Monoacylglycerol lipase is crucially involved in experimental colon carcinogenesis

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Background/Aim Colorectal cancer (CRC) is one of the most prevalent gastrointestinal malignancies in our country and worldwide (Siegel et al., 2015). The endocannabinoid 2-arachidonoyl-glycerol (2-AG) exerts antiproliferative actions in a number of tumoural cell lines, including colorectal cancer cells (Ligresti et al., 2003). Monoacylglycerol lipase (MAGL), a serine hydrolase which inactivates 2-AG, is highly expressed in aggressive human cancer cells (Nomura et al., 2010). Here, we investigated the role of MAGL in experimental colon carcinogenesis. **Methods** The *in vivo* role of MAGL was assessed using the xenograft and azoxymethane (AOM) models of colon carcinogenesis (Borrelli et al., 2014). MAGL expression was evaluated by RT-PCR and immunohistochemistry; 2-AG levels by HPLC-MS; vascular endothelial growth factor (VEGF) was quantified by RT-PCR ad western blot; FGF-2 (basic fibroblast growth factor) by western blot; cyclin D1 was quantified by RT-PCR; vessels were counted using immunostaining and immunofluorescence analyses. **Results** MAGL and 2-AG were abundantly detected in tumoural tissues. The MAGL inhibitor URB602 (5 mg/kg, IP) reduced tumour volume generated by xenograft injection of colorectal cancer cells in nude mice. The curative effect was associated to down-regulation of angiogenic factors (i.e. VEGF and FGF-2) and reduction in the number of vessels in the tumoural area. Also URB602 exhibited a pronounced reduction in cell proliferation resulting in down-regulation of Cyclin D1. In the experiments aiming at investigating the role of MAGL in chemoprevention, URB602 attenuated AOM-induced preneoplastic lesions, polyps and tumours in wild type, but not in MAGL-deficient mice. **Conclusions** MAGL, possibly through modulation of cell proliferation and angiogenesis, plays a key role in experimental colon carcinogenesis. Pharmacological inhibition of MAGL could represent an innovative therapeutic approach in colorectal cancer prevention and/or cure.

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