Targeting cancer metastasis

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Background

Metastasis is the spread of cancer cells from a primary tumour often via blood circulation to a distant site in the body and the leading cause of mortality in cancer patients. However, no specific anti-metastatic treatments are available for clinical use. One critical step during metastasis is the exit of circulating tumour cells (CTCs) from the blood circulation. Targeting the ability of CTCs to exit the blood circulation opens up the possibility of a novel way to combat cancer metastasis.

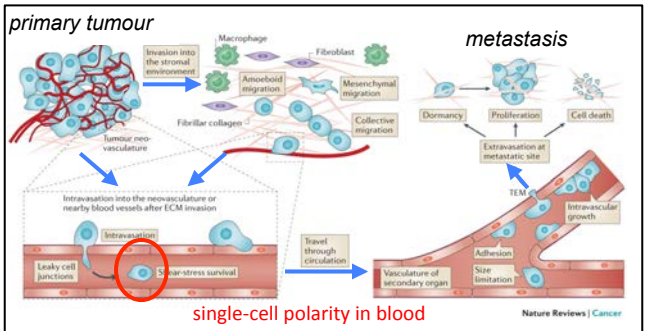


***Figure 1:* Stages of metastasis** (Reymond *et al* (2013), modif.

Single-cell polarity in liquid phase is a novel feature of CTCs that helps them attach to blood vessels, leave circulation and form metastases. Single-cell polarity correlates with the metastatic capacity of CTCs in mice and inhibition of single-cell polarity reduces metastatic seeding to the mouse lung.

On a cellular level, single-cell polarity is characterised by uneven distribution of the plasma membrane (PM), the underlying actin cytoskeleton and associated molecules. Mechanistically, tumour cells use the pole to attach to the vessel wall and orient the cell body.

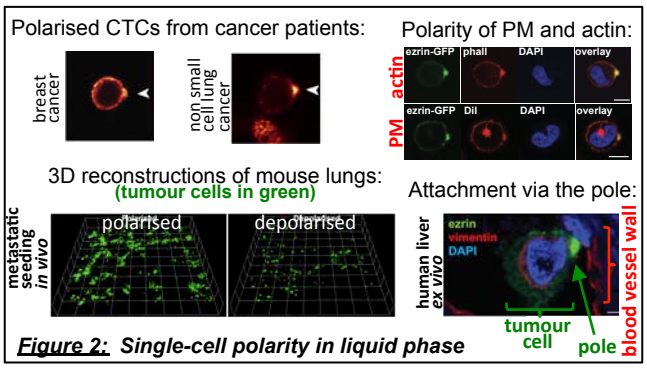
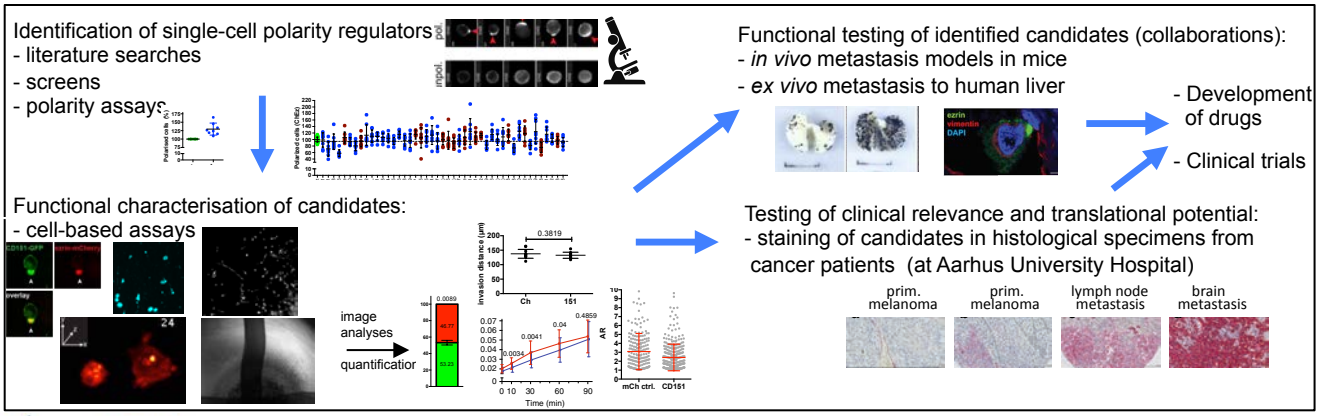


***Figure 2:* Single-cell polarity in liquid phase**

Projects: Identification and characterisation of regulators of single-cell polarity

All the projects aim to identify therapeutically targetable regulators of single-cell polarity in human cancer cells. Projects either focus on cell-intrinsic regulators such as plasma membrane- or actin-organising molecules or on systemic regulators that enhance or reduce polarisation in tumour cells.

Techniques: In addition to basic biochemical and molecular biological laboratory techniques, the projects will involve culturing, transfection and drug treatments of various cancer cell lines, fluorecence-microscopy-based polarity assays, tumorigeneity and viability assays, various cell migration assays and invasion assays in biomimetic 3D matrices. Expression and localisation of proteins will be assessed by immunofluorescence stainings. The subcellular localisation of proteins will be studied by confocal microscopy and flow imaging (a technique combining FACS and microscopy). The specific techniques acquired by the student will depend on the project.



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Reference:
Lorentzen A, et.al. Single cell polarity in liquid phase facilitates tumour metastasis. *Nature Communications* **2018** Feb 28;9(1):887.