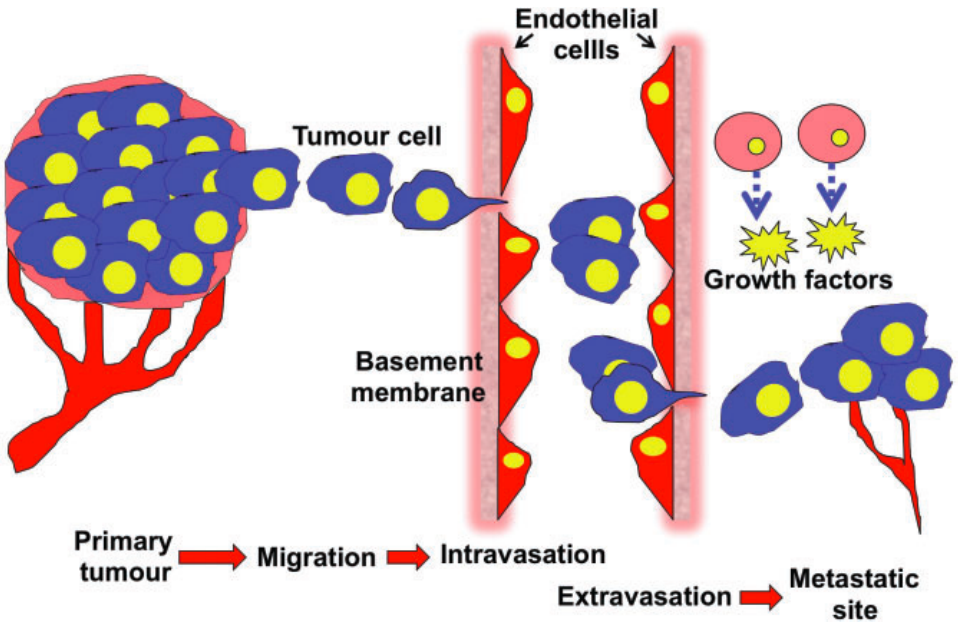
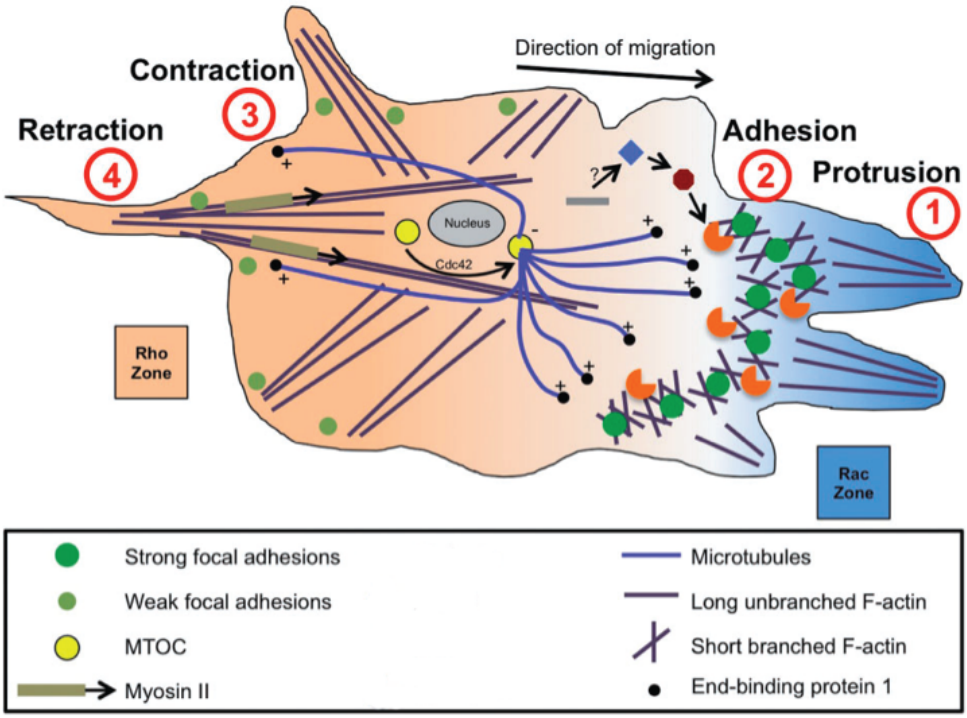
The Role of the Cytoskeleton in Cancer Metastasis
(Adapted from material published in Fife, *et al.,* Brit. J. Pharm., 2014)

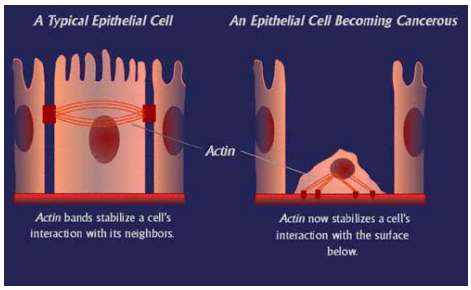


Step 1: Cancer cells detach from primary tumor and migrate through the surrounding ECM (extracellular matrix)
Step 2: Intravasation → Cancer cells degrade the basement membrane and travel across the endothelium
Step 3: Extravasation → Cells are transported through the vasculature, arrest in a capillary bed, and cross across the vasculature
Step 4: Cells grow and interact with the environment to form tumors away from the original site



Cells initiate motility by polymerizing actin filaments to create and extend membrane protrusions (1). The protrusions are stabilized via large protein complexes called focal adhesions (2), which adhere to the extracellular matrix. Movement is generated by the motor protein myosin, which "walks" along the actin cables, pushing the cell forward while contracting the rear of the cell (3), resulting in weakening of focal adhesions in this region and retraction of the cell (4).

Benign vs. metastatic tumor cells



http://www.cyto.purdue.edu/science/taste/cd1/a1017.htm

- After a cell interacts with the surface it can start to migrate – this is how metastasis of cancer starts.

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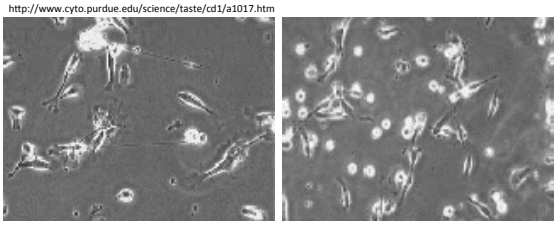
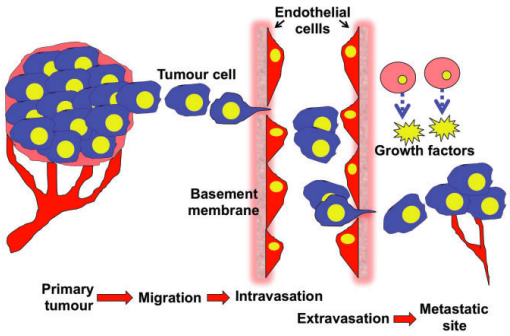


Benign tumor cells

Metastatic tumor cells



- Cell migration is essential to the process of metastasis.
- The cytoskeleton, particularly actin filaments/ microfilaments, plays a major part in cell movement.

https://www.youtube.com/watch?v=5tT25N5riaQ

- You are a group of cancer researchers gathering to discuss new ways of treating cancer. If cancers are treated before they metastasize the prognosis of the patient is much better.
- Read through the information provided and discuss with your groups what you think should be targeted when developing a new drug.

- What did you decide to target and why?
- What might be some of the problems with this approach?