P001 The role of the retinoblastoma protein (pRb) in the nuclear localisation of BAG-1: Implications for colorectal tumour cell survival.

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Although inactivated in a wide variety of human cancers, the retinoblastoma protein (pRb) has been shown to be over-expressed in colon carcinogenesis, linked to the cell survival function of the protein. However, the mechanisms by which pRb regulates apoptosis are still to be fully elucidated. We have established that the pRb interacts with the anti-apoptotic Bag-1 (Bcl-2 associated anathogene) protein, increasing its nuclear localisation. Interestingly, we have found that Bag-1 is predominantly nuclear in early colorectal adenomas, suggesting that nuclear Bag-1 may play a role in the development of colorectal cancer. However, little remains known about the function of nuclear Bag-1. We have established that maintenance of high nuclear BAG-1 increases the resistance of adenoma cells to γ-radiation induced apoptosis. Our work introduces a novel function for pRb, involving modulation of the subcellular localisation of BAG-1. We have found that nuclear BAG-1 is selected for in adenoma formation, and suggest that BAG-1 may promote colorectal tumour cell survival by making colonic epithelial cells less sensitive to DNA damage induced apoptosis.