

# CANNABIS CONSIDERATIONS: SEEKING BETTER PATIENT OUTCOMES



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**ATTESTATIONS**

Please indicate your understanding of and willingness to comply with each statement below. If you have any questions regarding your ability to comply, please contact the activity coordinator as soon as possible.

Agree	Disagree	
<input checked="" type="checkbox"/>	<input type="checkbox"/>	I have disclosed all relevant financial relationships (relevant relationships are those with companies whose products or services may be mentioned during my presentation). This information will be disclosed to learners on promotional materials distributed prior to the activity.
<input checked="" type="checkbox"/>	<input type="checkbox"/>	The content and/or presentation of the information with which I am involved will promote quality or improvements in healthcare and will not promote a specific proprietary business interest of a commercial interest. Content for this activity, including any presentation of therapeutic options, will be well-balanced, evidence-based and unbiased.

**I have no commercial ties with any company or individuals regarding the compounds to be presented and discussed.**

<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	their indications and contraindications in the care of patients. All scientific research referred to, reported or used in CME in support of justification of a patient care recommendation will conform to the generally accepted standards of experimental design, data collection and analysis.
<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If I am discussing specific health care products or services, I will use generic names to the extent possible. If I need to use trade names, I will use trade names from several companies when available, not just trade names from any single company.

**All Schedule 1 substances are by definition: "off-label"**

<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If I have been trained or utilized by a commercial entity or its agent as a speaker (e.g. speaker's bureau) for any commercial interest, the promotional aspects of that presentation will not be included in any way with this activity.
<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If I am presenting research funded by a commercial company, the information presented will be based on generally accepted scientific principles and methods, and will not promote the commercial interest of the funding company.

I have carefully read and considered each item in this form, and have completed it to the best of my ability.

Jeffrey Block, M.D.

Print Name

Signature





*Mind ∞ Body*

*Imhotep*

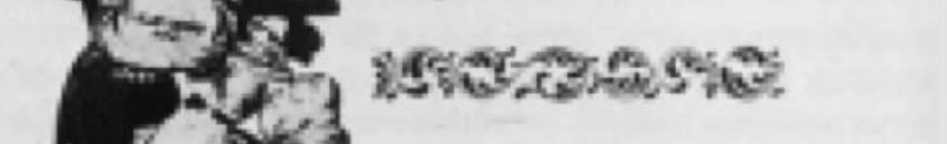
*Acharya Charaka*



# A GRAND EXHIBITION

OF THE GIGGETS PRODUCED BY INHALING  
NITROUS OXIDE, EXHILERATING, OR  
**LAUGHING GAS!**

WILL BE GIVEN AT *The Harmon Hall*  
Monday EVENING, 1877



10 GALLONS OF GAS  
will be  
prepared and administered  
to all in the audience  
who desire to inhale it.

MEN will be invited from the audience, to  
protect those under the influence of the Gas from in-  
sulting themselves or others. This course is adopted  
as no apprehension of danger may be entertained,  
probably no one will attempt to fight.



LIVING MADE EASY.



# “LAUGHING GAS”



Evaluated by F.D.A.  
Food & Drug Administration  
Safety & Efficacy  
Use - Abuse

“Marijuana”  
Cannabis sativa



Substances  
Scheduled by D.E.A.  
Drug Enforcement Administration  
Risks & Benefits  
Prohibited - Controlled

The Controlled Substances Act (CSA)

“Chocolate” Defined a “Scheduling” of Drugs”

Theobroma cacao

“Schedule 1” substances are designated as “prohibited” when:

1 - The drug or other substance has a high potential for abuse.

2 - The drug or other substance has no currently accepted medical use in treatment in the United States.

3 - There is a lack of accepted safety for use of the drug or other substance under medical supervision.

“Cocaine”  
Erythroxylum coca

Nicotiana tabacum

Reference.: Schedules of controlled substances - [Pub.L. 91-513](#), 84 [Stat. 1236](#), enacted October 27, 1970, codified at [21 U.S.C. § 801](#) et seq. [21 U.S.C. § 812](#)



The American Medical Association's  
William C. Woodward, M.D. addressed the  
U.S. House of Representatives Committee on Ways and Means  
concerning *The 'Marihuana' Tax Act of 1937.*

AMA

AMERICAN MEDICAL  
ASSOCIATION



Dr. William Woodward, serving as legislative counsel for the American Medical Association, publicly dispelled any impression that either the AMA or enlightened medical opinions sponsored this new law's politicized rationale.

He further emphasized that the AMA encourages unfettered scientific research & education; and that Cannabis' medicinal use should be regarded as:

**STATED MISSION:**

*“an unknown quantity, but might have  
important uses in medicine and psychology”* (May 4, 1937)  
**“TO BRING TOGETHER PHYSICIANS AND COMMUNITIES  
TO IMPROVE THE NATION'S HEALTH.”**

Cannabis' prohibition's side-effects have  
undermined it's research and education.

2019



## Modulating the endocannabinoid system in human health and disease – successes and failures

Pál Pacher and George Kunos

Laboratory of Physiologic Studies, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda, MD, USA

### Keywords

cannabinoids; clinical trials; disease; endocannabinoid system; human; pharmacology; therapeutic potential

### Correspondence

P. Pacher, Laboratory of Physiological

The discovery of the endocannabinoid system, comprising the G-protein coupled cannabinoid 1 and 2 receptors (CB<sub>1/2</sub>), their endogenous lipid ligands or endocannabinoids, and synthetic and metabolizing enzymes, has triggered an avalanche of experimental studies implicating the endocannabinoid system in a growing number of physiological/pathological functions. These studies have also suggested that modulating the activity of the en-

“...modulating ECS (endocannabinoid system) activity may have therapeutic potential in almost all diseases affecting humans...”  
“*Targeting the Endocannabinoid System*” (NIH Review - 2013)

### Introduction

Although *Cannabis sativa* (the marijuana plant) is one of the most ancient medicinal plants in the history of medicine [1], the clinical use of synthetic cannabinoids or medicinal plant extracts has been largely empirical and limited to a few specific indications related to pain, wasting disorders, and chemotherapy-induced nausea and vomiting, as a result of their socially undesirable psychoactive properties [2]. The discovery of endocannabinoids (ECs), which mimic some of the effects of synthetic cannabinoids *in vivo*, their G-protein coupled receptors, as well as their synthetic and metabolizing enzymes, has prompted preclinical studies aiming to explore the role of the endocannabinoid system (ECS) in health and disease [2–4]. These studies have been greatly facilitated by the introduction of mice deficient

in cannabinoid receptors or EC degrading enzymes, as well as selective cannabinoid receptor ligands and inhibitors of EC metabolism. The results of these studies have implicated the ECS in a variety of physiopathological processes, both in the peripheral and central nervous systems and in various peripheral organs [2]. Such studies have further suggested that modulating ECS activity may have therapeutic potential in almost all diseases affecting humans, including obesity/metabolic syndrome [5]; diabetes and diabetic complications [6]; neurodegenerative [7,8], inflammatory [9], cardiovascular [10–12], liver [13,14], gastrointestinal [15] and skin [16] diseases; pain [17,18]; psychiatric disorders [19,20]; cachexia [2]; cancer [21,22]; and chemotherapy-induced nausea and vomiting [23], amongst many others [2].

