Small cell lung carcinomas (SCLC) are highly aggressive, invasive and early metastasizing tumors. The process of metastasis is going along with phenotypical changes. Cells have to detach from the primary tumor, invade the surrounding stroma, enter the circulation and escape the detection of the immune system until reaching metastatic sites. Epithelial-mesenchymal transition (EMT) processes, initially known from embryonic development, have recently been described to play an important role for these processes. EMT is going along with phenotypical changes and disbanding cell-cell connections that result in a transition from a more epithelial phenotype to a more mesenchymal-like appearance. It is described that the reverse process mesenchymal-epithelial transition (MET) happens at the site of metastasis, and it is postulated that these processes are linked to radio- and chemoresistance. There is very little knowledge on EMT processes and its impact on metastasis in SCLC.

SCLC cell lines NCI-H69, NCI-H82, NCI-N592 are usually forming floating cell clusters when cultured in RPMI 10%FCS, only very few cells are growing adherent to tissue culture flask (3-7%). FACS analysis shows different subpopulations of size and density within a cell line. We started to analyze the phenotypical morphology of the cell lines NCI-H69, NCI-H82, NCI-N592 and NCI-H446. The addition of low concentrations of BrdU to the culture is inducing a phenotypical change to mainly adherent growing cells. These changes are accompanied by changes of typical EMT markers on gene and protein levels.

For the induction of phenotypical changes 10µM BrdU was added to the culture medium for 14-21 days. Medium was changed every second day by centrifuging and resuspension. Once the majority of cells appear adherent BrdU was not added anymore. The cells remain adherent and show normal growth patterns. We show that the phenotypical changes go along with changes in membrane structures like Tight Junctions, Desmosome, Gap Junctions, Vimentin and Cadherins. Mesenchymal markers are upregulated in adherent cells, whereas epithelial markers are downregulated. We are postulating that under the influence of BrdU SCLC cell lines undergoing a mesenchymal shift. Our in vitro model might be interesting to study in vivo incidences of EMT.