



Cannabinoids 101

Matthew Hill, Ph.D.

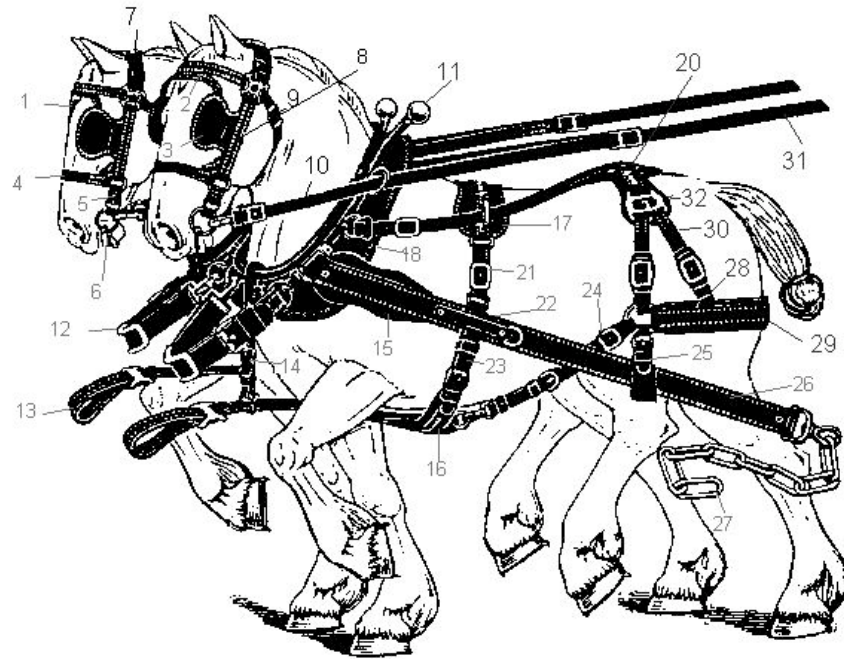
Hotchkiss Brain Institute

University of Calgary



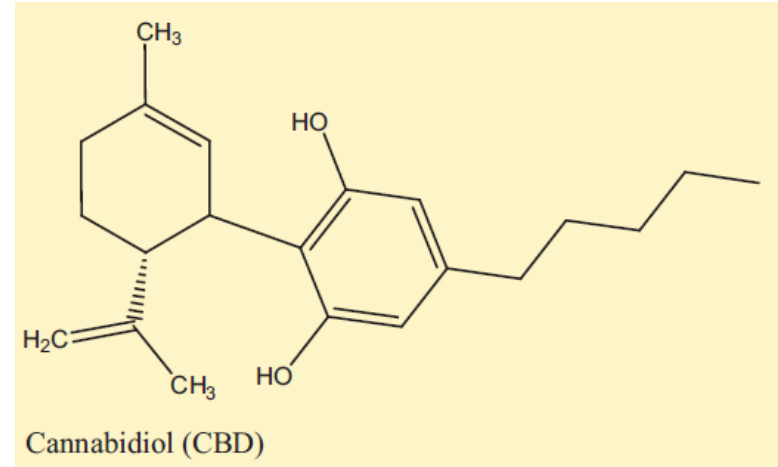
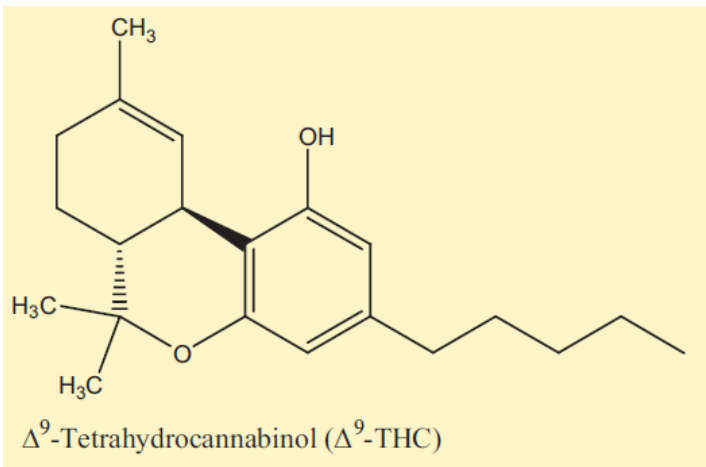
Defining the cannabinoid system

