# Multidimensional Signatures of Epithelial Mesenchymal Transition Plasticity


## ABSTRACT

Despite of *in vitro* and few *in vivo* evidences, approval of epithelial mesenchymal transition (EMT) in tumor histopathology is challenging. It may be due to less understood cellular plasticity including difficulty in distinguishing EMT undergoing cells and cancer associated fibroblast and involvement of small subset of transient cells in this transition. Hence, this study endeavoured to explore EMT plasticity in terms of cellular phenotypes, interaction ecology, mechanobiology and relating *in vitro* information at tissue level. To comprehend phenotypes, cellular morphometric and cytoskeletal characterization was evaluated in TGF-β1 induced EMT of epithelial normal (HaCaT) and cancer cell (AW 13516) population. To understand phenotypic interaction in population, intercellular connectivity was recorded. Phenotype and connectivity abundance estimated in population and dynamism appraised by Markov model. In comprehending biophysical cue on EMT, cellular morphology; molecular and biophysical properties were assessed of cells cultured on substrate with varying stiffness under TGF-β1. To sketch EMT signatures in histopathology, phenotypic, ultrastructural and transcriptomic profiling performed on oral potentially malignant disorders and cancer biopsies. Morphological study evidenced five phenotypes and two of them especially originated during EMT. Markov model evaluated inter-phenotypic transition that indicated emergence of intermediate forms. Cellular connectivity study found out three types connectivity during EMT. Connectivity has some biasness for specific cellular phenotypes. As per model, connectivity plasticity was more prominent in cancer cell population. Intriguingly, mechanobiological investigation noted that soft substrate inhibits cancer cell EMT. In histopathology, few EMT-like phenotypes were documented and their presence was linked to dysplasia. The EMT transcriptomic profile indicated aberrant expression of some genes and ultra structural study illustrated connectivity alteration. This study provides proof of EMT phenotypes and connectivity including their dynamism in the context of recognizing cellular plasticity during EMT. It also opened the trail to render *in vitro* information for advancing histopathological practices with appreciation for EMT in tumor.



**Keywords:** Epithelial mesenchymal transition, Phenotypic plasticity, Intercellular connectivity, Mechanobiology, Oral potentially malignant disorders, Oral squamous cell carcinoma.