# SPATIOTEMPORAL DYNAMICS OF ATP IN MIGRATING TUMOR CELL

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Metastasis is the spread of cancer cells to distant organs and is a primary cause of cancer mortality. Enhanced migratory behaviour of tumour cells in metastasis is a critical hallmark of cancer progression. Cell migration is driven by dynamic changes in matrix adhesions, complexes that regulate the linkage between the actin cytoskeleton and the extracellular matrix. **Aerobic glycolysis or "the Warburg effect" is another important hallmark of cancer**, which mediates the conversion of glucose to pyruvate and generation of ATP. Little is known on the role of altered glucose metabolism in tumour cell migration. In particular, **the spatiotemporal relationships between energy supply and the dynamics of matrix adhesions and actin are unclear.** To fully understand the relationship between glucose metabolism and tumour cell migration, we established an image-based pipeline that allows the *in situ* assessment of glycolysis-derived metabolites in migrating tumor cells. Indeed, in order to understand the relationship between metabolites concentration/fluxes and the migratory phenotype of tumour cells, we need to apply a systems microscopy strategy to obtain a detailed cell-to-cell spatiotemperal quantitative analysis of both metabolites and migratory parameters. For this project, we have used reporter cell lines that express ectopically different fluorescent FRET biosensors that allow the live monitoring of metabolites in migrating tumor lung carcinoma cells (H1299). Those FRET probes include glucose, pyruvate, lactate and a ATP sensor and in addition the cells express a reporter for the actin cytoskeleton in the red channel. As a proof of principle, we did conduct a compound screen to infer the role of glucose metabolism in the migratory behaviour of the H1299 cells. We developed an automated image analysis pipeline using Cell profiler in combination with custom-made R script.

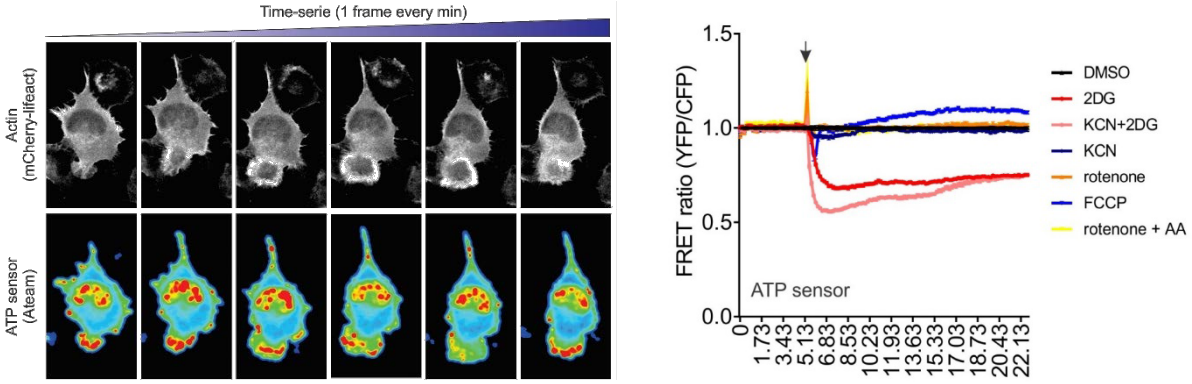


**Figure: A)** Simultaneous live imaging of actin dynamics and the ATP levels in a migrating tumor cell. **B**) Inhibition of glycolysis with 2DG results in a drop of cellular ATP and as a consequence prevent the cells to migrate. ATP reporter cell line exposed to various metabolic inhibitors (inhibitor of the glycolysis: 2DG; inhibitors of OXSPHO: KCN, FCCP, rotenone, antimycin).