- Exogenous compounds
 - Phytocannabinoids
 - THC, CBD, combinations
 - Synthetic cannabinoids
 - Nabilone, dronabinol
 - K2, “spice”
- Endogenous cannabinoids
 - Anandamide
 - 2-arachidonyl glycerol
- Receptor targets
 - CB1, CB2



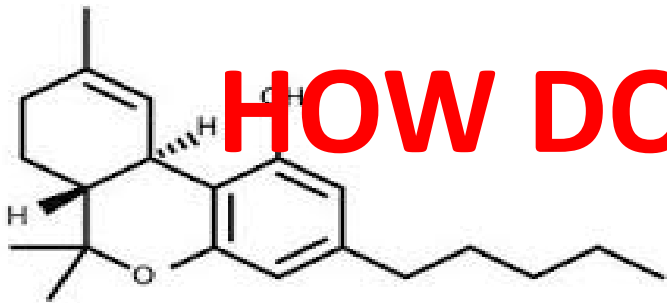
Targets of Phytocannabinoids

- The two main cannabinoids in cannabis that are studied are:
- THC
- CBD (cannabidiol)

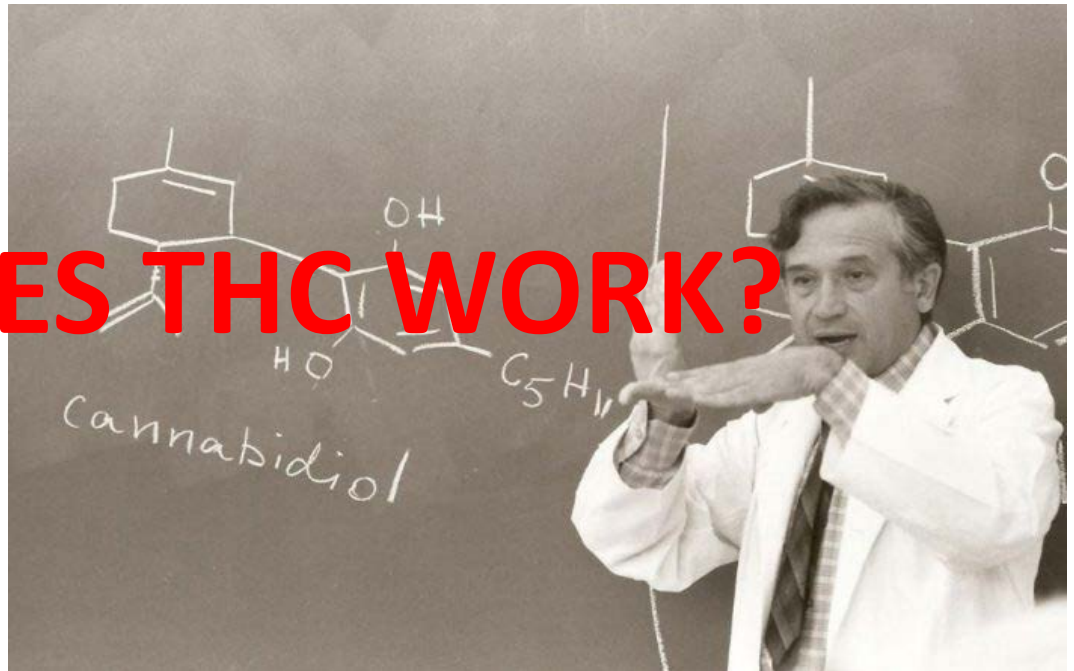


THC

- Discovery of THC as the psychoactive component of cannabis
- April 20, 1964
- Raphael Mechoulam (Hebrew University)

