The Physics of Cancer: The role of physical interactions and mechanical forces in Metastasis

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Presented by:
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The metastatic process

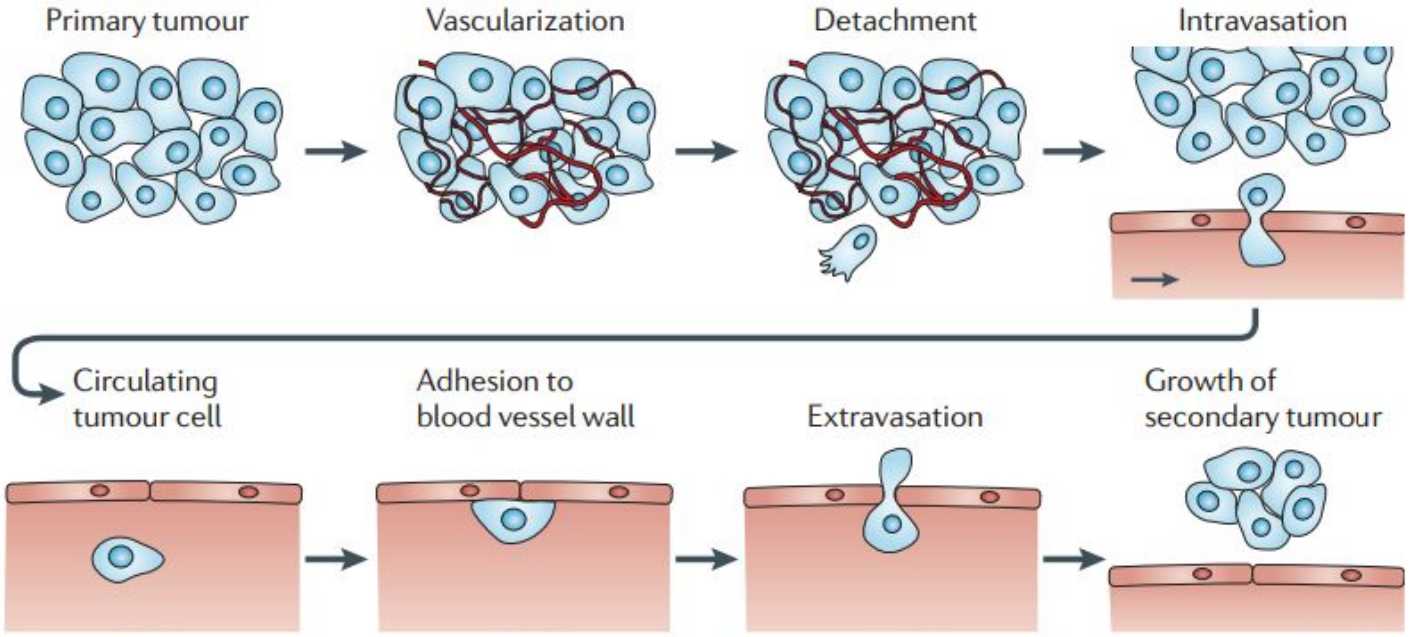


Figure 1 | **The metastatic process.** In this complex process, cells detach from a primary, vascularized tumour, penetrate the surrounding tissue, enter nearby blood vessels (intravasation) and circulate in the vascular system. Some of these cells eventually adhere to blood vessel walls and are able to extravasate and migrate into the local tissue, where they can form a secondary tumour.

