Hypoxia-induced metastasis : the role of the unfolded protein response

PROPOSITIONS
belonging to the thesis

Hypoxia-Induced Metastasis:
The Role of the Unfolded Protein Response

1. The growth of distant metastases is determined by the intrinsic properties of the tumor cells, the local microenvironment at the metastatic site, as well as the primary tumor microenvironment. (this thesis)

2. The unfolded protein response (UPR) is an important mediator of hypoxia-driven metastasis. (this thesis)

3. Hypoxic activation of the UPR promotes metastasis by increasing the tolerance of tumor cells to hypoxia and by inducing the expression of the metastasis-associated gene LAMP3. (this thesis)

4. Targeting HIF and/or UPR signaling presents a potential therapeutic strategy to prevent development of metastases. Strategies to target hypoxic cells should be combined with radiotherapy and chemotherapy, which are aimed at eliminating well-oxygenated tumor cells, including those with increased metastatic potential. (this thesis)

5. The amount of cancer research funding devoted to metastasis research is disproportionate to the clinical relevance of metastasis.

6. Personalized cancer medicine is the future of cancer treatment but faces copious practical challenges for widespread clinical implementation.

7. "Although the successful eradication of a cancer should require the elimination of all the cancer stem cells (CSCs), on the contrary side, the successful growth of a metastasis by definition requires the presence of at least 1 CSC."
(Hill *et al.* 2007)

8. One of the many unresolved questions regarding metastasis is how disseminated tumor cells can sometimes remain in a dormant state for up to several years after successful treatment of the primary tumor prior to developing into clinically detectable metastases, and how this switch occurs. A better understanding of the signaling pathways underlying tumor dormancy might lead to the identification of novel therapeutic targets directed against dormant cells and the prevention of tumor recurrence.

9. "Life can only be understood backwards; but it must be lived forwards."
(Søren Kierkegaard)

Hilda Mujcic, 12 September 2013