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Dissertations-Kurzfassung

Ms4a8a overexpression inhibits tumor growth of CT26 colon carcinoma cells in vivo

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Ms4a8a is a novel member of the MS4A gene family first identified in murine tumor associated macrophages. The MS4A protein family includes CD20, high affinity IgE receptor β chain (FcεRIβ), and at least 14 other members that are characterized by four membrane-spanning domains, two extracellular domains and two cytoplasmic regions. Most MS4A family members have been found to be expressed in hematopoietic cells and are discussed to be involved in intracellular regulatory processes via ion channel activity.

To analyze Ms4a8a expression in the mouse, a rabbit polyclonal serum against the cytoplasmic domain of the protein was generated. Immunohistochemical analysis identified Ms4a8a positive macrophage-like cells in the lung, on tubular structures in the kidney and in enterocytes at the top of the villi in the large intestine.

To analyze the function of MS4a8a in intestinal epithelial cells, the colon carcinoma cell line CT26 was transfected with a vector harbouring recombinant Ms4a8a cDNA under the control of the EF1 promoter. In comparison to control cells, the proliferation rate of Ms48a transgenic CT26 cells assayed by H3-thymidine incorporation was significantly reduced. In contrast, after transplantation into Balb/c wild type mice, MS4a8a positive CT26 clones reached a higher tumor-end-weight than the non-transfected clones, despite the lower *in vitro* proliferation rate.

To identify Ms4a8a-dependent gene expression, two transgenic and two control CT26 clones were evaluated by Affymetrix mouse genome 430 2.0 DNA arrays. After independent confirmation by real time RT-PCR, keratin 20 was identified as the most significant Ms4a8a target gene in CT26 cells. Keratin 20 is an intermediate protein of the keratin family.

In conclusion, Ms4a8a was characterized as a member of the MS4A family, which is expressed in enterocytes *in vivo* and regulates keratin 20 gene expression *in vitro*. A reduced proliferation rate of Ms4a8a transgenic CT26 colon carcinoma cells *in vitro* is mirrored by increased tumor growth *in vivo*. Further characterization of Ms4a8a CT26 tumor cells *in vivo* may help to identify Ms4a8a-mediated mechanisms that support tumor growth *in vivo*.