Wirtz et. al. 2011

Detachment and intravasation

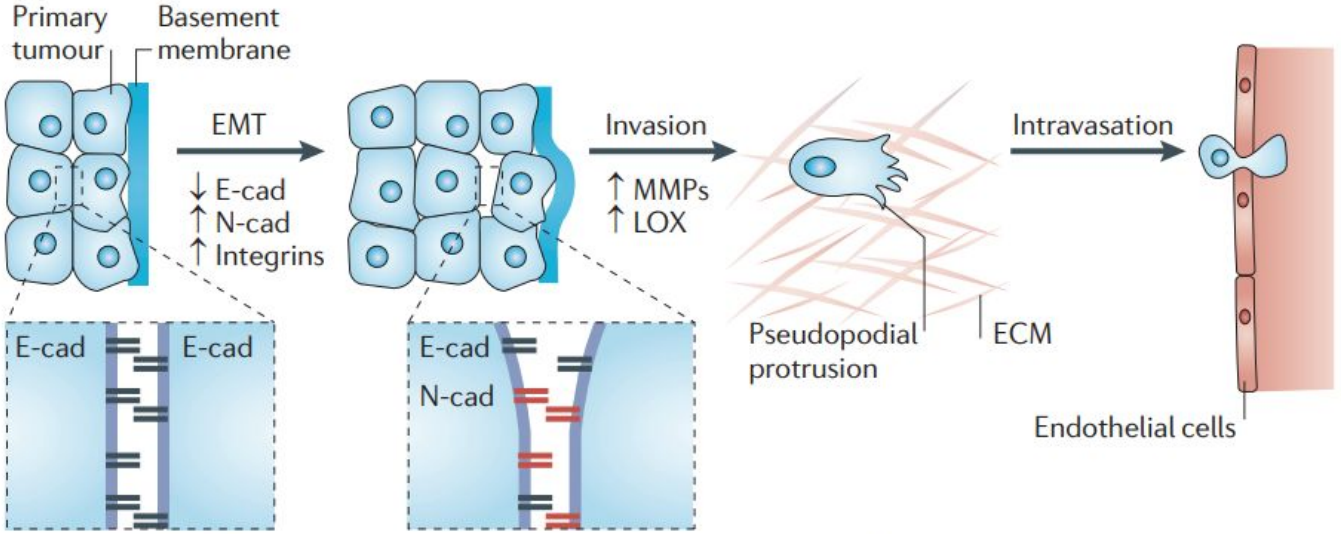
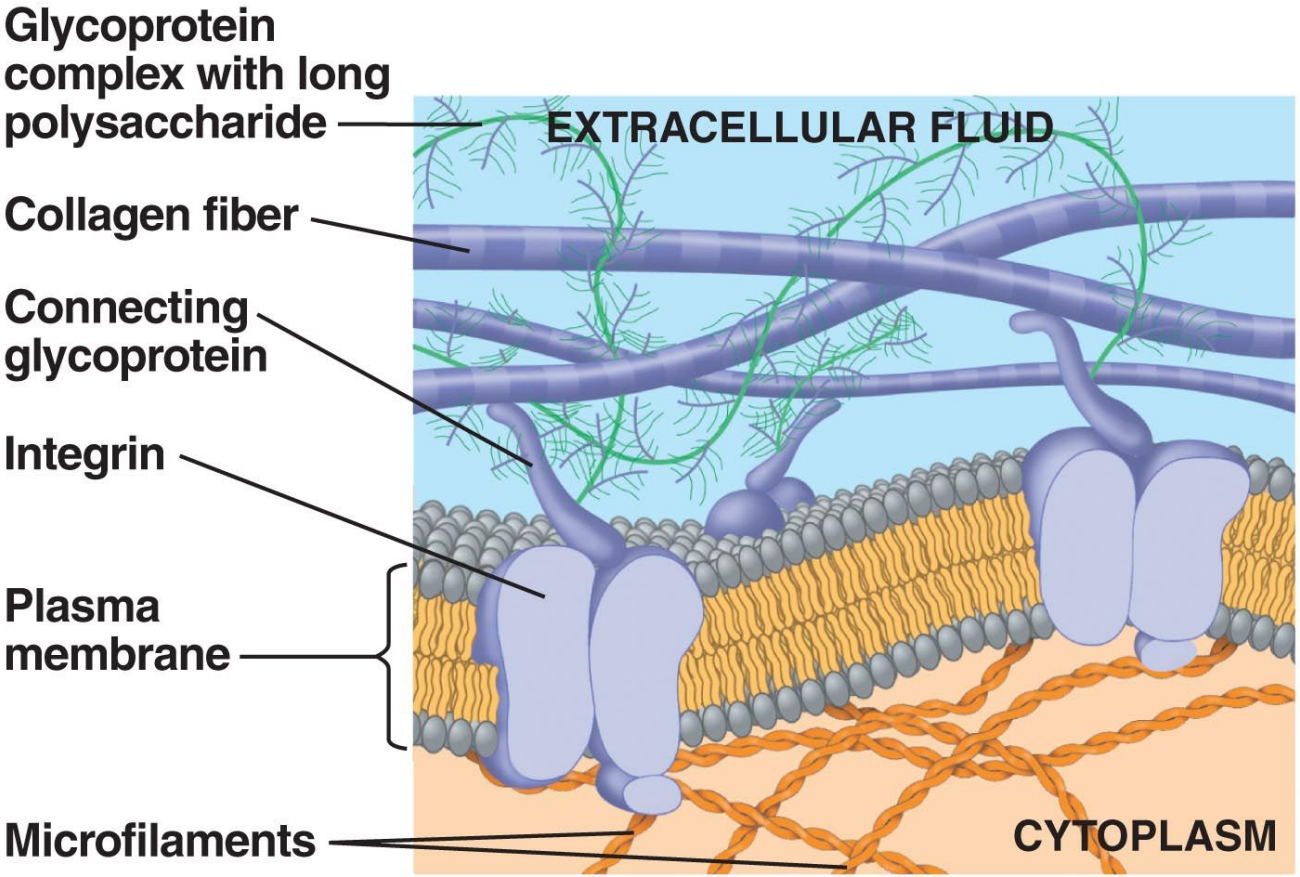


