# Computational systems biology in cancer brain metastasis

Cancer metastasis, especially cancer brain metastasis, is a complicated process representing the major cause for cancer-related deaths worldwide. A better understanding of the underlying mechanisms of such malignancies will enable us to develop more efficient therapeutic strategies. The progression of a primary tumor to metastatic disease is a multiple-step process involving detachment of primary tumor, local invasion, intravasation, transport, extravasation, and colonization at the secondary site, which is hard to address without integration of multiple disciplines.

In the initial step of metastasis, primary tumor cells intrude the surrounding stroma. Cancer cells gain invasive property via a process known as Epithelial to Mesenchymal transition (EMT) during which cancer cells change their morphology from epithelial to mesenchymal shape and at the same time, secrete molecules to degrade the extracellular matrix. Intruded cancer cells intravasate into the nearby blood vessels (called circulating cells), where they have to survive by stimulating particular survival signaling pathways before their successful colonization into a distant organ. The circulating cells also have to acquire special properties to extravasate from the circulation system. To do this, they generally mimic leukocytes and express particular molecules (chemokines and cytokines) to facilitate successful extravasation. For special organs such as brain which is protected by the blood brain barrier, extravasation is quite difficult. However, survival at the distant organ is more challenging for the extravasated cells as various foreign tissue factors may cause apoptosis of the cancer cells. Only cells that can better accommodate the foreign tissue environment can survive and grow as a secondary tumor.

Since the metastatic cascade involves so many complex steps, it is generally considered to be an inefficient process. However, once the metastasis does occur, it is fatal to the host. Therefore, a better comprehension of each step in the metastatic cascade is essential for the development of optimal therapeutic interventions. Research in the field of cancer metastasis has been ongoing for decades and various mechanisms of metastasis have been revealed. Unfortunately, most of which have merely added another layer of complexity to the metastatic cascade. Recent technological advances such as high throughput genomics, proteomics, and metabolomics analyses have provided better platforms for investigating this complicated disease at the systems level. The computational systems biology approaches, via integration of multiple systems and data types, are promoting new biomarker discoveries for metastatic diseases and demonstrating more suitable and personalized targeted therapeutics. Scientists from diverse fields, including mathematics, bioinformatics and computational biology disciplines, must foster communications and work together to better understand and disturb the elaborate and nonlinear process of cancer brain metastasis.

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## Publication

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