

**P027** Polyamine metabolism – a target for non-steroidal anti-inflammatory drugs in colorectal cancer cells?

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Non-steroidal anti-inflammatory drugs (NSAIDs) are known to prevent and cause regression of colorectal tumours in man. The classic action of NSAIDs is via inhibition of COX-1 and 2. However, there is an increasing body of evidence suggesting that the cytotoxic/chemopreventative actions are independent of COX inhibition. Our studies have focussed on the effects of NSAIDs on the polyamine metabolic pathway. Polyamines are endogenous growth factors in mammalian cells and their concentrations are increased significantly in colorectal tumours. In addition, increased ornithine decarboxylase activity and polyamine content has been shown to be essential for the transformation of cells. Thus inhibition of this pathway may result in the prevention or regression of tumours. In a variety of colorectal cancer cell lines we found that NSAIDs were cytotoxic and induced apoptosis. Concomitant with this there was a significant decrease in polyamine content. This response was independent of COX expression and toxicity could be reversed by the addition of exogenous polyamines. This implies that the polyamine pathway is a critical target in the cell death induced by NSAIDs in colorectal cancer cells.