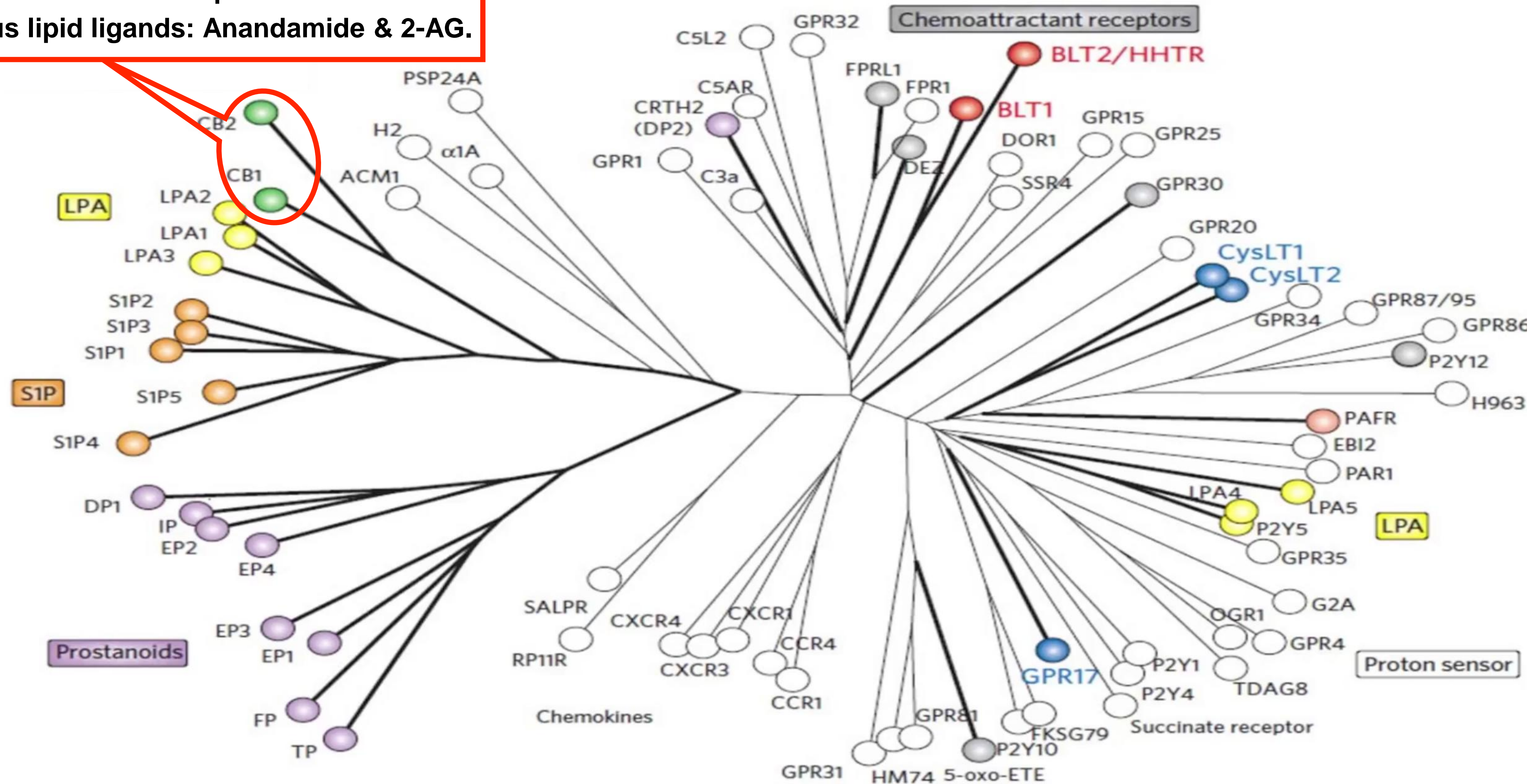
### Abbreviations

2-AG, 2-arachidonoylglycerol; AEA, anandamide or arachidonoyl ethanolamide; CB<sub>1/2</sub>, cannabinoid receptor 1 or 2; CBD, cannabidiol; CNS, central nervous system; EC, endocannabinoid; ECS, endocannabinoid system; FAAH, fatty acid amide hydrolase; MAGL, monoacylglycerol lipase; MS, multiple sclerosis; THC, Δ<sup>9</sup>-tetrahydrocannabinol; TRPV<sub>1</sub>, transient receptor potential cation channel subfamily V member 1.



# Endocannabinoid receptor system functions influence all other known physiologic systems.

CB1 & CB2 Cannabinoid Receptors interact with two endogenous lipid ligands: Anandamide & 2-AG.



Human Receptor Systems (2013)





## ETHICAL CHALLENGE:

Should a physician offer compassionate access to Cannabis for use as a medicine while it remains under Federal prohibition?

## ~~MEDICAL ALTERNATIVES~~

The AMA Principles of Medical Ethics states: *“Seeking relief from the intolerable physical, psychological or spiritual symptoms of disease is a natural instinct that contributes to a substance’s therapeutic use.”*

*“A physician, by law, and also recognize treatment of intolerable symptoms is the noble task that society bestows upon its healers to provide humane relief.”*

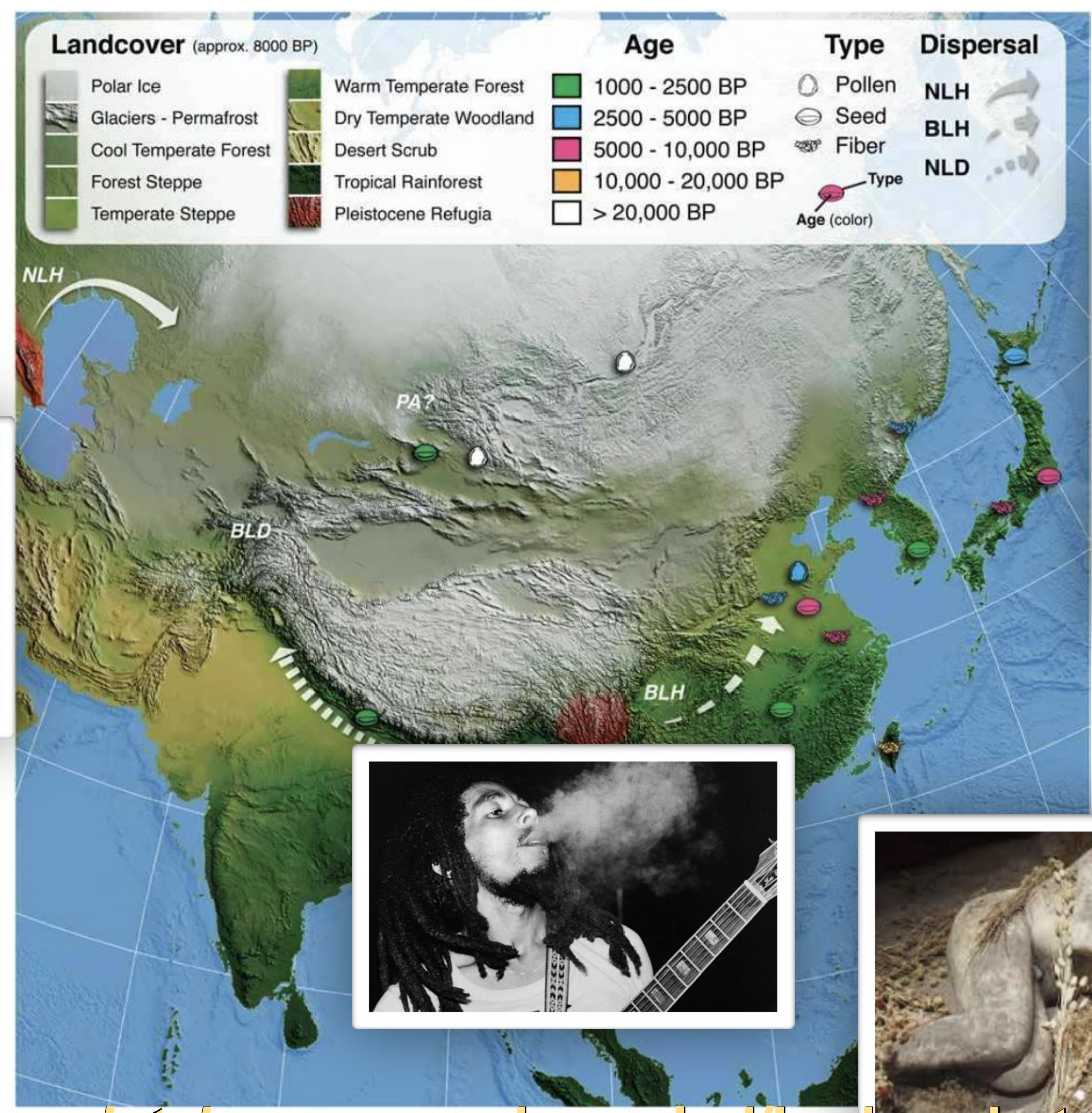
*that all interests of the patient.”*

Source: AMA Physician’s Code of Ethics: <http://www.ama-assn.org>

**JSB**



# During the Pleistocene Ice Age Adaptable Human Beings and Cannabis Plants Survived in Cannabis' Current "Refugia" Distribution



China (700 BCE)

s tomb.

