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Therapeutic and diagnostic antibodies to CD146: Thirty years of research on its potential for detection and treatment of tumors and discovery of new pathways

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CD146 (MCAM, MUC18, S-Endo1) is a transmembrane glycoprotein belonging to both CAM and mucin families. It exists as different splice variants and is cleaved from the membrane by metalloproteases to generate a soluble form. CD146 is expressed by numerous cancer cells as well as being one of the numerous proteins expressed by the vascular endothelium. It has also been identified on smooth muscle cells, pericytes, and some immune cells. This protein was initially described as an actor involved in tumor growth and metastatic dissemination processes. Some recent works highlighted the role of CD146 in angiogenesis. Interestingly, this knowledge allowed the development of therapeutic and diagnostic tools specifically targeting the different CD146 variants. The first anti-CD146 antibody designed to study the function of this molecule, MUC18, was described by the Pr. J.P. Jonhson in 1987. We will discuss the 30 following years of research focused on the detection, study, and blocking of this protein in physiological and pathological processes. We will also focus on new recent data including MCAM variants in a larger proteasome composed of NADPH isoform 1 and ADAM17 which have been widely described as being involved in tumor growth. Indeed, characterization of novel NOX1 and ADAM17 inhibitors and the use of Knock-out animals enlightens us on the role of MCAM membrane and soluble variants in tumor development and allows us to develop new strategies to block these pathways.

Recent Publications

1. **Stalin J**, Nollet M, Dignat-George F, Bardin N and Blot- Chabaud M. Therapeutic and diagnostic antibodies to CD146: Thirty years of research on its potential for detection and treatment of tumors. Antibodies. Accepted 1st November 2017 (review).
2. Nollet M, **Stalin J** et al. A novel anti-CD146 antibody specifically targets cancer cells by internalizing the molecule. Oncotarget. Accepted in November 2017.
3. **Stalin J**, Nollet M et al. Targeting soluble CD146 with a neutralizing antibody inhibits vascularization, growth and survival of CD146-positive tumors. Oncogene. 2016 Oct 20;35(42):5489-5500.
4. **Stalin J**, Harhouri K et al. Soluble CD146 boosts therapeutic effect of endothelial progenitors through proteolytic processing of short CD146 isoform. Cardiovasc Res. 2016 Aug 1;111(3):240- 51.
5. **Stalin J**, Harhouri K et al. Soluble melanoma cell adhesion molecule (sMCAM/sCD146) promotes angiogenic effects on endothelial progenitor cells through angiomotin. J Biol Chem. 2013 Mar 29;288(13):8991-9000.

Biography

Jimmy Stalin is a post-doctoral researcher in the pathology department of Fribourg University. He joined this research group after a brief post-doctoral position in Beat Imhof group (Geneva University). He completed his PhD and undergraduate studies at Aix-Marseille University (France). His research interests lie in the area of physiological and pathological angiogenesis but also in the comprehension of tumor stromal cells modulation after therapy. He also closely collaborate with pharmaceutical company (Genkyotex) and research group (CERIMED) to generate and characterize antibodies and inhibitors targeting various proteins.

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