Figure 2 | **The physics of invasion and intravasation.** The epithelial-to-mesenchymal transition (EMT) is associated with a loss of adhesion through downregulation of E-cadherin (E-cad) and a change in morphology. Invasion by tumour cells of the surrounding tissue and subsequent motion is dictated by the physicochemical properties of the extracellular matrix (ECM). By squeezing between blood vessel endothelial cells, tumour cells can enter the vascular system. All of these steps involve physico-chemical processes, such as adhesion and deformation, that are dependent on the local environment. LOX, lysyl oxidase; MMPs, matrix metalloproteinases; N-cad, N-cadherin.

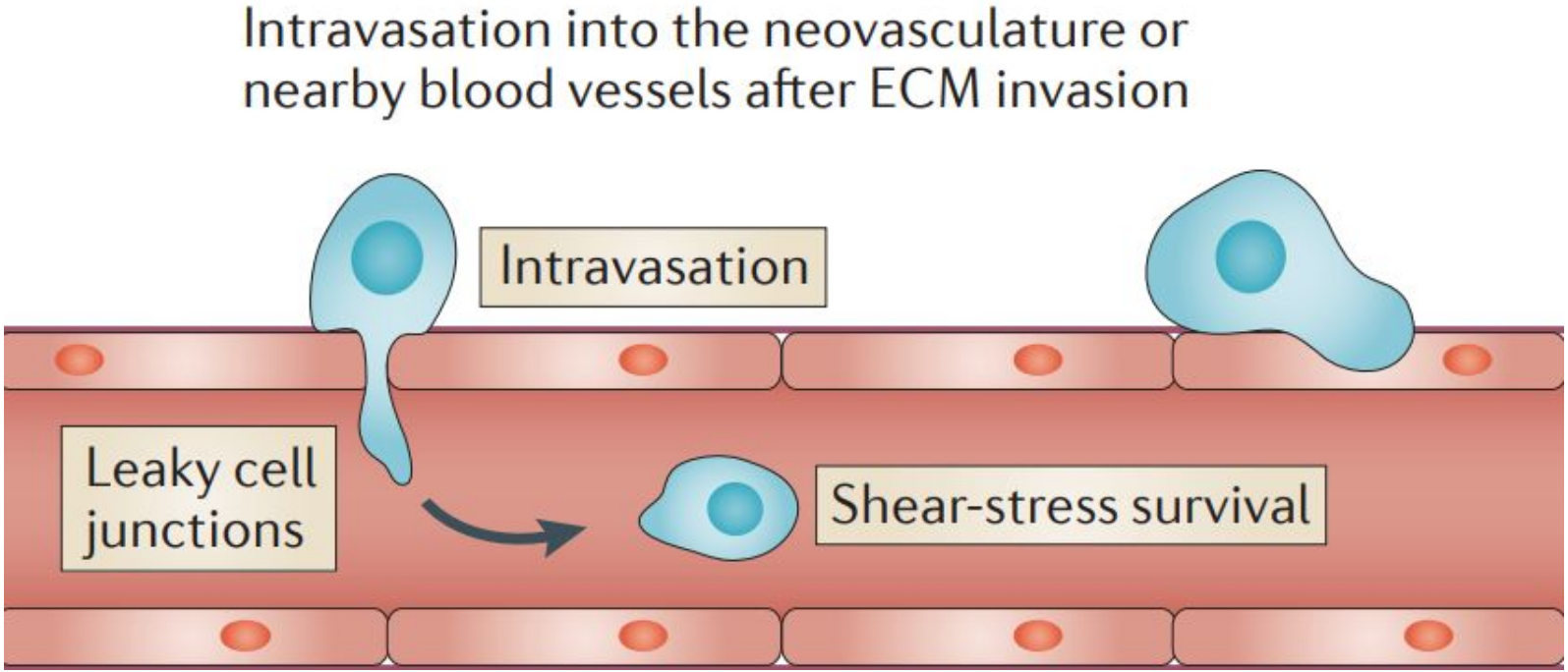
