Identification and Characterization of TGF-beta induced Long Noncoding RNAs in Lung Cancer

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Lung cancer is the most lethal cancer worldwide due to high ratio of recurrence and high probability to undergo metastasis. As epithelial-mesenchymal transition (EMT) plays a major role during metastasis, how EMT is regulated by periphery in the lung cancer is particularly important. Although initiation of EMT can be triggered by TGF-beta found to be overexpressed in lung cancer, how EMT can be affected by TGF-beta signaling in different disease stages and its contribution to the heterogeneity of tumor cells are still unclear. This hampers our ability to effectively treat and block metastasis in lung cancer. Recently, long noncoding RNAs have emerged as a new player for tumor metastasis. We therefore hypothesize that lncRNAs mediated TGF-beta signaling might be involved during EMT in lung cancer. Using RNA-seq, we identified changes in lncRNAs profiles during different time points after TGF-beta treatment in A549 cells. Early responded lncRNAs are major regulators in signaling and will be selected as primary candidates for further study. Expression patterns will be re-validated by other lung cancer cell line with TGF-beta treatment. The lncRNA candidates that have altered expression levels in response to TGF-beta will be chosen to determine their effects on migration and gene regulation using wound healing and expression microarray. In situ hybridization will eventually be carried out to correlate the expression level of lncRNA in lung cancer clinical samples and re-probe with EMT markers. The regulation of lncRNA in EMT would be validated with lncRNA knockout with TGF-beta stimulation in A549 cells. The abilities of migration and invasion in knockout cells would be determined in vivo. In the end, we found the candidate lncRNA play a critical role in EMT with TGF-beta stimulation in lung cancer.