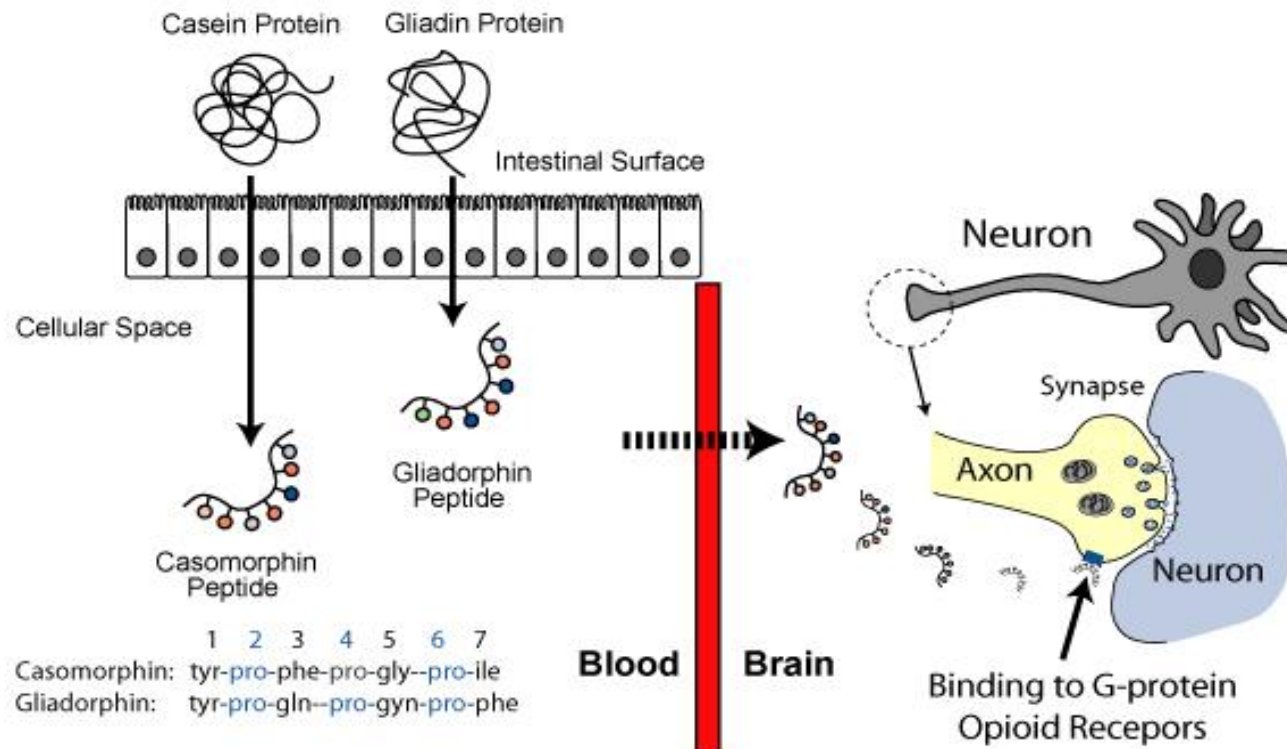


Intestinal
Mucosal Cells

Blood Stream



Neuronal Receptors for Casein and Gliadin Peptides

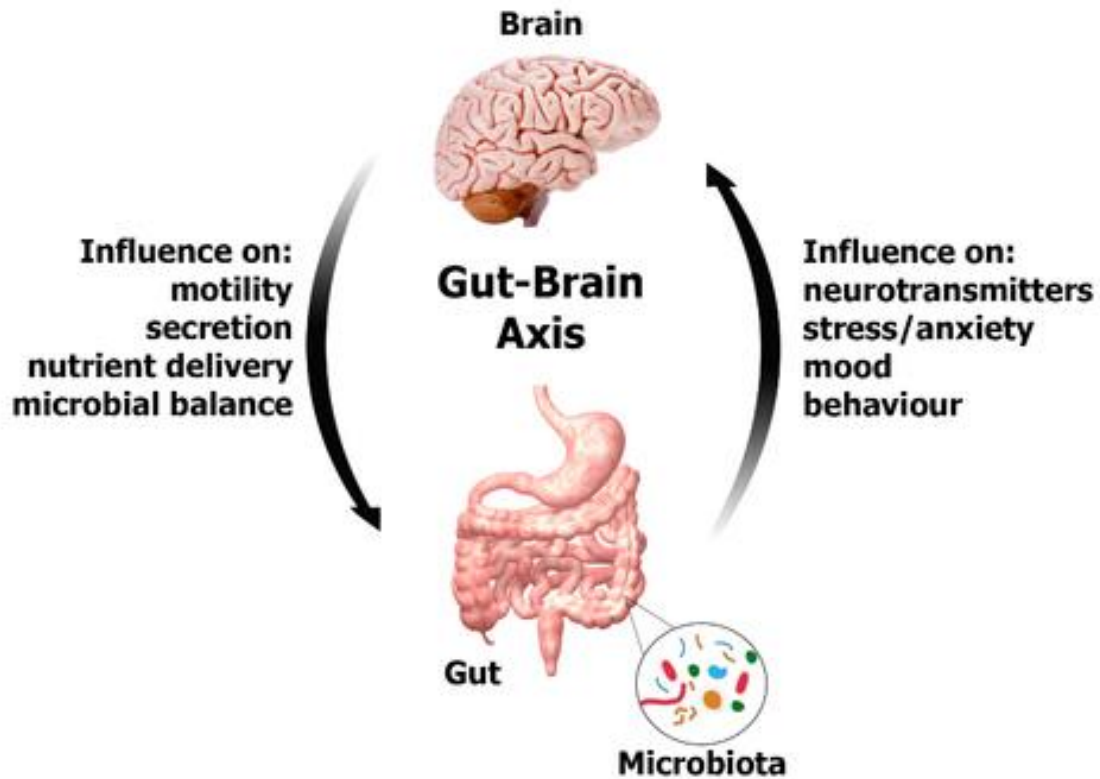


https://www.peds.ufl.edu/divisions/genetics/programs/autism_card/casein

A vertical image showing a close-up of a green, textured plant stem or leaf against a blurred background. The stem is dark green and has a bumpy, segmented appearance. The background is a mix of light and dark green, suggesting other foliage out of focus.