Wirtz et. al. 2011

Extra Cellular Matrix



Shana Chon. 2014

Intravasation



Reymond et. al. 2013

Blood Stream

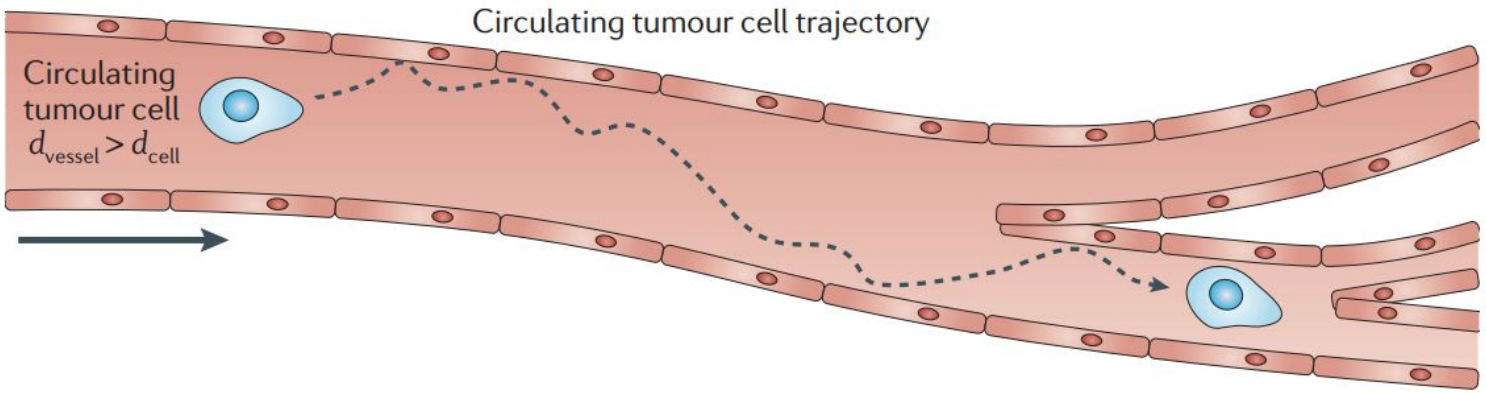
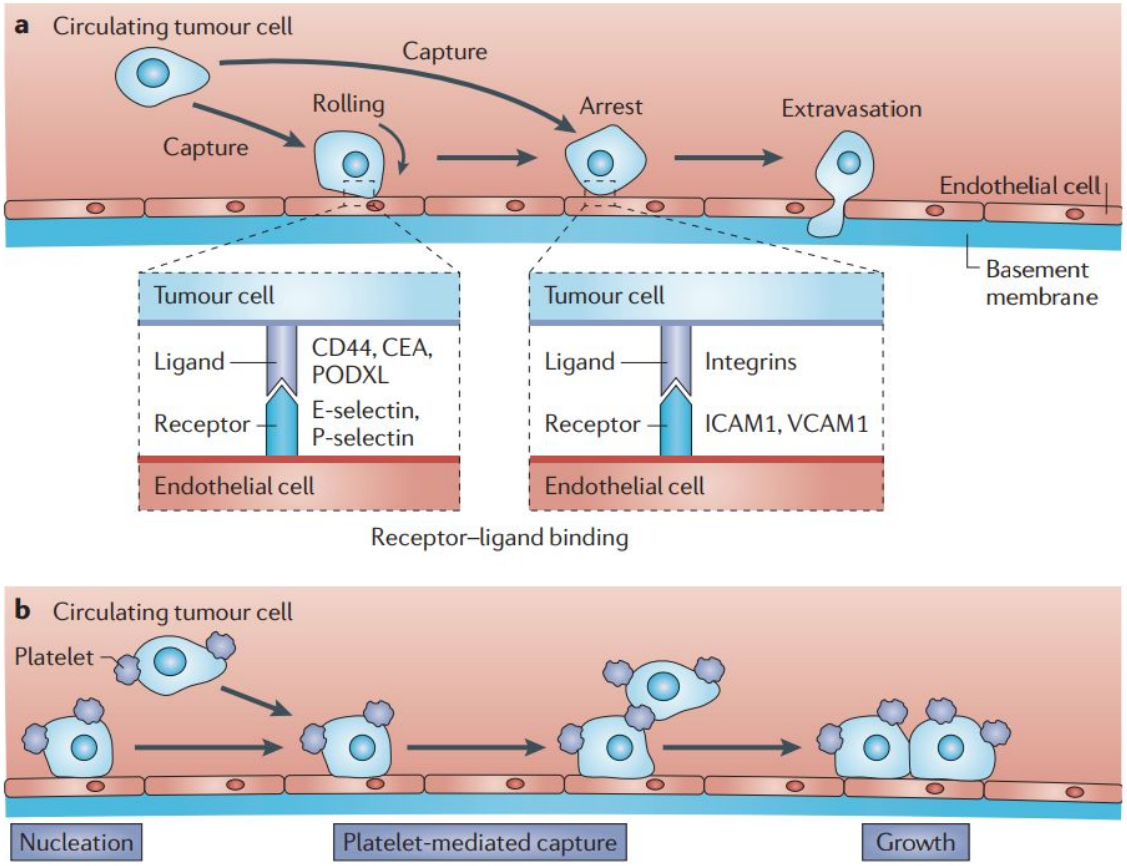


Figure 3 | **Arrest of circulating tumour cells.** Tumour cells with a diameter (d_{cell}) less than the diameter of the blood vessel wall (d_{vessel}) will follow a trajectory that is determined by the local flow pattern and by collisions with host cells and blood vessel walls. Collisions with a blood vessel wall may lead to arrest. Tumour cells with diameter greater than the diameter of a blood vessel will be arrested owing to mechanical trapping (physical occlusion).