Drug varieties were used as mind/body substances.

Hemp varieties were used as textiles.

Cannabis - Evolution and Ethnobotany  
Clarke & Merlin: Univ. of Cal Press 2013





# CONTRAINDICATIONS TO CANNABIS USE

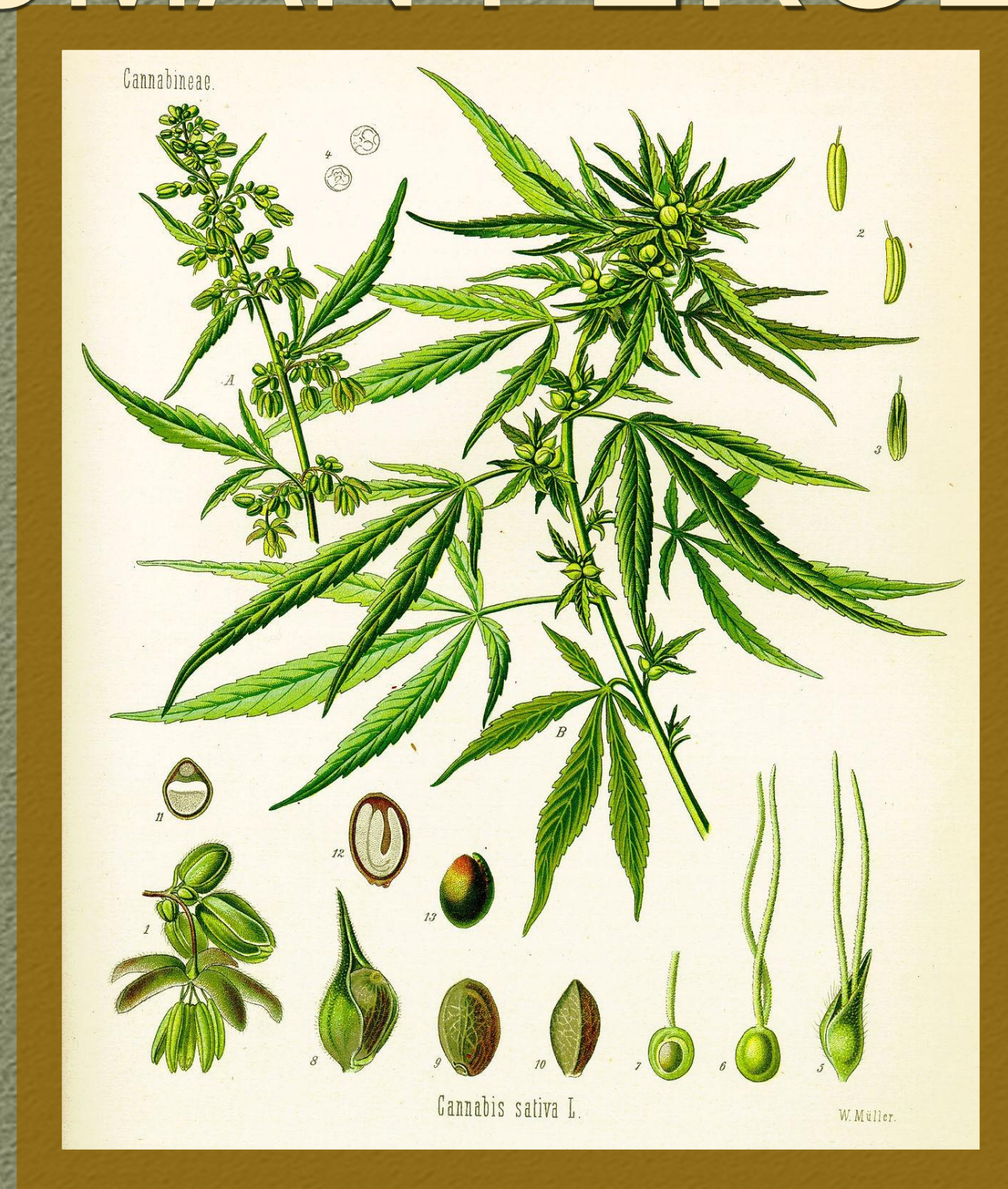
- ▶ Existing disease or genetic predisposition to psychotic disorders (schizophrenia).
- ▶ Pre-existing significant cardiac disease.
- ▶ Pregnancy.



# PLANT-DERIVED BIOACTIVE CHEMICALS INTERACT WITH 3 RECEPTOR SYSTEMS TO REDUCE HUMAN PERCEPTION OF PAIN



- MORPHINE -  
- ENDORPHINS  
(1974)



- THC / CBD -  
- ENDOCANNABINOIDS  
(1992 & 1994)



- CAPSAICIN -  
- ENDOVANILLOIDS  
(1997)



WELL-DOCUMENTED IN THE 19TH & 20TH CENTURY AS BEING EFFECTIVE FOR PAIN, CHLORODYNE WAS ALSO ABUSED.

