Metabolic regulation of metastatic growth

Fact Sheet

Project Information

MetaRegulation

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Project closed

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14 February 2018

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1 June 2018

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31 May 2023

Funded under
EXCELLENT SCIENCE - European Research Council (ERC)

Total cost
€ 2 000 000,00

EU contribution
€ 2 000 000,00

Coordinated by
VIB VZW
Belgium

Objective

Metastatic growth of cancer cells requires extracellular matrix (ECM) production. The current understanding is that transcription factors regulate ECM production and thus metastatic growth by increasing the expression of collagen prolyl 4-hydroxylase (CP4H). In contrast, we recently discovered that metabolism regulates CP4H activity independently of the known transcription factors. Specifically, we found that loss of pyruvate metabolism inhibits CP4H activity and consequently ECM–dependent breast cancer cell growth. Based on this discovery we propose the novel concept that metabolism regulates metastatic growth by increasing ECM production.

In this project we will investigate the following questions: 1) What is the mechanism

by which pyruvate regulates CP4H activity in breast cancer cells? To address this question we will investigate pyruvate metabolism and ECM production in 3D cultures of various breast cancer cell lines using 13C tracer analysis, metabolomics, and two-photon microscopy based ECM visualization. 2) How can this novel metabolic regulation be exploited to inhibit breast cancer-derived lung metastases growth? To address this question we will inhibit pyruvate metabolism in metastatic breast cancer mouse models using genetically modified cells and small molecules in combination with immuno- and chemotherapy. 3) How can this novel regulation be translated to different metastatic sites and cancers of different origin? To address this question we will determine the in vivo metabolism of breast cancer-, lung cancer-, and melanoma-derived liver and lung metastases (using metabolomics and 13C tracer analysis), and link it to ECM production (using two-photon microscopy based ECM visualization).

With this project we will deliver a novel concept by which metabolism regulates metastatic growth. In a long-term perspective we expect that targeting this novel metabolic regulation will pave the way for an unexplored approach to treat cancer metastases.

Fields of science (EuroSciVoc)

medical and health sciences > clinical medicine > oncology > **lung cancer**

natural sciences > physical sciences > optics > **microscopy**

medical and health sciences > clinical medicine > oncology > **breast cancer**

Keywords

in vivo cancer metabolism | metastasis | metabolic regulation | extracellular matrix production

Programme(s)

H2020-EU.1.1. - EXCELLENT SCIENCE - European Research Council (ERC) MAIN PROGRAMME

Topic(s)

ERC-2017-COG - ERC Consolidator Grant

Call for proposal

ERC-2017-COG

See other projects for this call

Funding Scheme

ERC-COG - Consolidator Grant

Host institution

VIB VZW

Net EU contribution

€ 2 000 000,00

Total cost

€ 2 000 000,00

Address

SUZANNE TASSIERSTRAAT 1
9052 ZWIJNAARDE - GENT
Belgium

Region

Vlaams Gewest > Prov. Oost-Vlaanderen > Arr. Gent

Activity type

Research Organisations

Links

Contact the organisation Website
Participation in EU R&I programmes
HORIZON collaboration network

Beneficiaries (1)

VIB VZW

Belgium

Net EU contribution

€ 2 000 000,00

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