

Endocannabinoid Anandamide: A Bioactive Lipid and Novel Regulator of Angiogenesis & Neurogenesis

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We have recently showed that endogenous cannabinoid anandamide and its metabolically stable analog methanandamide activate endothelial nitric oxide synthase (eNOS) to produce nitric oxide acting on a Gi-coupled, endothelial non-CB₁/CB₂ putative "anandamide receptor". Using *in vitro*, *ex vivo* and *in vivo* models of angiogenesis we have found that in endothelial cells methanandamide acting on non-CB₁/CB₂ putative "anandamide receptor" produced pro-angiogenic responses but methanandamide-mediated activation of CB₁ receptors produced anti-angiogenic responses. More recently using GFP expressing transgenic zebrafish (Fli-1) we have found that knock down of zCB₁ receptor produced alteration in the capillary formation in 74 hpf morphant embryos. In a related study we have also found that anandamide can regulate developmental and adult neurogenesis under physiological and pathophysiological condition. Taken together, results from these studies suggest that endogenous cannabinoid anandamide and its receptors (CB₁ and non-CB₁ anandamide receptors) regulate angiogenesis and neurogenesis and can be considered as a novel target for the therapeutic modulation angiogenesis and neurogenesis.