www.institut-icanna.com



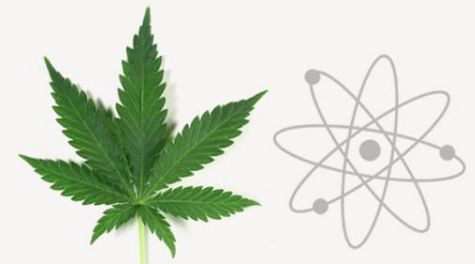
„Intervention“ mit cannabinoiden

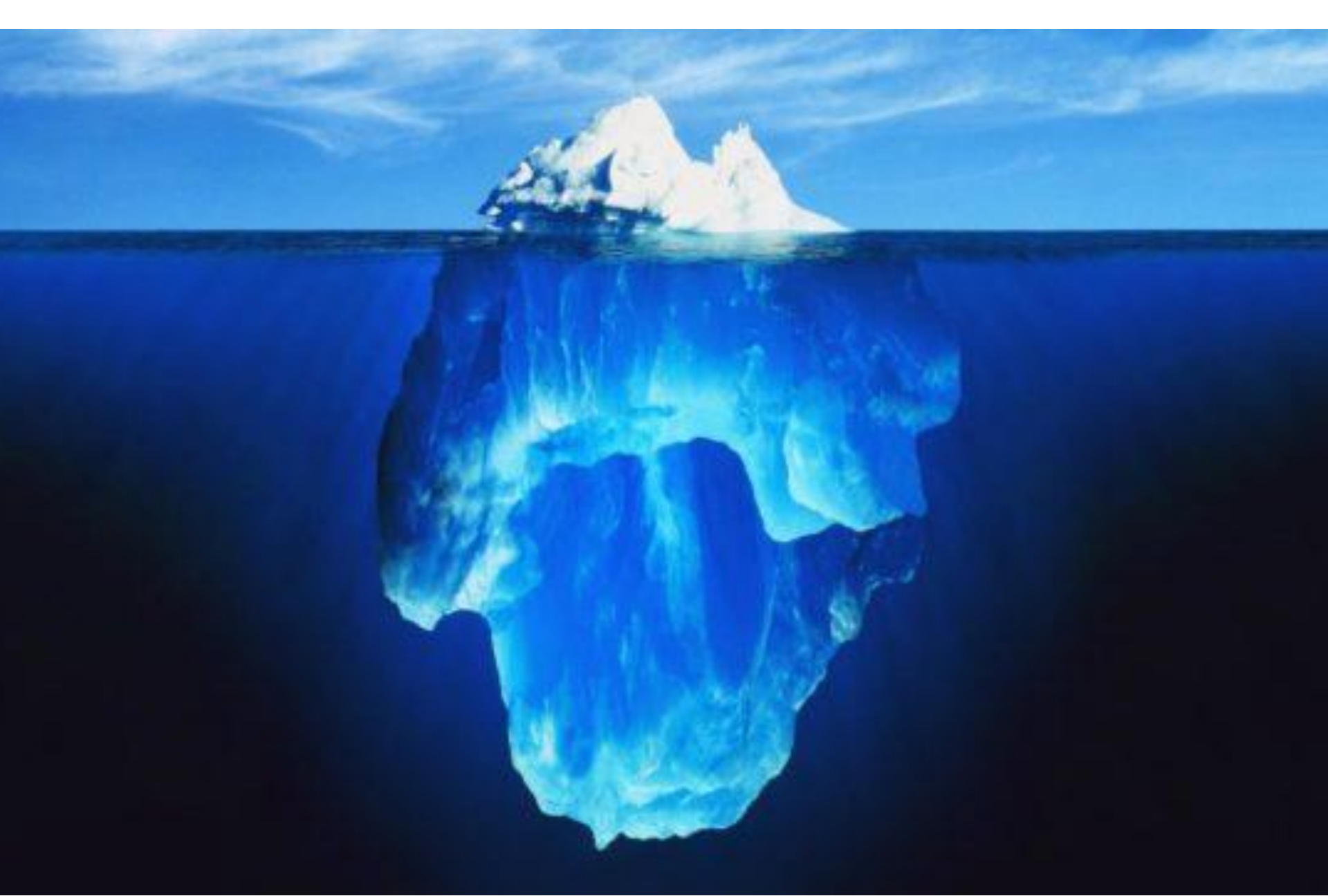
CBGA	Cannabigerolic Acid
CBGVA	Cannabigerivarinic Acid
CBG	Cannabigerol
CBGV	Cannabigerivarin
THCA	Tetrahydrocannabinolic Acid
THCVA	Tetrahydrocannabivarinic Acid
THC ($\Delta 9$)	$\Delta 9$ -tetrahydrocannabinol
THCV	Tetrahydrocannabivarin
CBNA	Cannabinolic Acid
THC ($\Delta 8$)	$\Delta 8$ -tetrahydrocannabinol
CBN	Cannabinol
CBDA	Cannabidiolic Acid
CBDVA	Cannabidivarinic Acid
CBD	Cannabidiol
CBDV	Cannabidivarin
CBCA	Cannabichromic Acid
CBCVA	Cannabichromivaric Acid
CBC	Cannabichromene
CBCV	Cannabichromivarin
CBLA	Cannabicyclol Acid
CBL	Cannabicyclol

HANF

1064 active Substanzen

Entourage effect





Cannabinoide sind mit unserem Leben verbunden seit die Evolution der Menschheit begonnen hat.



Homöostase von der zellulären und molekularen Ebene



**“UNDERSTANDING CAN OVERCOME ANY
SITUATION, HOWEVER MYSTERIOUS OR
INSURMOUNTABLE IT MAY APPEAR TO BE.”**

NORMAN VINCENT PEALE

© Lifehack Quotes



ICANNA

International Institute for Cannabinoids

**VIELEN DANK FÜR IHRE
AUFMERKSAMKEIT**

