Actions of cannabinoids on amoebae

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Endocannabinoids, e.g. Anadamide (AEA), are lipid compounds which together with their receptors (CB1, CB2), and the enzymes that metabolise them, form the human endocannabinoid system (ECS); affecting mood, cognition, appetite, pain, memory etc. Similar effects are activated by cannabis due to Δ9-tetrahydrocannabidiol (THC, psychoactive) and cannabidiol (CBD, non-psychoactive) receptor-binding. However, many of their effects cannot be attributed solely to CB1/CB2 binding and another 63 molecular targets have been proposed to play a role. Single-celled eukaryotes do not possess these cannabinoid receptors, or many of the 63 'alternative targets', yet they respond to cannabinoids. They offer an opportunity to examine the validity/importance of these 'alternative targets' with regards to the evolution of the human ECS. This knowledge would also increase the potential therapeutic use of CBD.

CBD and AEA were tested on 27 amoebae by comparing population density after 3 days growth to a control. Thirteen strains were negatively affected; 11 by both and 2 by CBD only. There was no taxonomic trend in susceptibility. The first 'alternative target' tested was the Peroxisome Proliferator-Activated Receptors (PPARs); nuclear receptor proteins divided into three types (α, β and γ). Blocking these receptors with commercial antagonists showed that when the PPARα receptor was blocked, the negative effect of CBD (but not AEA) on *V. vermiformis* population growth was reduced in a dose-dependent manner (in 5 out of 7 strains). CBD induced lower feeding rates in *V. vermiformis* and this was abolished by blocking the PPARα receptor with 10μM antagonist. Testing *V. vermiformis* with natural agonists for PPARα (Oleoylethanolamine, Palmitoylethanolamide) showed a similar response to CBD, i.e. lower growth and feeding in their presence which was abolished by blocking the PPARα receptor. PPARs have yet to be identified in protists, hence a target for CBD in *V. vermiformis* is considered to be a 'PPARα-like' receptor.