BOTANICAL PLANT EXTRACTS IDENTIFIED FOR PAIN

ENDOGENOUS RECEPTORS IDENTIFIED FROM PLANTS

Morphine

Cannabis

Capsicum

Endorphins

Endocannabinoids

Endovanilloids



# CANNABINOID SIGNALING AT THE SYNAPSE

# ENDOCANNABINOID RECEPTORS AND THEIR LIGANDS

TWO NATURAL LIGANDS' RETROGRADE FEEDBACK CONSTANTLY MODULATES THE RELEASE OF ALL NEUROTRANSMITTERS

**PRESYNAPTIC NEURON**

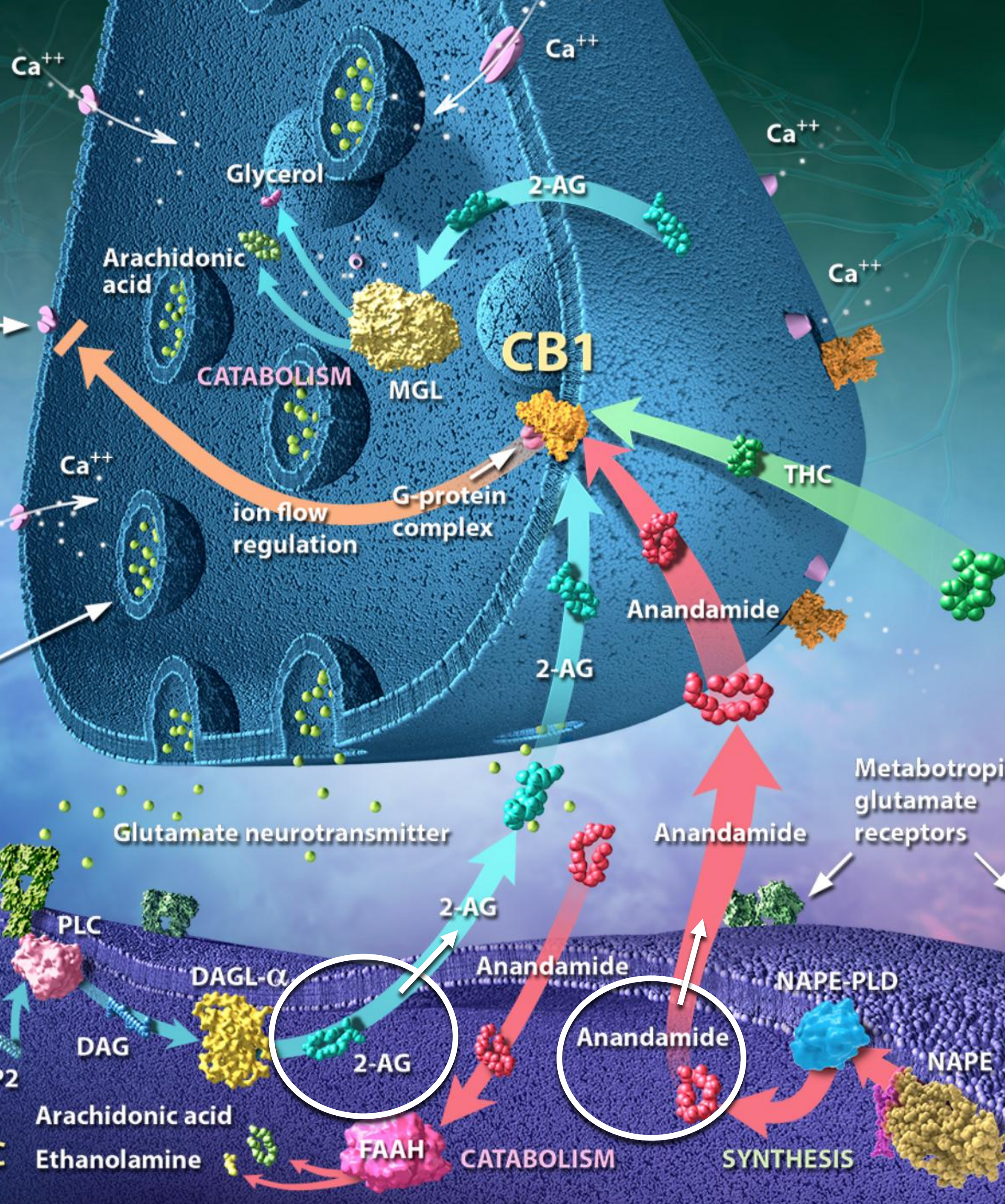
Calcium channel

Calcium ion flow

Neurotransmitter vesicle

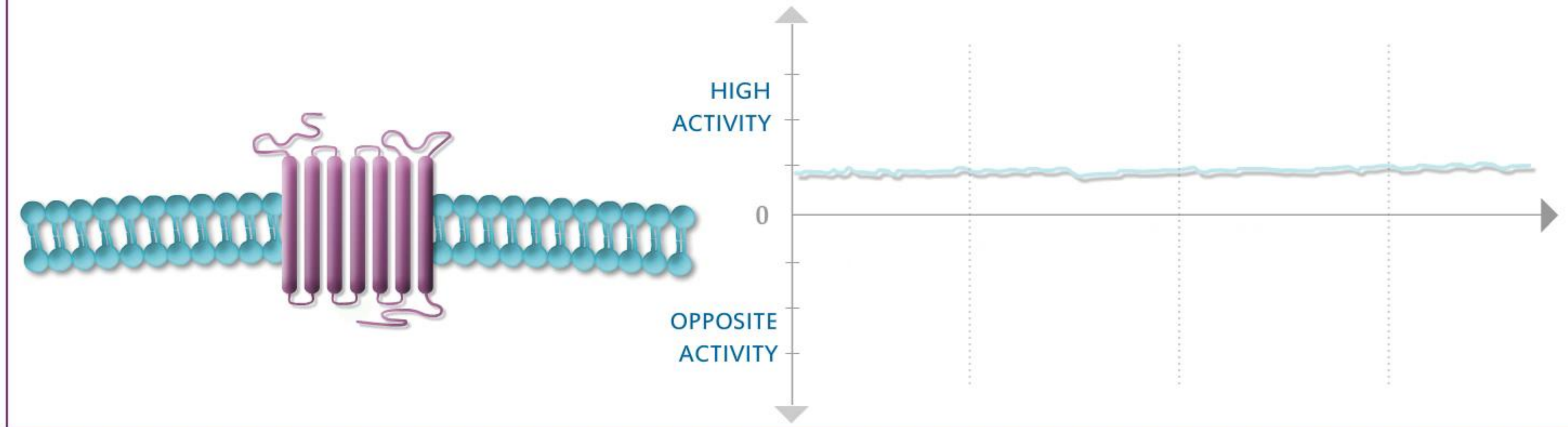
Metabotropic glutamate receptor

**POSTSYNAPTIC NEURON**



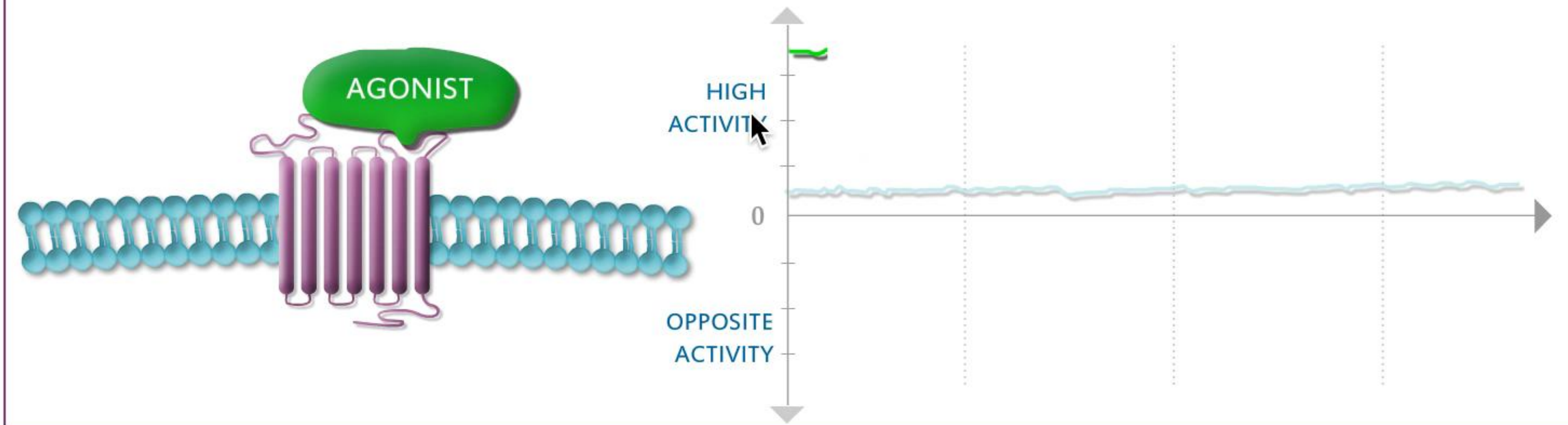
This animation differentiates full agonists (usually synthetic compounds) and partial agonists (especially useful in systems such as the ECS which are under tonic control):

### CANABINOID RECEPTORS HAVE A CONSTITUTIVE (BASAL) ACTIVITY



This animation illustrates the difference between inverse agonism and neutral antagonism at a constitutively active receptor:

### AGONISM OF THE RECEPTOR INCREASES ACTIVITY FROM THE BASAL LEVEL



**POSITIVE  
REGULATION:**

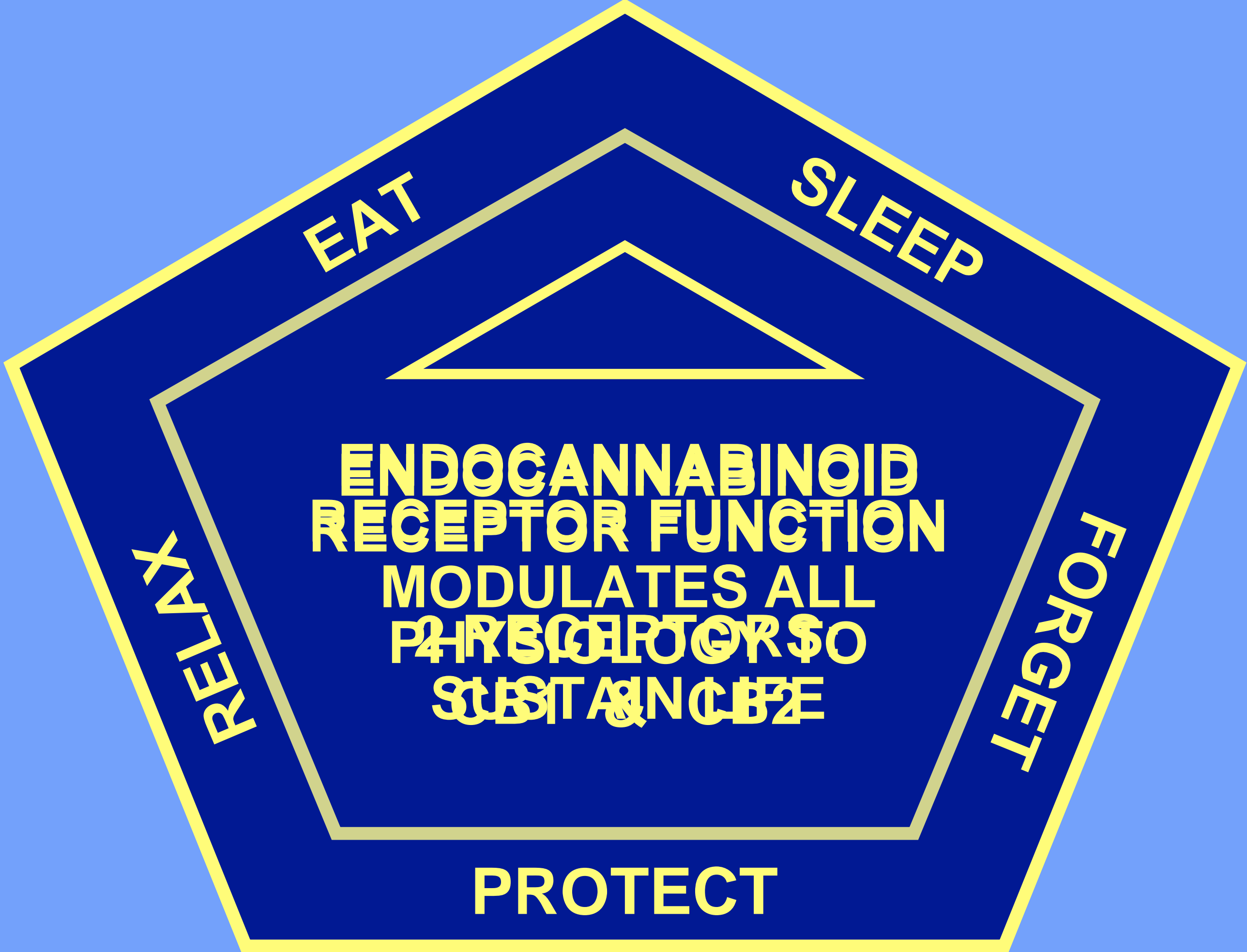
## CANNABINOID RECEPTOR ACTIVITY

**NEGATIVE  
REGULATION:**





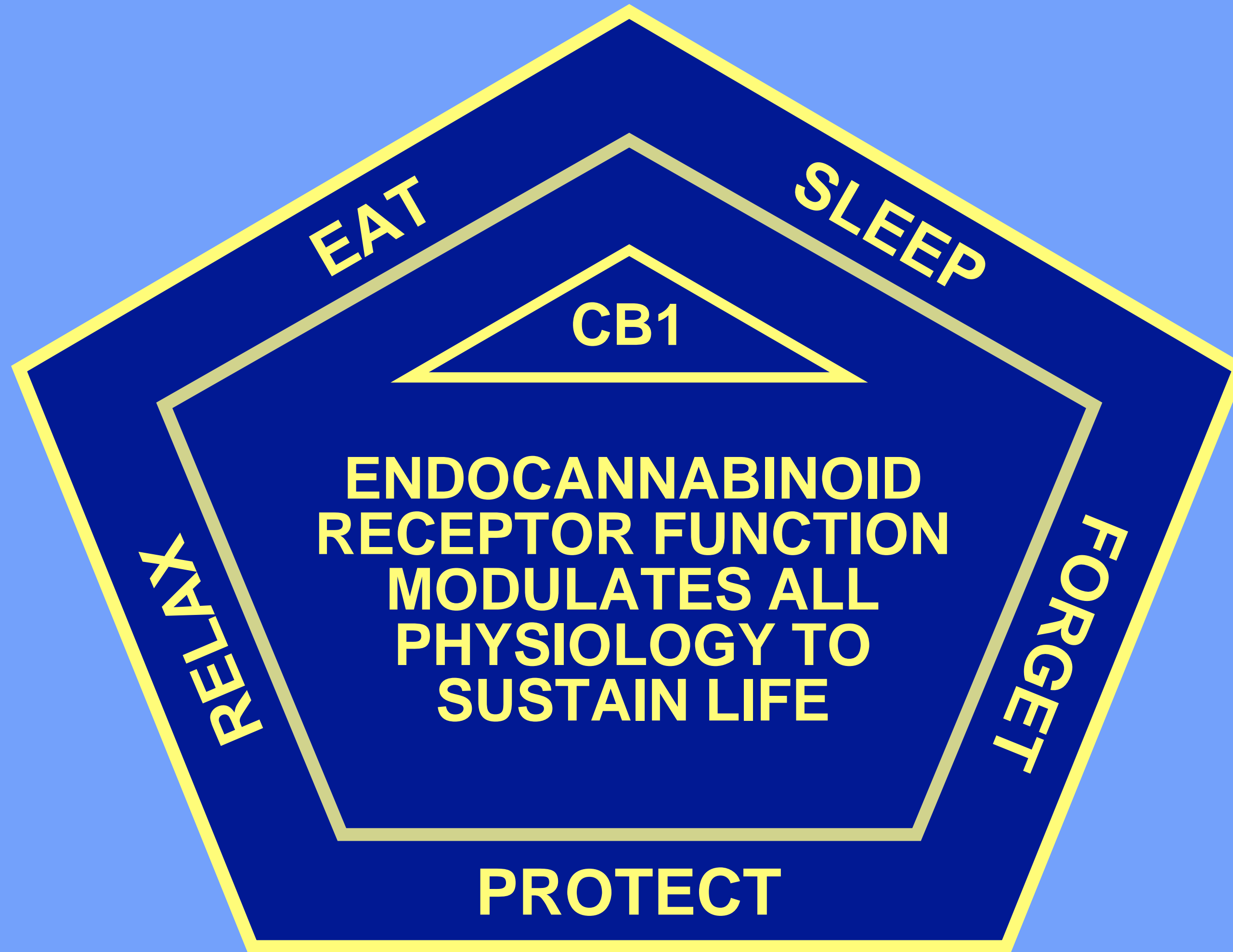
**CONCEPTION**



**DEATH**



**CONCEPTION**



**DEATH**



**CB1:**

**EAT**



**SLEEP**



**Eating & sleeping are essential for growth and reproduction.