# Mechanisms of the Epithelial to Mesenchymal Transition Induced by SNAIL Overexpression

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**INTRODUCTION**: Metastasis is responsible for most of the deaths related to cancer. Therefore, the most effective methods to decrease cancer morbidity and mortality consist in early detection, prevention and treatment of metastasis. Epithelial to mesenchymal transition (EMT) is one of the processes involved in cancer progression and metastasis. EMT induces cellular and microenviromental changes that result in loss of the epithelial phenotype and acquisition of mesenchymal properties, thus promoting cellular invasive and migratory capabilities. Overexpression of some transcription factors such as SNAIL also induces EMT and is correlated to cancer aggressiveness. **OBJECTIVES:** Identify specific mechanisms and proteins involved in the induction of EMT and metastasis. **MATERIAL AND METHODS:** The breast adenocarcinoma cell line MCF7 was induced to EMT by SNAIL overexpression. In order to provide in-depth proteomic analysis, subcellular proteome enrichment followed by GEL-LC-MS/MS was performed. Quantitative analysis relied on SILAC. **RESULTS AND DISCUSSION:** Subsets of proteins identified in each enriched subproteome led to a complementary list of 4289 proteins identified with high confidence. Among regulated proteins, ITGB1 was found to be involved in the process. ITGB1 was upregulated during SNAIL-induced EMT in both membrane and nuclear enriched fractions. Of note, ITGB1 has been correlated to cancer malignancy and aggressiveness in different cancer types. Activity inhibition of HDAC1, a downregulated protein during EMT, also upregulated ITGB1 specifically in the membrane enriched fraction, as well as

upregulated SNAIL. Network analysis of proteins regulated by SNAIL overexpression identified ITGB1 as a major hub and involved in several cellular processes such as cell communication and differentiation, regulation of signal transduction and control of cell death. **CONCLUSIONS:** ITGB1 seems to be essential to EMT and correlates to SNAIL and HDAC1. Control of such mechanism might represent an effective approach for clinical management of metastatic cancer.

**KEY WORDS:** EMT, SNAIL, ITGB1

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