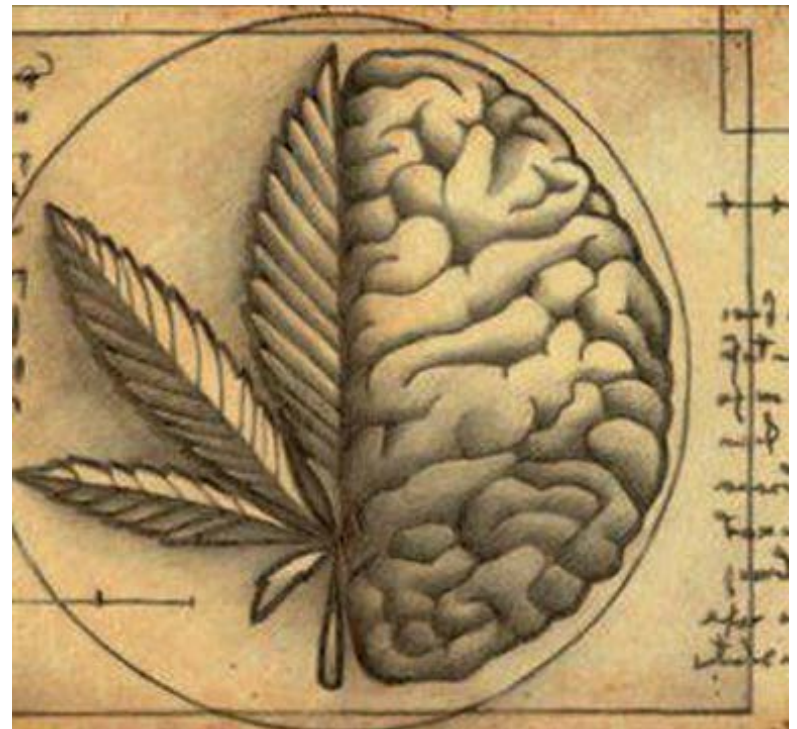


HOW DOES THC WORK?



Cannabis and the Endocannabinoid System

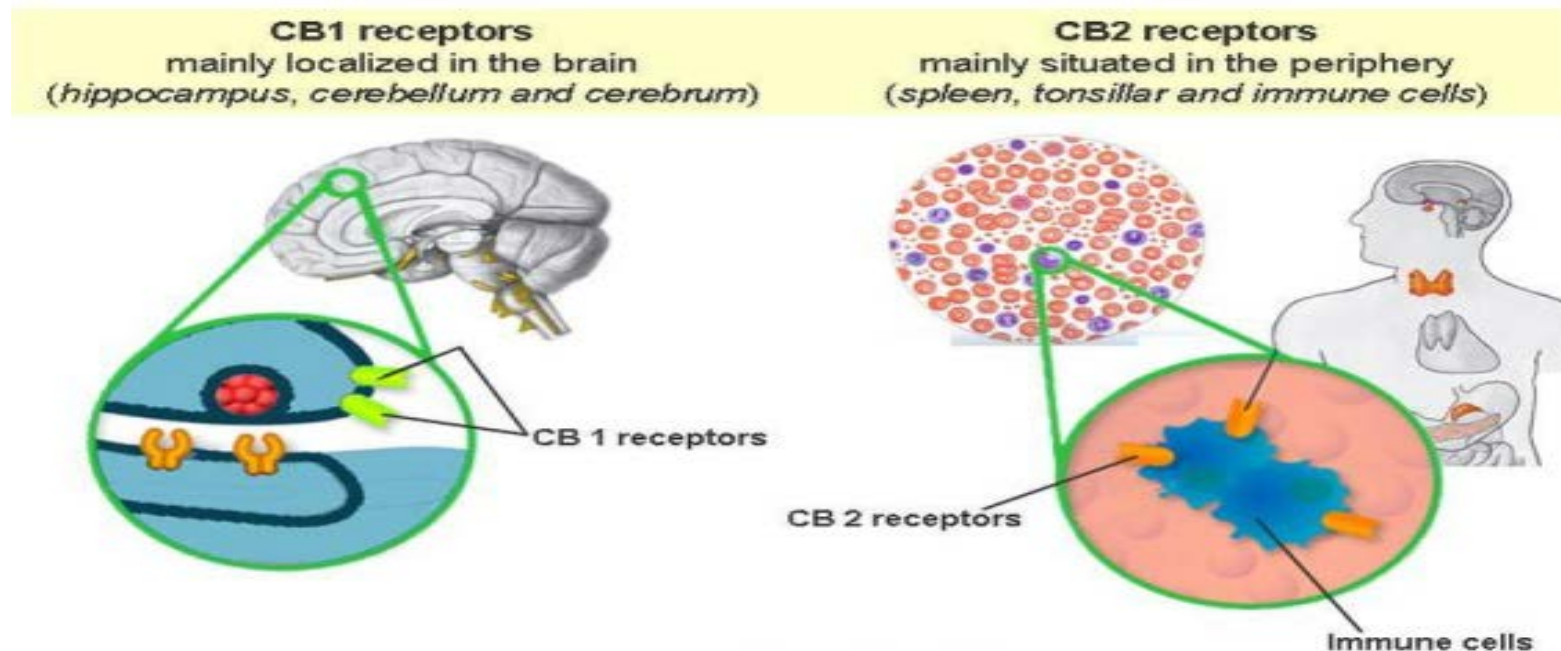
- THC, the psychoactive constituent of cannabis, exerts its effects on the brain and body through activation of the endocannabinoid system



