

**P023** The Endogenous Cannabinoid, Anandamide, Induces Cell Death in Colorectal Carcinoma Cells: Importance of Cyclooxygenase-2  
H.A.Patsos, D.J.Hicks, A.Greenhough, R.Dobson, A.C.Williams, C.Paraskeva

*Cancer Research UK Colorectal Tumour Biology Group,  
Department Pathology & Microbiology, University of Bristol,  
BS8 1TD, UK*

Cyclooxygenase-2 (COX-2) is important in the process of tumorigenesis and is up-regulated in most colorectal cancers. COX-2 can also metabolise the endogenous cannabinoid, anandamide, into prostaglandin-ethanolamides. Endogenous cannabinoids, including *N*-arachidonoyl ethanolamide (anandamide), have attracted considerable interest as novel anti-neoplastic agents. We investigated whether anandamide induced cell death in colorectal carcinoma (CRC) cells and whether the high levels of COX-2 in tumour cells could be utilized for their specific targeting for cell death by anandamide. Anandamide dose-dependently inhibited the growth of moderate (HT29) and high (HCA7/C29) COX-2 expressing CRC cell lines, but had little effect on the very low COX-2 expressing CRC cell line (SW480). Induction of cell death was partially rescued by the COX-2 selective inhibitor NS398. Furthermore, inhibition of fatty acid amide hydrolase (FAAH) potentiated the non-apoptotic cell death, indicating that anandamide-induced cell death was mediated via the metabolism of anandamide by COX-2, rather than its degradation into arachidonic acid and ethanolamine. Taken together these findings suggest anandamide may be a useful chemopreventive/therapeutic agent for colorectal cancer, since anandamide targets cells that are high expressors of COX-2, and may also be useful in eradication of tumour cells that have become resistant to apoptosis.