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| **CANCER 10**  **Invasion: regulation of cell mIGRATION**  Dr Vania Braga   1. **How does detachment from primary tumour and migration occur?**   **2) What are the molecular mechanisms that regulate** **motility?**   * microfilaments * regulation of actin dynamics * cytoskeletal proteins * signalling proteins |
| **Migration of primary glial cells**  Scratch wound assay |
| **Migration of a glial tumour cell line** |
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| **Filopodia**  Finger-like protusions rich in actin filaments  **actin vinculin**  16050Molecular Biology of the Cell |
| **Lamellipodia**  Sheet-like protusions rich is actin filaments  16092 |
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| **Cell Movement**  Control is needed:   * within a cell to coordinate what is happening in different parts * regulate adhesion/release of cell-extracellular matrix receptors * from outside to respond to external influences –   sensors  directionality  **Motility: hapoptatic *versus* chemotatic**  **Cell movement = changing cell shape** |
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| **Why is it important to learn about cytoskeletal proteins?**  Which one of these diseases is not caused by deregulation of actin cytoskeleton?   1. High blood pressure 2. Wiskott-Aldrich Syndrome – WAS (immunodeficiency, eczma, autoimmunity) 3. Epidermolysis Bullosa (hereditary blistering diseases) 4. Bullous Pemphigoid (autoimmune disease) 5. Alzheimer (neurodegenerative) |
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| **Signalling mechanisms that regulate the actin cytoskeleton:**  1 - ion flux changes (i.e. intracellular calcium)  2 – control by phosphoinositide signalling  3 - signalling cascades via small GTPases  **Control of actin filament networks by Ca2+**  **Gelsolin**   * Ca2+ dependent severing * exposes - (fast depolymerising) end   **α-actinin**   * Crosslinks actin filaments * binding decreased at high Ca2+ |
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| **Further reading:**  **1)** Molecular Biology of the Cell  **2)** Cell Biology. 2002. T.Pollard & W.Earnshaw. pg 551-670, Elsevier Science  **3)** Condeelis J, Singer RH, Segall JE. THE GREAT ESCAPE: When Cancer Cells Hijack the Genes for Chemotaxis and Motility. Ann Rev Cell Dev Biol. 2005;21:695-718.  **4)** Jaffe AB, Hall A. RHO GTPASES: Biochemistry and Biology. Ann Rev Cell Dev Biol. 2005, 21:247-269.  **5)** Sahai E. Mechanisms of cancer cell invasion. Curr Opin Genet Dev. 2005, 15(1):87-96. |