BP 2: Physics of Cancer

Time: Monday 9:30–11:00 Location: H43

Invited Talk BP 2.1 Mon 9:30 H43

Multicellular Streaming in Solid Tumours — •Josef Käs[1], Franziska Wetzel[1], Anatol Fritsch[1], Steve Pawlizak[1], Linda Oswald[1], Steffen Grosser[1], Lisa Manning[2], Cristina Marchetti[2], Michael Höckel[1], and John Condeelis[3] — [1]Leipzig University — [2]Syracuse University — [3]Albert-Einstein College

As early as 400 BCE, the Roman medical encyclopaedist Celsus recognized that solid tumours are stiffer than surrounding tissue. However, cancer cell lines are softer, and softer cells facilitate invasion. This paradox raises several questions: Does softness emerge from adaptation to mechanical and chemical cues in the external microenvironment, or are soft cells already present inside a primary solid tumour? If the latter, how can a more rigid tissue contain more soft cells? Here we show that in primary tumour samples from patients with mammary and cervix carcinomas, cells do exhibit a broad distribution of rigidities, with a higher fraction of softer and more contractile cells compared to normal tissue. Mechanical modelling based on patient data reveals that, surprisingly, tumours with a significant fraction of very soft cells can still remain rigid. Moreover, in tissues with the observed distributions of cell stiffnesses, softer cells spontaneously self-organize into lines or streams, possibly facilitating cancer metastasis.

BP 2.2 Mon 10:00 H43

Stochastic tunneling and metastable states during the somatic evolution of cancer — Peter Ashcroft[1], Franziska Michor[2], and •Tobias Galla[1] — [1]School of Physics and Astronomy, The University of Manchester, UK — [2]Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute and Department of Biostatistics, Harvard School of Public Health, Boston, MA, USA

Tumors initiate when a population of cells accumulates a certain number of genetic and/or epigenetic alterations. Sometimes an intermediate mutant in a sequence does not reach fixation before generating a double mutant, this is referred to as 'stochastic tunelling'. Here, we focus on stochastic tunneling in a Moran model. Our analysis reveals fitness landscapes and mutation rates for which finite populations are found in long-lived metastable states. The escape from these states is driven by intrinsic noise, and their location affects the probability of tunneling. In these regimes it is the escape from the metastable states that is the key bottleneck; fixation is no longer limited by the emergence of a successful mutant lineage. We use the Wentzel-Kramers-Brillouin (WKB) method to compute fixation times, successfully validated by stochastic simulations. Our work fills a gap left by previous approaches and provides a more comprehensive description of the acquisition of multiple mutations in populations of somatic cells.

Reference: P. Ashcroft, F. Michor, T. Galla, Genetics 199 (2015) 1213.

BP 2.3 Mon 10:15 H43

Liquid-like and Solid-like Behaviour of Breast Cancer Cell Lines in 3D Aggregates — •Linda Oswald, Steffen Grosser, Steve Pawlizak, Anatol Fritsch, and Josef Käs — University of Leipzig, Institute of Experimental Physics I, 04103 Leipzig, Germany

Three-dimensional aggregates of biological cells become increasingly relevant in research as they resemble in vivo situations much closer than two-dimensional assays. These tissue models are usually described by viscous liquid theories on long time scales. Recent experiments on 3D segregation of breast cancer cell lines questioned this approach.

Based on this finding, we create aggregates of MCF-10A, MDA-MB-436, which form compact spheroids, and of MDA-MB-231 cells, forming loose aggregates only. We perform fusion experiments of the spheroids allowing to assess the ratio of tissue surface tension to viscosity. While MDA-MB-436 spheroids fuse mainly as expected from the viscous liquid theory, MCF-10A spheroids show a rich diversity in fusion behaviour, such as changing fusion speeds and complete fusion arrest accompanied by superficial morphological changes.

BP 2.4 Mon 10:30 H43

Comparison of the visco-elastic properties of cancer and normal cells by step-response AFM — •Carmela Rianna, Holger Doschke, Jens Schäpe, and Manfred Radmacher — Institute of Biophysics, University of Bremen, Germany

We have measured the visco-elastic creep response of cancer cells on different stiffness polyacrylamide gels and compared it with normal cells of the same type. In conventional force indentation curves the viscous and elastic properties cannot be measured separately. So, these data are usually only analyzed in terms of elastic response, even though the response of the cell to a moving AFM tip is viscous and elastic at the same time. Applying a force step in contact and recording the creep relaxation of the cell allows separating the viscous and elastic response independently. This can be converted in the storage and loss modulus as is usually done in soft matter rheology. We have cultured cells on three different substrates: polyacrylamide gels of 5 kPa and 50 kPa, respectively, and "infinitely" stiff Petri dishes. Normal cells showed an increase of the storage modulus from 1 kPa, to 1.5 kPa to 2.2 kPa with increasing sample stiffness. Whereas cancer cells showed a storage modulus around 1.2 kPa, more or less independent of sample stiffness. The loss modulus was around 400 Pas for cancer cells, where normal cells showed an increase from 250 Pas, to 600 Pas and to 700 Pas with increasing stiffness. There is a large difference in adaption of cancer and normal cells to the substrate stiffness. Whereas normal cells sense the softness of the substrate and adapt to it, cancer cells do not change their visco-elastic properties according to it.

BP 2.5 Mon 10:45 H43

Cell sorting in breast cancer cell lines: Driven by differential adhesion? — Steve Pawlizak[1], Anatol Fritsch[1], •Steffen Grosser[1], Linda Oswald[1], Dave Ahrens[1], Tobias Thalheim[1], M. Lisa Manning[2], and Josef Alfons Käs[1] — [1]University of Leipzig, Institute of Experimental Physics I, 04103 Leipzig, Germany — [2]Syracuse University, Department of Physics, Syracuse, NY 13244, USA

Demixing of differentiating cells into different compartments, resulting in tissues with stable boundaries, is a crucial process during embryogenesis, which is usually thought of being driven by differential adhesion of the cells. This stable sorting of cells is disrupted in metastasis, questioning if differential adhesion plays the decisive role here, too.

We use a panel of three different breast cancer cell lines from different sides of the epithelial-mesenchymal transition to test the differential adhesion hypothesis (DAH) in this environment. We employ a variety of measurement techniques to asses mechanical properties of cells on the single-cell level, comprising cell-cell adhesion, cell stiffness, cell shapes, and cadherin densities. We compare these results to multicellular 3D sorting experiments and show that the results are at odds with predictions from the DAH. The behaviour of multi-cellular aggregates even shows deviations from the basic assumption of tissue liquidity on long timescales.

These findings suggest that dynamical effects such as directional motility or jamming might be key players in cancer development.