**

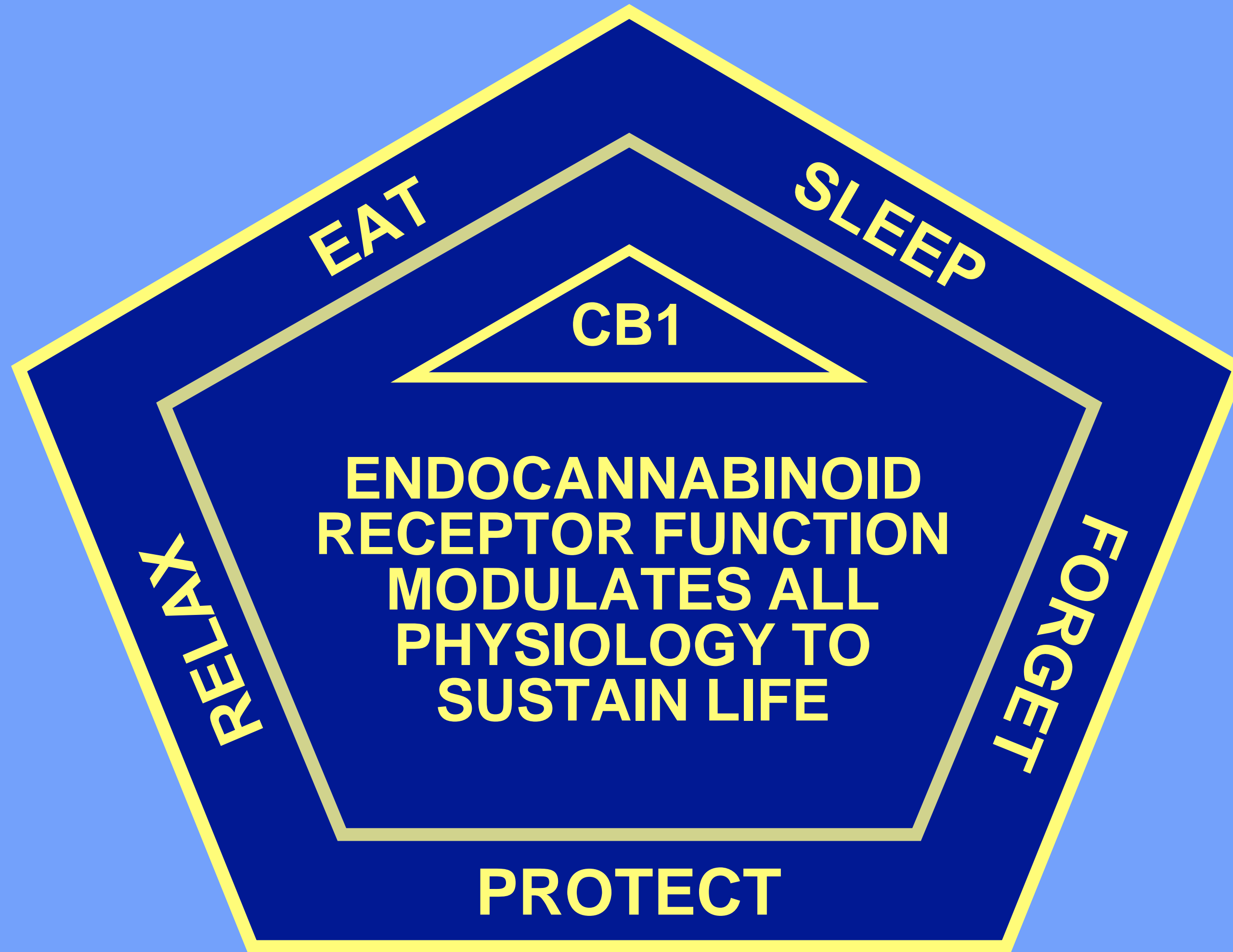


**The coordinated systemic functions of endocannabinoids  
explain a holistic but scientifically elusive**

**“Brain : Gut Connection”**



**CONCEPTION**



**DEATH**

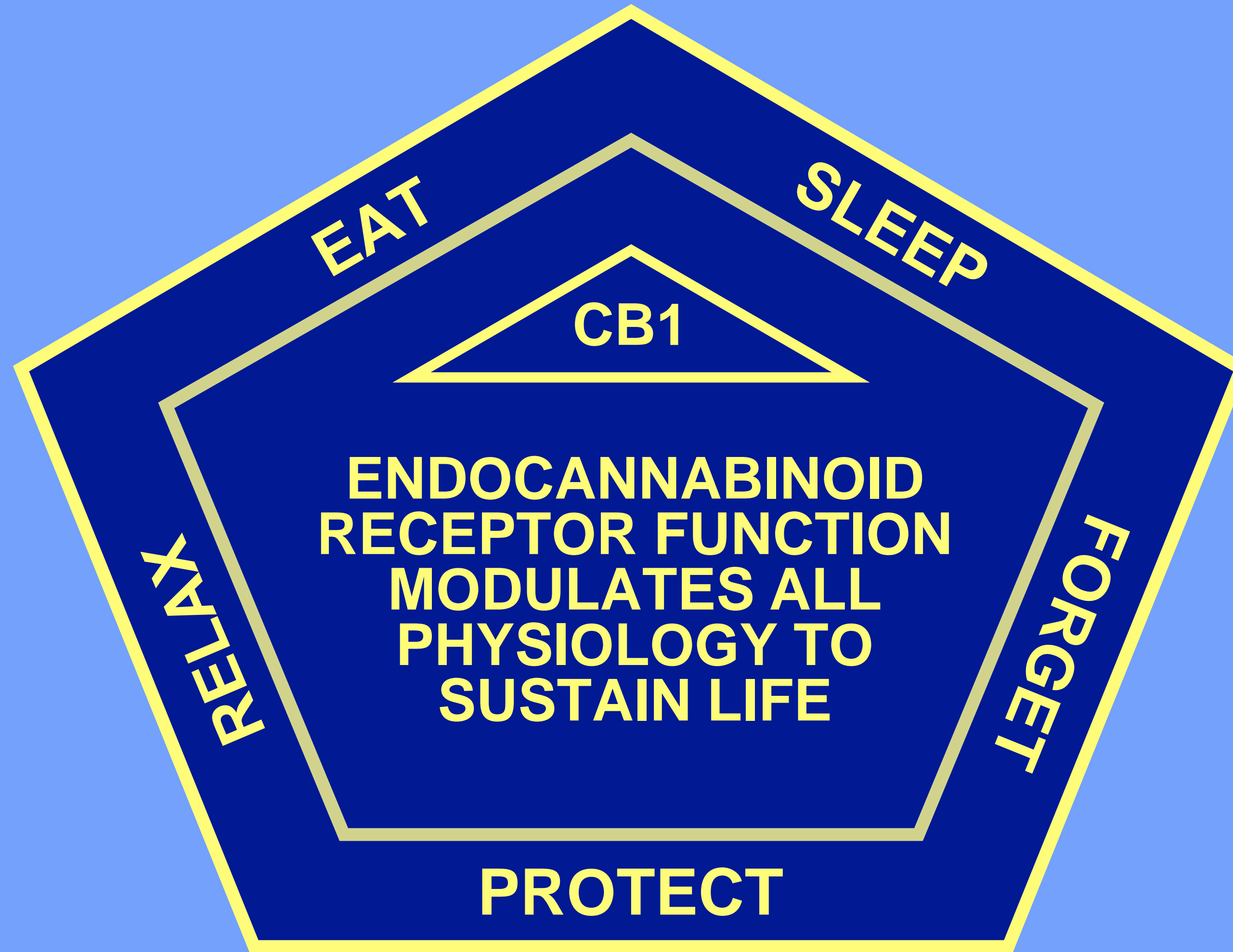


The need to relax is essential to  
recover from life's relentless  
stressors.

