Objective

Current anti-angiogenesis based anti-tumor therapy relies on starving tumors by blocking their vascular supply via inhibition of growth factors. However, limitations such as resistance and toxicity, mandate conceptually distinct approaches. We will explore an entirely novel and long-overlooked strategy to discover additional anti-angiogenic candidates, based on the following innovative concept: ‘rather than STARVING TUMORS BY BLOCKING THEIR VASCULAR SUPPLY, we intend TO STARVE BLOOD VESSELS BY BLOCKING THEIR METABOLIC ENERGY SUPPLY’, so that new vessels cannot form and nourish the growing tumor. This project is a completely new research avenue in our group, but we expect that it will offer refreshing long-term research and translational opportunities for the field.

Because so little is known on endothelial cell (EC) metabolism, we will (i) via a multi-disciplinary systems-biology approach of transcriptomics, proteomics, computational
network modeling, metabolomics and flux-omics, draw an endothelio-metabolic map in angiogenesis. This will allow us to identify metabolic regulators of angiogenesis, which will be further validated and characterized in (ii) loss and gain-of-function studies in various angiogenesis models in vitro and (iii) in vivo in zebrafish (knockdown; zinc finger nuclease mediated knockout), providing prescreen data to select the most promising candidates. (iv) EC-specific down-regulation (miR RNAi) or knockout studies of selected candidates in mice will confirm their relevance for angiogenic phenotypes in a preclinical model; and ultimately (v) a translational study evaluating EC metabolism-targeted anti-angiogenic strategies (pharmacological inhibitors, antibodies, small molecular compounds) will be performed in tumor models in the mouse.

Field of science

/natural sciences/chemical sciences/inorganic chemistry/inorganic compounds
/natural sciences/biological sciences/biochemistry/biomolecules/proteins/proteomics

Programme(s)

Topic(s)

Call for proposal

ERC-2010-AdG_20100317

Funding Scheme

ERC-AG - ERC Advanced Grant

Host institution

VIB VZW

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Rijvisschestraat 120
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Activity type
Research Organisations

EU contribution
€ 2 365 224

Website
Contact the organisation

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**Last update:** 2 August 2019  
**Record number:** 98951

**Permalink:** [https://cordis.europa.eu/project/id/269073](https://cordis.europa.eu/project/id/269073)

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