

*The Cannabis Papers:
A citizen's guide to cannabinoids (2011)
By Publius Essay #33*

CB3 it is! – reproducing revolutions

Cannabinoids and a newly discovered receptor

We've been researching, writing and publishing this collection of essays for about six years. While learning about CB1 and CB2 receptors, we noticed that many researchers were hypothesizing a third receptor – **a CB3 receptor**. Then in the last month of work, in June 2011, this article appeared on PubMed: *Modulation of the novel cannabinoid receptor – GPR55 – during rat fetoplacental development*.

That's the research reporting discovery of the elusive CB3, referred to as *GPR55*. That will add clarity and open up new hypotheses concerning cannabinoids.

Cultures advance much like science. Suddenly a hypothesis is made real. Born is a word used in such moments. It has been said the founders delivered a nation. It has also been said founders are delivered by their mothers.

This essay focuses on the cannabinoid receptor's role in reproduction by highlighting a bit of research for each receptor. We've also taken the liberty of pairing Jay, Hamilton and Madison with a receptor.

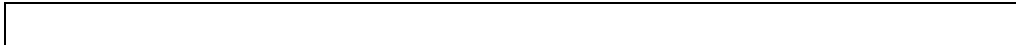
CB1

John Jay, revolutionary and First Chief Justice of the US Supreme Court

The effect of ovarian hormones on the synthesis of anandamide depends on different physiological conditions, oestrous cycle and early pregnancy, and on the presence of the activated blastocyst. Thus, ovarian hormones, as signals that emanate from the mother, operate in conjunction with the blastocyst intrinsic programme, regulating the synthesis of anandamide in a specific manner during crucial reproductive events that may compromise pregnancy outcome.

Reproductive Biomedicine 2009

Cannabis is the primary focus of the war on drugs. Nearly half of all US drug arrests are for cannabis. That translates into 800,000 citizens arrested by law enforcement for modulating their receptors. The federal government has many constitutional powers, as *Publius 1787-88* detailed in *The Federalist Papers*. Policing biological receptors involved in all aspects of human life is not one of the powers enumerated.



CB2

Alexander Hamilton, revolutionary and First Secretary of the US Treasury

This review will focus on the involvement of type-2 cannabinoid (CB2) receptors in reproductive biology, covering both the male and female sides. It will also discuss the potential relevance of the immunological activity of CB2 at the maternal/foetal interface, as well as the distinctiveness of CB2 versus type-1 cannabinoid (CB1) receptors that might be exploited for a receptor subtype-specific regulation of fertility. In this context, the different signalling pathways triggered by CB1 and CB2 (especially those controlling the intracellular tone of nitric oxide), the different activation of CB1 and CB2 by endogenous agonists (like anandamide and 2-arachidonoylglycerol) and the different localization of CB1 and CB2 within membrane subdomains, termed “lipid rafts,” will be discussed. It is hoped that CB2-dependent endocannabinoid signalling might become a useful target for correcting infertility, in both men and women.

British Journal of Pharmacology 2008

The drug war allows authorities to monitor our past cannabis use and prevent future use. If herbal cannabis use climbs, prohibitionists need more money for the drug war. If use falls, they need more money to keep up the fight. That is a politically cynical Catch-22 masquerading as social policy.

CB3

James Madison, revolutionary and POTUS 4

Together with the endogenous cannabinoids (ECs) and the respective metabolizing-enzymes, the cannabinoid receptors complete the endocannabinoid system (ECS).

Two cannabinoid receptors have been described so far, CB1 and CB2, though a third has been suggested, CB3. In order to investigate the expression of GPR55, referred as **the novel cannabinoid receptor 3 (CB3)**, in the uterine maternal tissues during normal pregnancy we analyzed its expression by Q-PCR, Western blot and immunohistochemistry during fetoplacental period. **GPR55** was found in uterine natural killer (uNK) cells pointing to an involvement in the immunological reactions that occur during pregnancy. The prominent expression of **GPR55** in decidual cells suggests a role in mediating cannabinoid signaling during fetoplacental development. The data presented here may clarify the role of GPR55 in fetoplacental development and highlights the presence of **a new target for cannabinoid signaling during pregnancy**.

Placenta 2011

Despite 70 years of cannabis prohibition, we can still note that cannabis has improved human lives more substantially than cannabis laws have repressed human freedom – and we can take that to be a good sign of things to come. Despite the best efforts of prohibitionists, the CS is going to win this war. No surprise though – like the CS, this plant is resilient in ways we don't even comprehend yet.

Publius
(2011)

Search terms

GPR55; Cannabinoid receptors; CS and reproduction, pregnancy and blastocyst; Publius 1787-88; John Jay; Alexander Hamilton; James Madison.

Research and selected readings

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