CB1: RELAX



**CONCEPTION**



**DEATH**



# CB1: FORGET

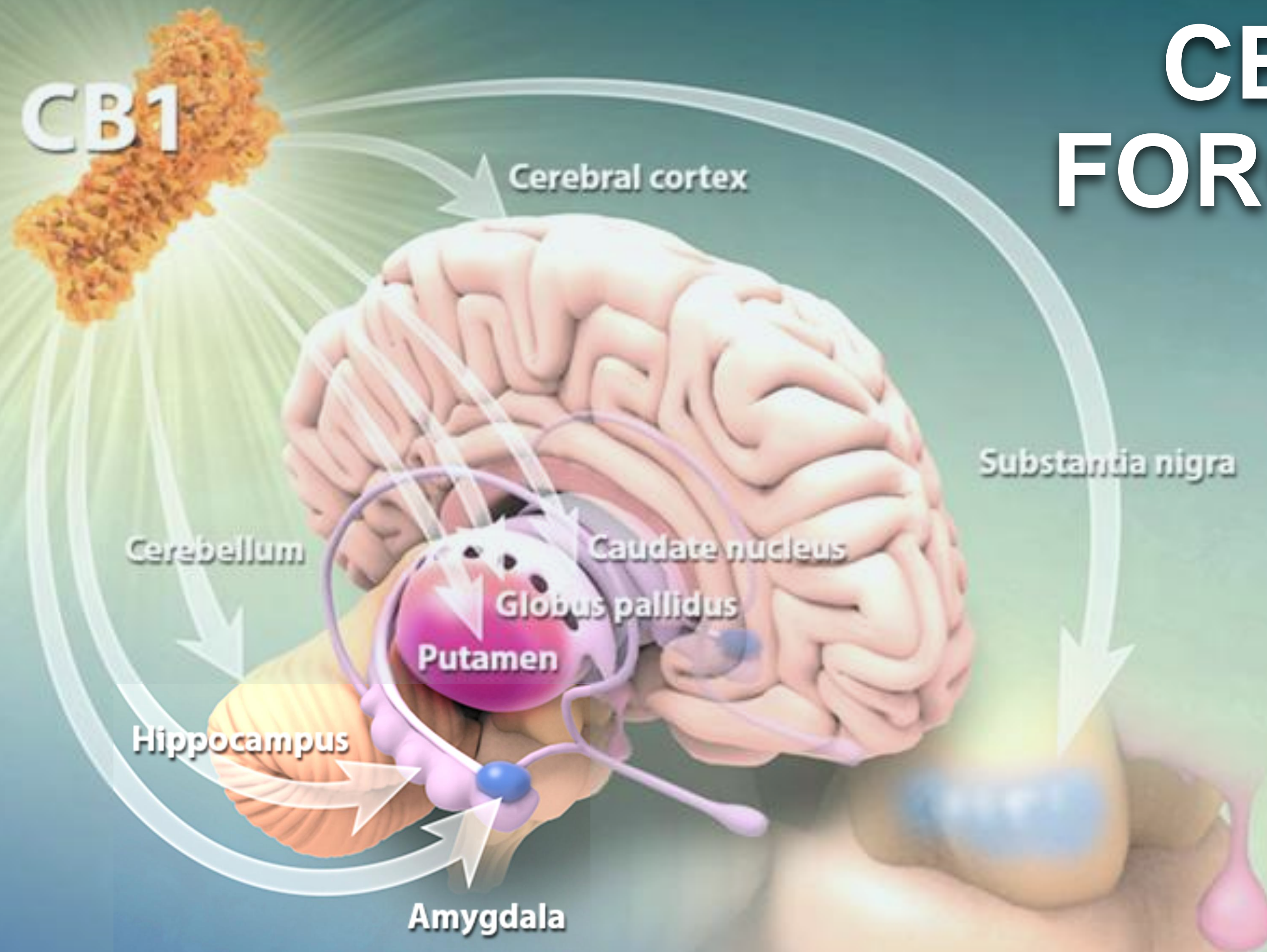


More than an inconvenience:  
**The *ability* to forget is essential for survival.**





# CB1 FORGET



**The hippocampus processes memories.**



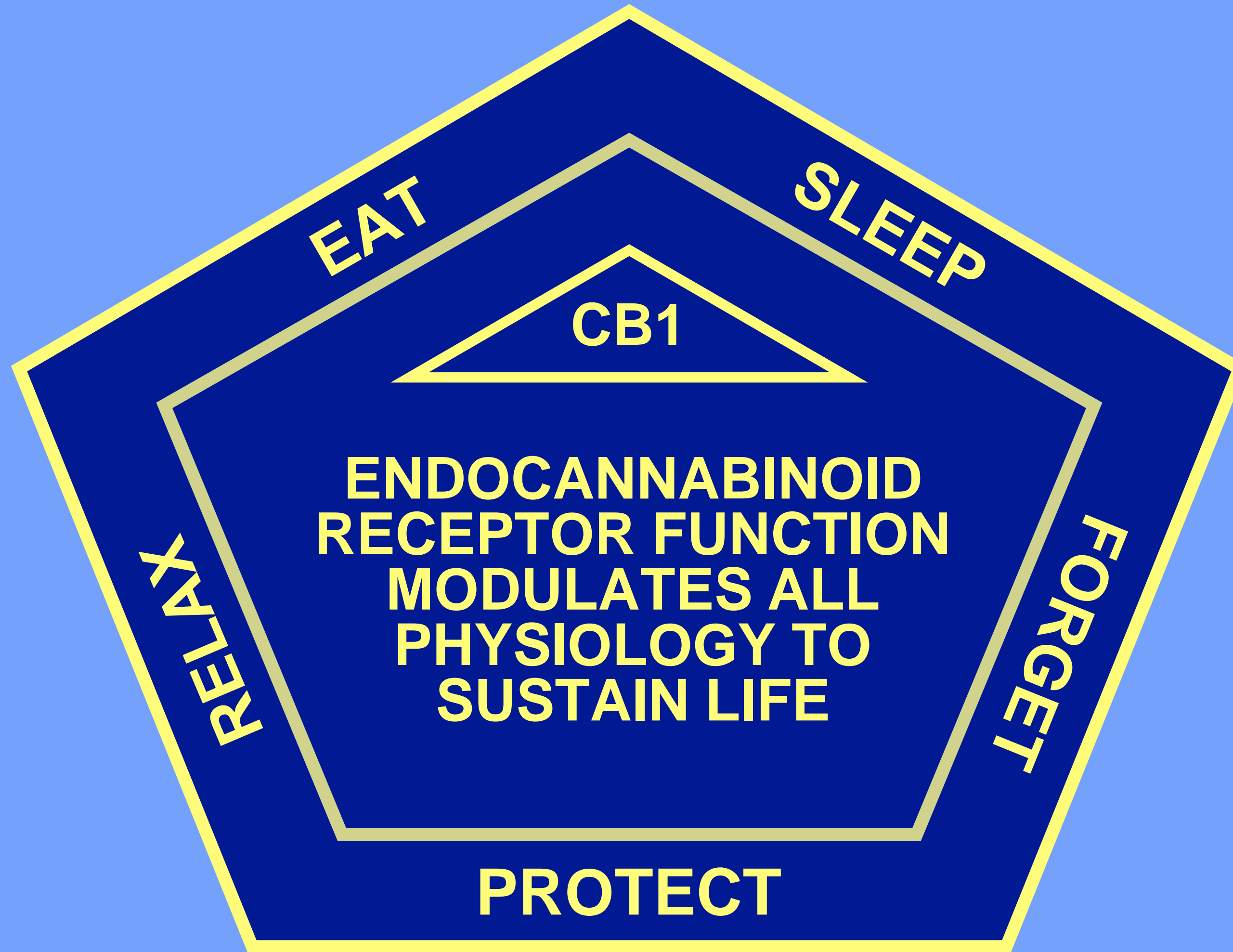
Memories are selectively filtered by cannabinoids.



