Olfm3-3 - a Novel Mediator of Angiogenesis

A growing number of cancer therapeutics function by inhibiting tumor angiogenesis. Targeting the vascular endothelial growth factor (VEGF) has resulted in several commercially successful therapeutics since the VEGF receptor is expressed almost exclusively on endothelial cells, which are key players in angiogenesis. However, VEGF targeting therapies have limited long-term benefits and some patients develop resistance to the therapy. Resistance is due to various mechanisms, including up-regulation of alternative pro-angiogenic signaling pathways, increased and tight pericyte coverage of newly formed vessels making blocking access of VEGF-targeting therapeutics to endothelial cells. Furthermore, upon cessation of VEGF therapy, pericytes remain present in the tumor microenvironment and provide a scaffold for rapid revascularization of the tumors.

Prof. Beat Imhof and his team at the University of Geneva have developed a strategy to inhibit tumor growth by targeting Olfactomedin-like 3 (Olfml3), a molecule that has been found to promote angiogenesis by signaling to both endothelial cells and pericytes. Olfml3 is a novel proangiogenic factor that is produced by activated tumor endothelial cells and accompanying pericytes. They have found that blockade of Olfml3 by anti-Olfml3 antibodies is highly effective in reducing tumor growth by blocking blood vessel formation and their stabilization by pericyte coverage. In vitro, Olfml3 targeting is sufficient to inhibit endothelioma cell migration and sprouting. Olfml3 alone or through binding to BMP4 enhances the SMAD signaling pathway required for BMP4-induced angiogenesis. Therefore, Olfml3 blockade provides multiple levels for controlling tumor growth by targeting two distinct cell types within the tumor microenvironment.

Development stage

- Proof of concept in tumor animal studies using siRNA and polyclonal antibodies (see images)
- Isolated rat monoclonal antibodies to human Olfml3 are being characterized

Advantages

- Defined Mechanism of Action
- Enhanced targeting in the tumor microenvironment with strategy to reduce development of resistance

Intellectual Property

World-wide intellectual property protection for this technology:

Available for licensing or partnering

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