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The endocannabinoid anandamide inhibits colon cancer cell growth by modulating different survival and proliferating pathways

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The Endocannabinoid System (ECS) comprising the CB1 and CB2 receptors and their endogenous ligands is a central signalling system regulating food intake and energy balance. It is also present in peripheral tissues where it is involved in cell proliferation and survival. It has been shown that in colon cancer cells, the CB1 receptor antagonist SR171416 reduces colon cancer cell growth by acting as an inverse agonist rather than an antagonist [1]. Starting from this observation and from evidence indicating that some biological responses to cannabinoids depend on estrogen levels and some selective estrogen receptor modulators can bind the CB1 receptor [2], we aimed to study the effects of the CB1 receptor ligand anandamide (AEA) on colon cancer cell proliferation and its ability to modulate some survival and proliferating pathways including Akt, MAPK/ERK and estrogen receptor (ER) b signalling which is the predominant ER pathway in colonic epithelium. We used an AEA-analogue and a selective inhibitor of fatty acid amide hydrolase (FAAH) that enhances intracellular levels of AEA and studied proliferation and cell cycle progression on human adenocarcinoma cells DLD1 and SW620. Our results showed that increased levels of AEA significantly reduced cell proliferation in both cell lines at 24 and 48 h also inducing an S phase cell cycle accumulation. The AEA-induced inhibition of cell growth was mediated by a reduced expression of phoshoAkt and phosphoERK and, at the same time, by an induction of ERβ expression. These data suggest that AEA can reduces colon cancer cell proliferation by interfering with different signalling pathways.

References

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Keywords
Endocannabinoid system, anandamide, colon cancer cells, Akt and MAPK/ERK pathways, oestrogen receptor β signaling