中文題目：CD133+肺癌幹細胞之上皮間質轉換狀態之分子調控與疾病復發之相關性

英文題目：Molecular Portraits of Epithelial and Mesenchymal Status in CD133+ Stem-like Lung Cancer Cells and The Relevance to Disease Free Survival

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Background: Epithelial-mesenchymal transition (EMT) and the existence of CD133-positve stem-like lung cancer cells play important roles in drug resistance. A recent finding showed circulating tumor cells (CTCs), which enriched of cancer stem cells (CSCs), exhibit dynamic changes in epithelial and mesenchymal composition during the treatment course. We therefore hypothesize that the epithelial-type and mesenchymal-type CSCs may have different drug response.

Methods: The expression of EMT markers in 15 lung cancer cell lines was analyzed using Western blot and flow cytometry. The E-cadherin+/CD133+, E-cadherin-/CD133+, E-cadherin+/CD133- and E-cadherin-/CD133- subpopulations of PC14 cell line were sorted by fluorescence assisted cell sorting. The phenotypes and genotypes of the four sub-populations were examined using microarray, sphere formation, immunofluorescence, invasion, migration and MTT assays. The drug resistant signature was identified by comparing the gene expression profile from four subpopulations and Gene Expression Omnibus (GEO) database.

Results: The existence of both epithelial and mesenchymal subpopulations could be observed in A549, H358, H520 and PC14 cell lines. The E-cadherin+/CD133+ subpopulation exhibited higher sphere formation ability and was more resistant to the treatment of chemotherapy agents compared to the E-cadherin-/CD133+ subpopulation. The mesenchymal type (E-cadherin-) cells showed higher tumor initiation ability in the animal model. Gene expression profiling showed 86 genes were bioinformatically predicted as drug resistant signature and were correlated with the disease free survival of the patients with lung cancer. Among the drug resistant signature genes, 20 genes were significantly related to the patient's prognosis.

Conclusion: The epithelial-type lung CD133+ stem-like lung cancer cells are more resistant to chemotherapy and a panel of gene signatures can be used to predict the worse prognosis of lung cancer patients.

Key words: lung cancer, cancer stem cell, epithelial-mesenchymal transition, drug resistance