Cannabis and the Endocannabinoid System

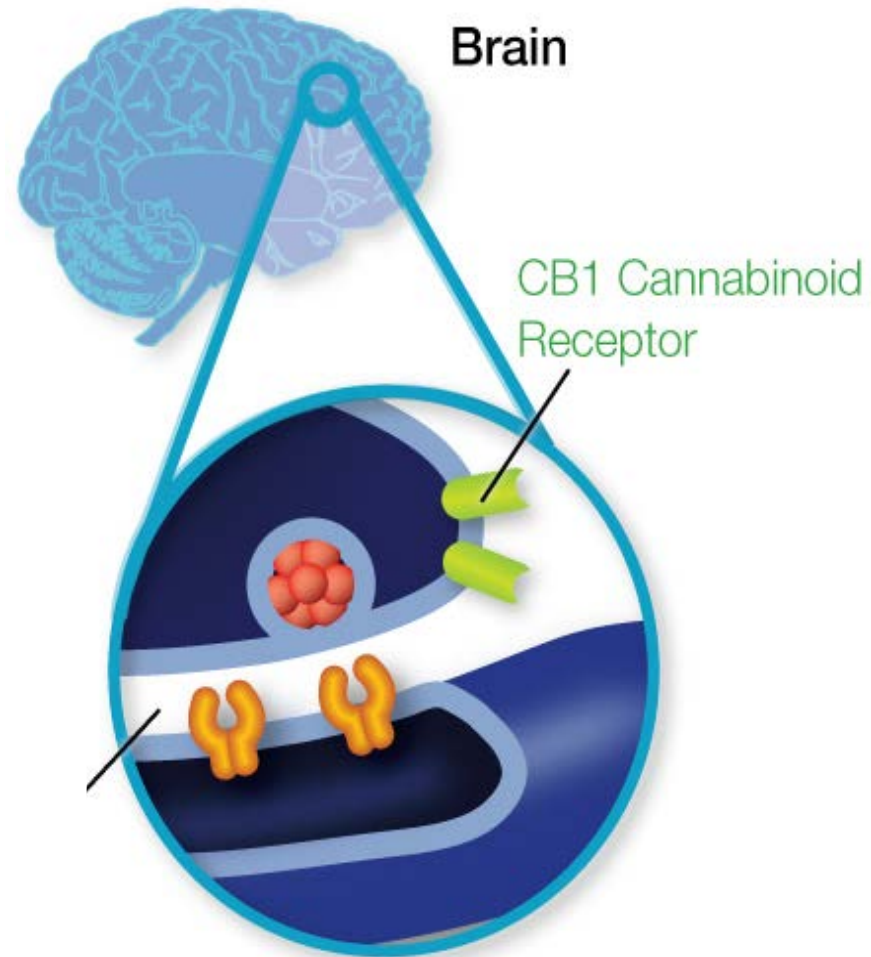
- THC binds to the same receptors that endocannabinoids exert their physiological effects through.
 - CB1 receptors (in the brain)
 - CB2 receptors (in immune cells)

