CD93 protein suggests new strategy to inhibit cancer

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One strategy for cancer therapy is to inhibit the development of blood vessels in the tumour. Researchers at Uppsala University show in a new study how the protein CD93 interacts with the protein network that is required for tumour vessels to form properly. Blocking this interaction could be used as a means to hamper blood vessel development and slow down the cancer. The study is published by Journal of Clinical Investigations.

Blood vessels in tumours have a different molecular composition as compared to normal vessels. This results in an abnormal function of the tumour vessels, which can affect how the tumour grows and responds to treatment. One way of improving cancer therapy could therefore be to inhibit the formation of the malfunctioning blood vessels in the tumour. To do this, more knowledge is required about the components involved in the process when the tumour vessels are formed.

Anna Dimberg's research group at the Department of Immunology, Genetics and Pathology has studied how the protein CD93, which is produced by blood vessels in many cancer types, including brain tumours, affects the formation of tumour vessels. The study, which has been published by Journal of Clinical Investigations, shows that CD93 has a central role in the formation of the extracellular matrix, i.e. the material outside of the cells in a tissue.

"We found that CD93 has a main role in organising the fibronectin network that surrounds the blood vessels. These are incredibly exciting

results since the extracellular matrix is important for well-functioning blood vessels and can also affects the function of many other cells in the tumour's microenvironment, including the cancer cells," says Roberta Lugano who is a postdoc in the group and has been responsible for the study.

The fibronectin network is needed for the newly formed blood vessels to mature into functioning, stable vessels. In animal models of brain tumours where CD93 was lacking in the blood vessels, the researchers saw that no fibronectin network was formed around the newly formed vessels. This was associated with a reduced capacity to transport blood and an increased permeability to fluid and plasma proteins.

The researchers have also characterised how CD93 and the fibronectin network are related at the molecular level. CD93 is located in the cells of the blood vessel walls where it binds to fibronectin via interaction with the protein MMRN2. The CD93/MMRN2 complex is needed to reorganise soluble fibronectin into a network of fibres. It also appears that this mechanism is especially important for the tumour blood vessels.

"Our results suggest that one could inhibit blood vessel development in tumours by preventing the interaction between CD93 and MMRN2. That could lead to defectively functioning tumour vessels and slow down cancer development. This is something that we plan to test in our future studies," says Anna Dimberg, researcher at Department of Immunology, Genetics and Pathology at Uppsala University.

More information: Roberta Lugano et al. CD93 promotes integrin-β1 activation and fibronectin fibrillogenesis during tumor angiogenesis, *Journal of Clinical Investigation* (2018). DOI: 10.1172/JCI97459

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