Metastases

The spread of a cancer from one organ or part to another non-adjacent organ or part.

Metastases cause 90% of human cancer deaths. The metastatic cascade involves local invasion, intravasation, extravasation, metastatic site colonization, and proliferation. While individual mediators of these processes have been investigated, interactions between these mediators remain less well defined.

Lau et al. previously identified a complex between receptor tyrosine kinase c-Met and β1 integrin in metastases. Using novel cell culture and in vivo assays, they found that c-Met/β1 complex induction promotes intravasation and vessel wall adhesion in triple-negative breast cancer cells, but does not increase extravasation. These effects may be driven by the ability of the c-Met/β1 complex to increase mesenchymal and stem cell characteristics. Multiplex transcriptomic analysis revealed upregulated Wnt and hedgehog pathways after c-Met/β1 complex induction. A β1 integrin point mutation that prevented binding to c-Met reduced intravasation. OS2966, a therapeutic antibody disrupting c-Met/β1 binding, decreased breast cancer cell invasion and mesenchymal gene expression. Bone-seeking breast cancer cells exhibited higher c-Met/β1 complex levels than parental controls and preferentially adhered to the tissue-specific matrix. Patient bone metastases demonstrated a higher c-Met/β1 complex than brain metastases. Thus, the c-Met/β1 complex drives intravasation of triple-negative breast cancer cells and preferential affinity for bone-specific matrix. Pharmacological targeting of the complex may prevent metastases, particularly osseous metastases [1].

Classification

see Metastases Classification.

Treatment

Intracranial metastases treatment.

Prognosis

Metastases is the leading cause of cancer mortality.

Metastatic cancer is notoriously difficult to treat, and it accounts for the majority of cancer-related deaths.

1)
Lau D, Wadhwa H, Sudhir S, Chang AC, Jain S, Chandra A, Nguyen AT, Spatz JM, Pappu A, Shah SS, Cheng J, Safaee MM, Yagnik G, Jahangiri A, Aghi MK. Role of c-Met/β1 integrin complex in the metastatic cascadein breast cancer. JCI Insight. 2021 May 18:138928. doi: 10.1172/jci.insight.138928. Epub ahead of print. PMID: 34003803.