Mode of action



Cannabinoids 101

- Cannabinoids act at CB₁ receptors to inhibit neurotransmitter release

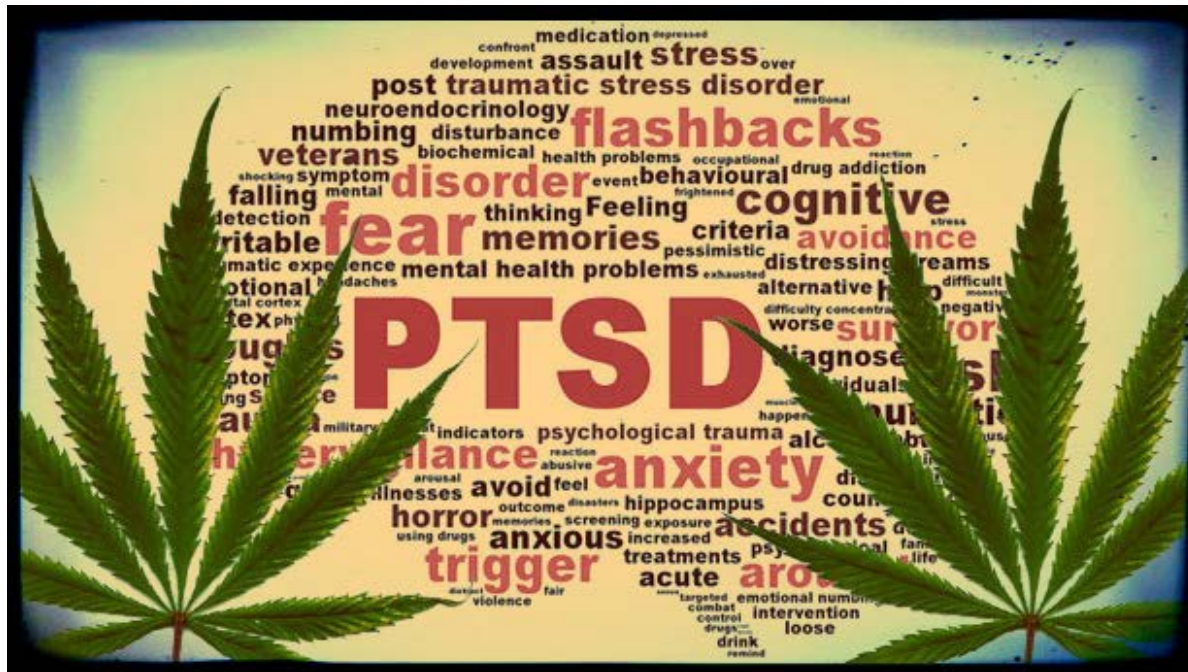


Cannabis and the Endocannabinoid System

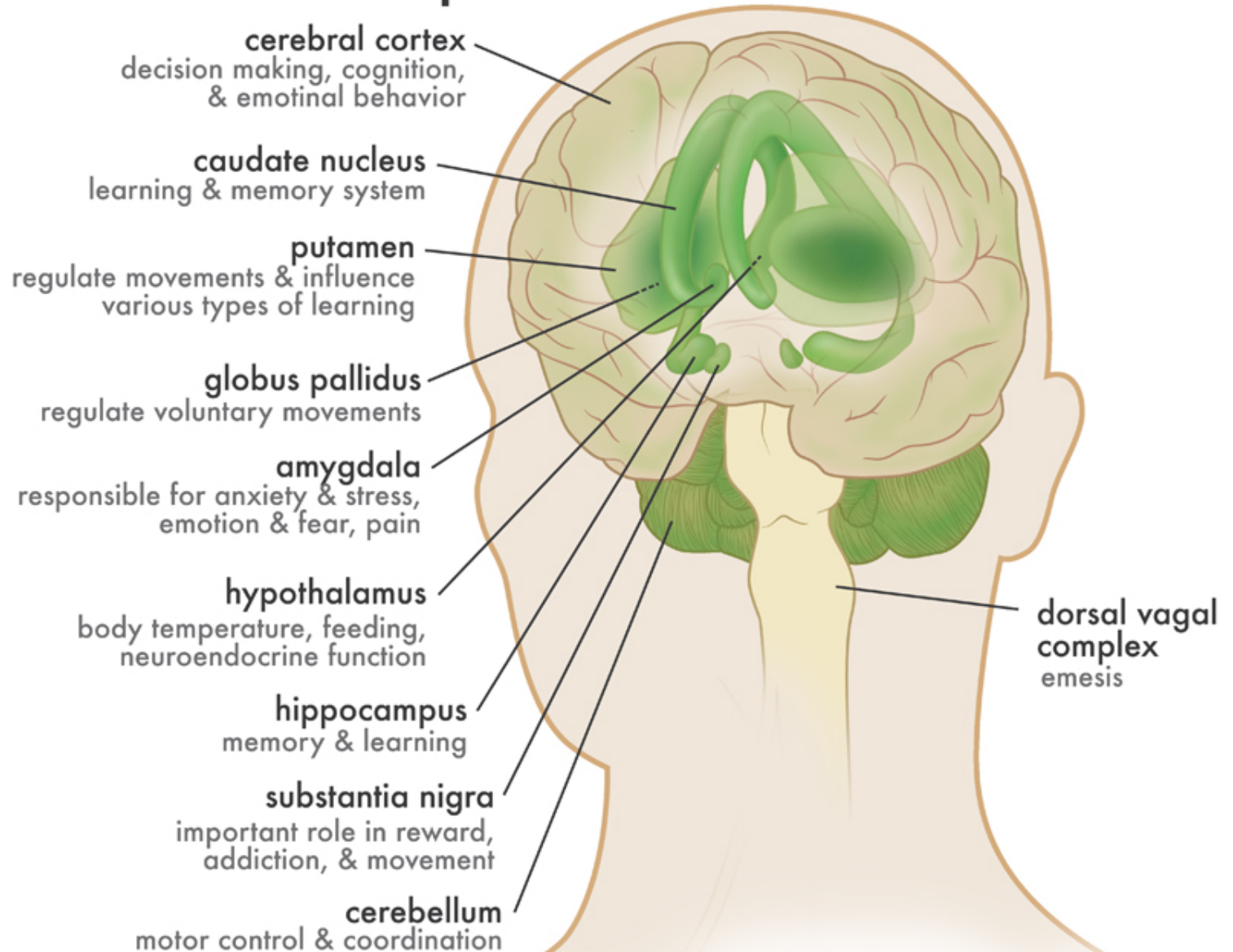


Cannabinoids and Anxiety

- Endocannabinoids naturally act to promote recovery from stress, reduce anxiety and dampen the rumination of emotionally aversive memories.
- Cannabis use in PTSD may be an attempt to compensate for an endocannabinoid deficit



Distribution of CB1 receptors



CB1 Receptors – Its Complicated

PANCREAS



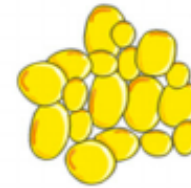
- Insulin release and signaling
- β -cell function