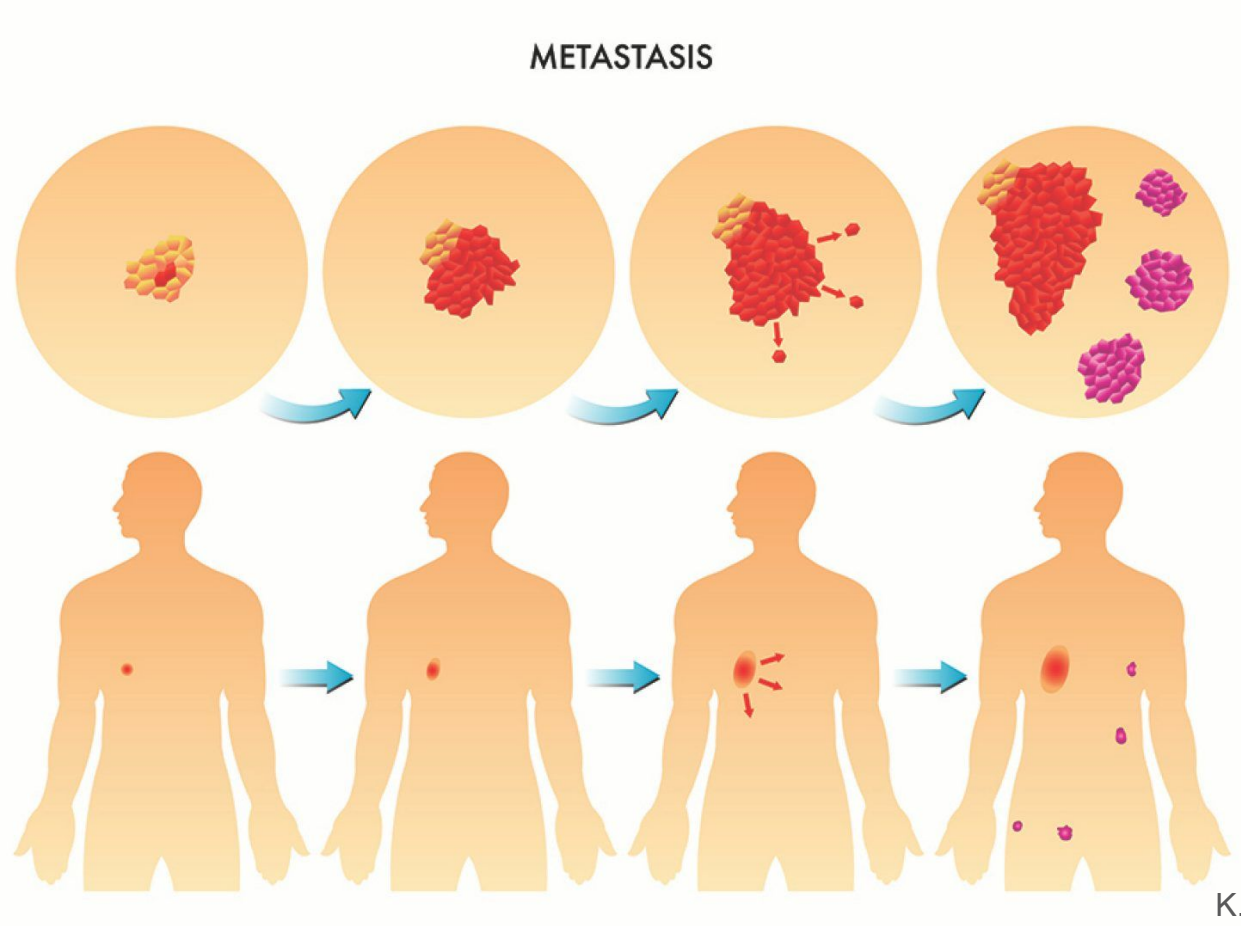
Wirtz et. al. 2011

Adhesion and Extravasation



Wirtz et. al. 2011

Secondary tumours (location of metastatic sites)



K. Werner. OncoLog, 2016

Conclusions

- Spread of cancer is dominated by physical and chemical interactions with diverse microenvironments.
- Intravasation, extravasation and cell motility are modulated by mechanical forces.
- Trajectory of a cell tumor, adhesion and subsequently extravasation are linked to the shear flow in the vascular system.
- *In vitro* tests fail in clinical trials, basically due to the fact that this systems do not replicate well the microenvironments present in humans.
- Understanding the physical processes that take place in the complex metastasis process is a fundamental step in developing new treatments to save many lives.