CB1: FORGET



**CONCEPTION**



**DEATH**



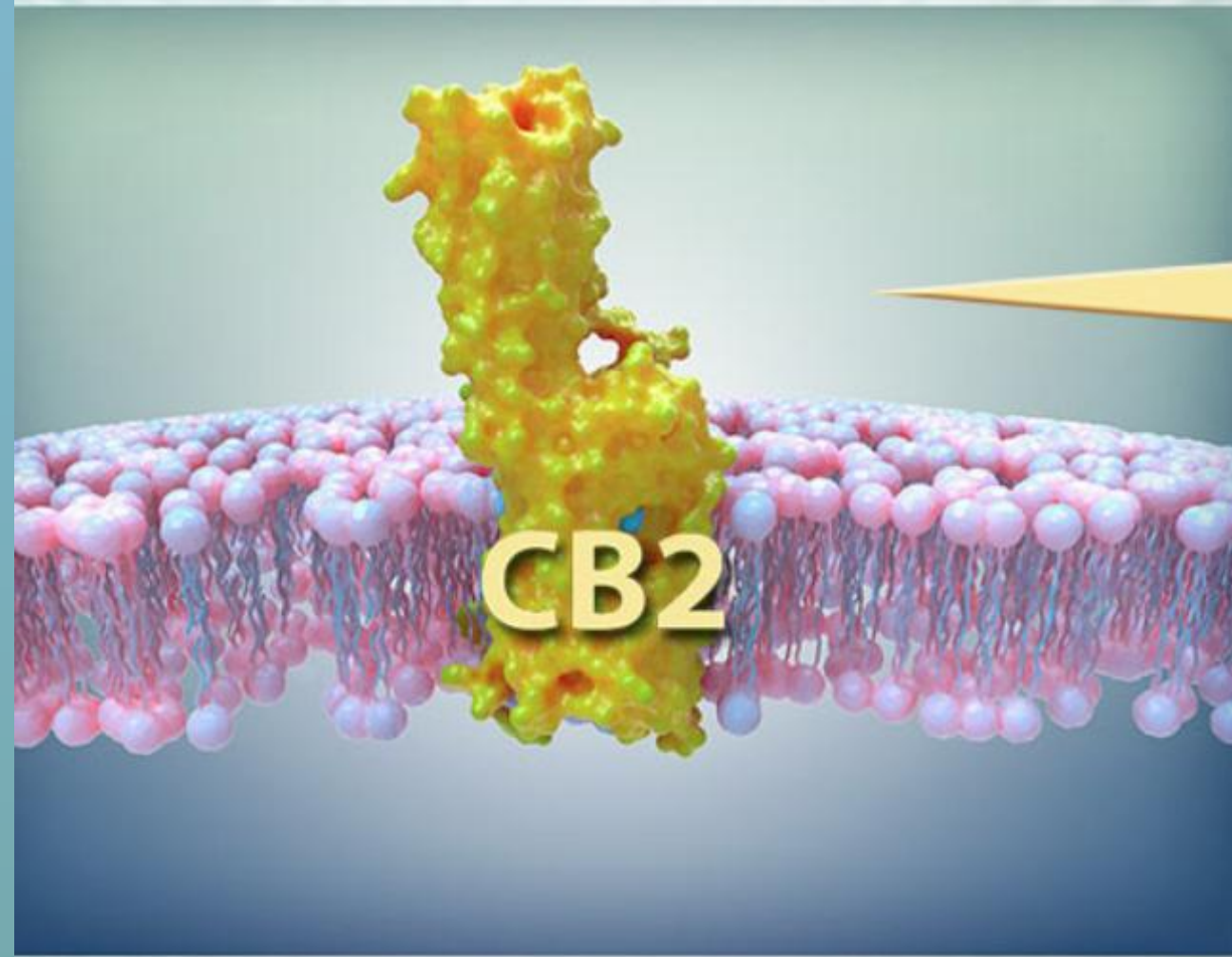
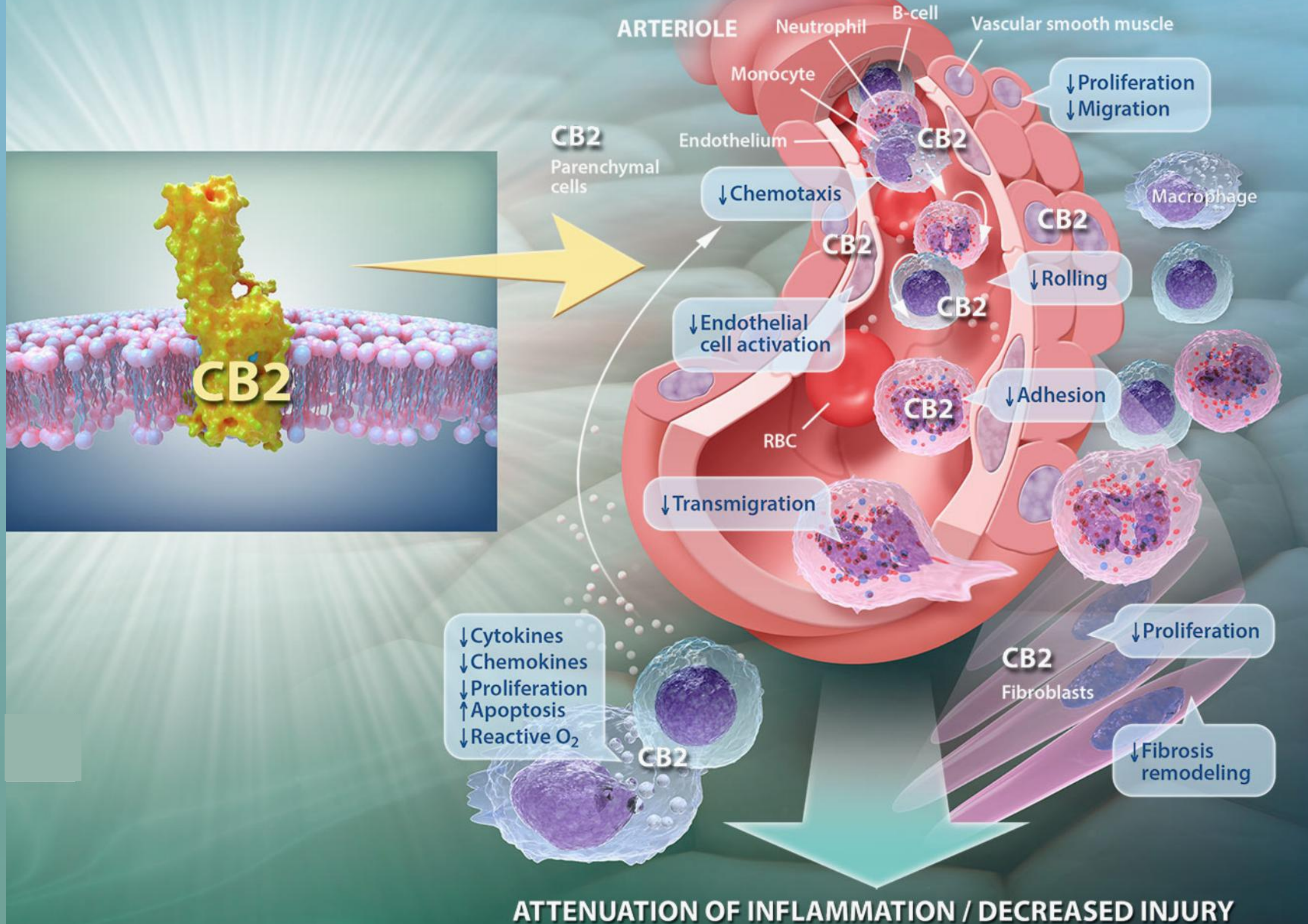
# CB2: PROTECT



**Cannabinoids respond to mitigate the progression of disease.**



# Inflammation & Tissue Injury



*In Vivo* PET Scan  
Ahmad, et al  
2013 AD

Cannabinoid  
Receptor (CB2)  
Locations

Acupuncture  
Point  
Locations

灸取穴参考



Western Medicine's New Science Future Meets Eastern Medicine's Traditional Past

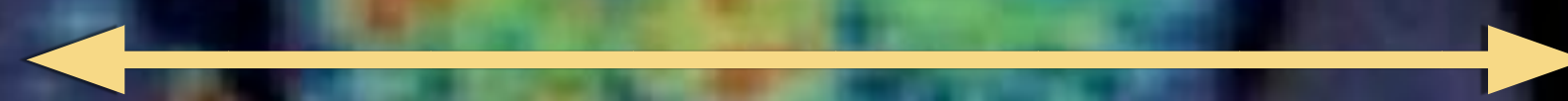
# INTEGRATIVE MEDICINE

“Health”

“Qi”

Immunity ↔ Life

Flow  
↔  
Life





Take home  
message....

A temptation's indulgence offers choices....  
that caution us to be careful with what we wish  
for,  
because science & reason matter.

JSB 2014





Jeffrey S. Block, M.D.

[www.NurturingNature.com](http://www.NurturingNature.com)