Highly heterogeneous breast cancers are the most commonly diagnosed cancer in women worldwide. Majority of breast cancer related deaths are a consequence of inoperable metastatic disease. Therefore, understanding how tumor cells invade other tissues and contribute to the heterogeneity and generation of more resistant to treatment cancer cells are fundamental challenges in cancer research. Carcinomas are the cancer type that arise from epithelial tissues, that normally are well organized with cells connected tightly with each other. Epithelial-to-mesenchymal transition (EMT) is a dynamic process that endows epithelial cells with enhanced motility and invasiveness by dynamic changes like loss of connections between epithelial cells and increased motility as a single cell, allowing them to spread and invade surrounding tissue. One important aspect of EMT's role in cancer is that EMT contributes to the generation of circulating tumor cells (CTCs). CTCs are tumor cells released into blood and/or lymphatic vessels that can circulate in the human body, which are predestined sources of metastasis as the “seeds”. EMT was also suggested being important in the formation of so-called cancer stem cells, cells which are more resistant to therapies and can survive in the body for long periods of time and give rise to new tumor and disease recurrence. Although the contribution of EMT to initial tumor cell invasiveness has been confirmed, its role in whole process of metastasis remains debated. Most importantly it remains a challenge to observe EMT in vivo in human carcinomas. One major difficulty is caused by the transient, reversible nature of EMT, since cancer cells which went through EMT, invaded tissues and spread to the blood stream, once at the distant organ, can go back to epithelial state and form metastatic tumor growth. Because only a small minority of carcinoma cells may be invasive and undergo an EMT in primary tumors, the functional characterization, cancer stem cells potential and changes in gene expression in such cells can be masked by the bulk of non-metastatic cells. Detecting such transient cells will be critical to assess the contribution of EMT to the behavior of high grade carcinomas. Another major challenge in such studies is to identify reliable molecular markers to define cells that are undergoing EMT in human tumors. Data from our laboratory indicate that relatively novel protein catulin is highly expressed in different types of invasive carcinoma cells. In vitro data indicate that an up regulation of catulin expression correlates with the transition of tumor cells from an epithelial to mesenchymal morphology and removal of catulin in human cancer cell lines dramatically decreases the migratory and invasive potential of those cells. We also reported that catulin is highly expressed in the malignant human breast cancers and correlates with aggressive behavior of those tumors. As α-catulin expression and function correlates with early onset of tumour cell invasion, we developed a reporter system, using catulin regulatory element and fluorescent protein, which will allow us to mark, track and isolate a small minority of carcinoma cells that may be invasive and undergo an EMT in primary tumours as well as give rise to CTCs. Analysis of those cells will lead to characterization of early detection markers of invasion and also understanding of early signalling pathways involved in tumour invasion and more importantly to development of targeting strategy against invasive cancer stem cells. We also established three-dimensional tumor spheroid-based functional assays for newly characterized targets validation. This functional test combined with data obtained using our reporter system will give us a strong indication of potential new markers of invasion and novel targets for anti-metastasis therapeutics.