Expression and secretion of factors involved in angiogenesis and invasion was assessed by quantitative PCR and ELISA.
Results and discussions The melanoma cells showed a preference for growth in the meninges and ventricles after intracerebral injection, and intertumor heterogeneity in the aggressiveness of meningeal tumours reflected differences in angiogenic activity and expression of VEGF-A and interleukin 8 (IL-8). In contrast, growth and invasion of the brain parenchyma relied primarily on vascular co-option. The response to bevacizumab treatment depended on the angiogenic signature of the tumour cells and on the intracranial growth site. Bevacizumab treatment resulted in delayed meningeal tumour growth and prolonged survival in cell lines showing high VEGF-A expression and high angiogenic activity in the meninges, whereas no difference in survival was observed between bevacizumab-treated and vehicle-treated mice in cell lines showing low VEGF-A expression and lower angiogenic activity in the meninges.
Conclusion The melanoma cell lines showed different response to bevacizumab treatment, and these differences reflected differences in intracranial vascularisation patterns and in expression of VEGF-A.

PO-316 ISOQUERCETIN: A NOVEL AGENT TO INCREASES VASH1 AND SUPPRESS COLON CANCER

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Introduction Angiogenesis represents an important factor supporting the growth and propagation of many tumours; however, current antiangiogenesis agents exhibit limited efficacy or elevated adverse effects. As natural plant-based products with numerous beneficial physiologic effects, flavonoids represent attractive alternatives as cancer therapeutics. To the best of our knowledge, this study represents the first demonstration that the flavonoid isoquercetin (Q3G) functions as a novel inhibitor of angiogenesis in colorectal cancer by targeting vasohinibin 1 (VASH1). Vasohibin-1 (VASH1) is an endogenous angiogenesis inhibitor. However, the clinical relevance of VASH1 in colon cancer and its regulations on cancer angiogenesis and cancer cell biological characteristics are still unknown. The aim of this study was to evaluate the flavonoid isoquercetin (Q3G) as a novel VASH1-targeted inhibitor of angiogenesis in colorectal cancer.
Material and methods Balb-c nude mice were implanted with human colon adenocarcinoma HT-29 cells. The tumour volume was monitored daily. Following euthanasia, tumours were subjected to histological analysis (histologic grade, microvessel count) and immunohistochemical determination of VASH1 expression. Statistical analysis of the data (ANOVA and polynomial regression) adopted a 5% significance level.
Results and discussions We identified that acute but not prophylactic administration of Q3G in a mouse xenotransplant tumour model Q3G increased VASH1 expression, decreased vascular proliferation, and inhibited tumour growth. Our studies suggest that Q3G therefore represents a vascular disrupting agent, inhibiting tumour growth by limiting tumour blood supply and neovascularization through the upregulation of the angiogenesis inhibitory factor, VASH1.
Conclusion Thus, Q3G targeting of VASH1 expression may serve as a novel antiangiogenesis strategy for treating colorectal cancer.

PO-317 A NOVEL BISPECIFIC ANTIBODY TO HARNESS THE HERG1-β1 MACROMOLECULAR COMPLEX FOR CANCER THERAPY.

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Introduction Among hindrances in cancer treatment, the lack of appropriate markers to be exploited for targeted therapy, and the need of new potential drugs are two big challenges. hERG1 potassium channels area novel class of oncological targets and one of the most intriguing aspects of their involvement in tumour establishment and progression is the interaction with adhesion molecules, such as integrins. It has been recently demonstrated that macromolecular complexes formed between hERG1 and β1 integrins selectively occurs in many types of cancer (Becchetti A et al., 2017). In this scenario, hERG1 could be exploited as a therapeutic target providing non cardiotoxic strategies aimed at blocking hERG1.
Material and methods A scDb, a bifunctional single-chain diabody, directed against hERG1/β1 complex, was developed via SOE-PCR methodology. Such antibody was tested on HCT116 cells in lateral motility and western blotting experiments. Moreover immunohistochemistry (IHC) was performed on metastatic colorectal cancer (mCRC) paraffin embedded samples using the scDb, an anti-hERG1 and an anti-b1 integrin.
Results and discussions Performing IHC on sequential sections of mCRC confirmed the specificity of the scDb for both hERG1 and b1 integrin. *In vitro* data provide evidences that the administering of the bispecific antibody has an impact on lateral motility. Moreover, signalling pathways are also affected by the antibody treatment, as AKT phosphorylation and HIF1α levels are decreased when the molecule is administered.Such findings might suggest a possible effect of the bispecific antibody on the VEGF-A signalling pathway, which are consistent with our previous hypothesis (Becchetti A et al., 2017) of a possible cross-talk leading to a deep impact on VEGF expression and, thus, on neoangiogenesis.
Conclusion scDb-hERG1/β1 could be used as a potential new treatment for cancer patients and as an early molecular diagnostic marker. In fact, the selective expression of hERG1/β1 complex in cancer cells and its role in angiogenesis and cancer progression suggests that a molecule selectively targeting the complex will be an invaluable tool for cancer treatment.

PO-318 INTESTINE-SPECIFIC HOMEOBOX GENE ISX INTEGRATES IL6 SIGNALING, TRYPTOPHAN CATABOLISM, AND IMMUNE SUPPRESSION

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