LIVER



- Lipid storage
- Insulin sensitivity

ADIPOSE TISSUE

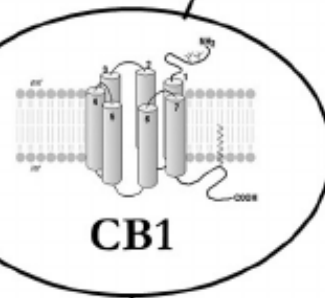


- Glucose uptake
- Insulin sensitivity
- Adipogenesis

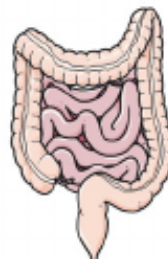
MUSCLE



- Glucose uptake
- Insulin sensitivity



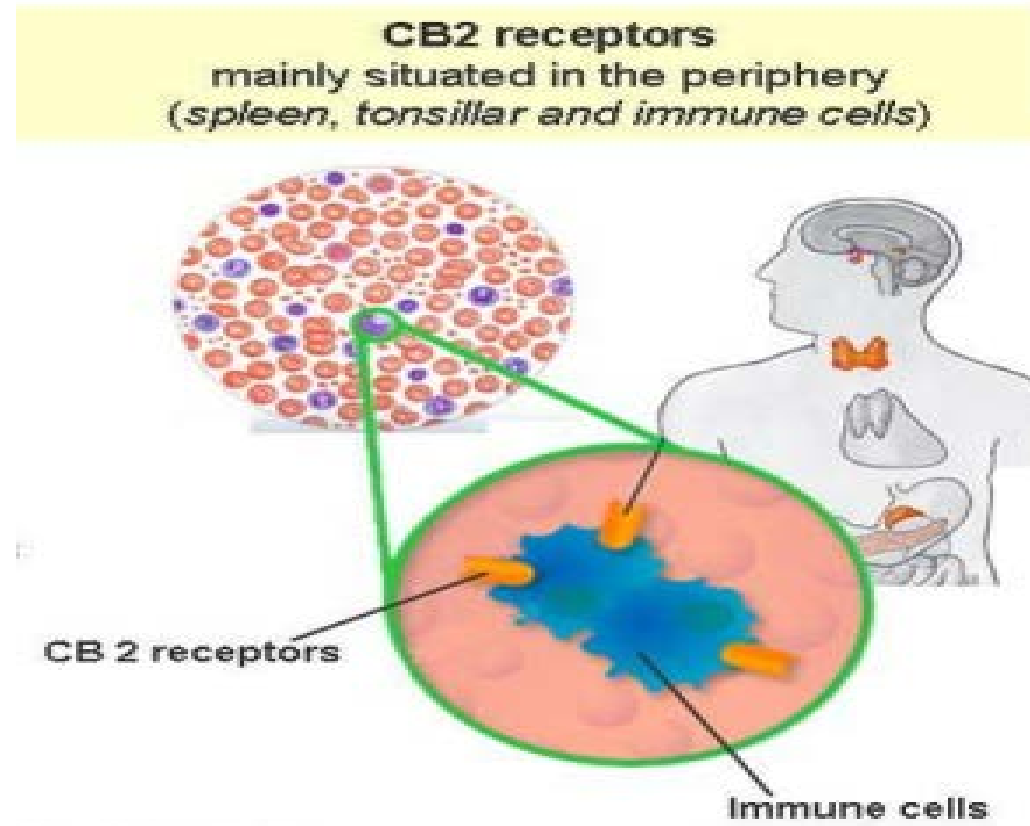
GASTROINTESTINAL TRACT AND GUT MICROBIOTA



- Gut barrier function
- Gut permeability
- Metabolic endotoxemia

Lets Not Forget About CB₂!

- Cannabinoid type 2 receptor (**CB₂**)
 - Primarily found in immune cells
 - Acts to suppress release of pro-inflammatory molecules
 - Doesn't seem to do much to normal immune system but reduces hyperactivity



Cannabidiol



- CBD has an unclear mechanism, but does NOT bind to CB₁ or CB₂ receptors.
- CBD has been shown to:
 - Inhibit Adenosine uptake
 - Interact with Serotonin receptors
- Anti-epileptic, Anti-inflammatory, Anxiolytic

What do we know about how cannabis effects the brain?

- Two forms of studies:
 - 1) Human epidemiological:
 - often poorly controlled between groups
 - cannot capture pre-existing differences
 - 2) Animal studies:
 - dosing and route of administration not reflective of reality
 - study components of cannabis in isolation as opposed to whole plant

What do we know about how cannabis effects the brain?

- What we need to do:
 - 1) **Human studies:**
 - longitudinal, within subject (ABCD study)
 - 2) **Animal studies:**
 - model route of administration (inhalation)
 - examine impact of whole cannabis or oils, not discrete components

What do we know about how cannabis effects the brain?

- Should we be worried....

