

JOINT EVENT

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Regenerative medicine: Gene and stem cell therapy for lung injury**Cheng-Wen Wu**

National Yang-Ming University, Taiwan

Lung diseases, such as acute respiratory distress syndrome (ARDS) or chronic obstructive pulmonary disease (COPD), are both major public health problems but currently without any effective pharmacologic approach for the treatment. Stem cell therapy based on transplantation of *in vitro* propagated stem/progenitor cells has been proposed as a potential solution to restore lung functions. However, due to the complexity of cell source and lung microenvironment, whether transplanted cells have differentiated for reconstitution of airway/alveolar epithelium were questioned. Furthermore, safety issues have raised concerning the use of stem cells *in vivo*. Although past gene therapy studies using viral vectors in human has been hampered due to adverse effects and safety issues, recent clinical trials have shown remarkable therapeutic benefits and an excellent safety record with improved vector designs. Our lab has focused on *in vivo* gene delivery of stemness genes in somatic lung epithelial cells using PEI nanoparticles for lung injury treatment. In a mouse model of elastase-induced emphysema, we found that the transient gene delivery of COPX-1 in alveolar epithelial cells post-injury induced efficient regeneration of alveolar epithelium and improved pulmonary function. The regenerated regions showed normal alveolar epithelial phenotype and extracellular matrix components, without the symptoms of neoplasia. Our study suggests that *in vivo* delivery of stemness genes in somatic cells in pathologic loci is a feasible approach for tissue regeneration. The target cells could proliferate and differentiate more efficiently due to the native identity and microenvironment. *In vivo* gene delivery may hold promise for the future treatment of lung diseases such as ARDS or COPD.

Recent Publications

1. S Y Hong, Y R Kao, T C Lee and C W Wu (2018) Upregulation of E3 ubiquitin ligase CBLC enhances EGFR dysregulation and signaling in lung adenocarcinoma. *Cancer Res*. DOI: 10.1158/0008-5472.CAN-17-3858.
2. T F Lee, Y C Tseng, W C Chang, Y C Chen, Y R Kao, T Y Chou, C C Ho and C W Wu (2017) YAP1 is essential for tumor growth and is a potential therapeutic target for EGFR-dependent lung adenocarcinomas. *Oncotarget* 8(52):89539-89551.
3. K C Wen, P L Sung, Y T Chou, C M Pan, P H Wang, O K Lee and C W Wu (2017) The role of EpCAM in tumor progression and the clinical prognosis of endometrial carcinoma. *Gynecol Oncol*. DOI: 10.1016/j.ygyno.2017.11.033.
4. S H Hsiao, Y T Chou, S E Lin, R C Hsu, C L Chung, Y R Kao, H E Liu and C W Wu (2017) Brain metastases in patients with non-small cell lung cancer: the role of mutated-EGFRs with an exon 19 deletion or L858R point mutation in cancer cell dissemination. *Oncotarget* 8(32):53405-53418.
5. T W Lin, M T Chen, L T Lin, P I Huang, W L Lo, Y P Yang, K H Lu, Y W Chen, S H Chiou and C W Wu (2017) TDP-43/HDAC6 axis promoted tumor progression and regulated nutrient deprivation-induced autophagy in glioblastoma. *Oncotarget* 8(34):56612-56625.

Biography

Cheng-Wen Wu is an Academician of Academia Sinica, and Distinguished Chair Professor of National Yang-Ming University in Taiwan. He was a pioneer in biophysical approach to molecular biology, best known for his work on presenting biophysical evidence of the 4-step mechanism of gene transcription, and the discovery of the presence of zinc ions in eukaryotic transcription factor TFIIIA, the first example for the class of proteins known as zinc finger proteins. After returning to Taiwan, he made many important contributions to the studies of cancer metastasis in lung cancer, and of acute and chronic lung injuries such as ARDS and COPD, two of the serious health threats to the Taiwanese population, with important clinical significances. Recently, he is interested in applying stemness concept for analyzing tumor progression in lung cancer as well as gene and stem cell therapies of lung injuries. He has published over 264 scientific articles in international journals and has won numerous prestigious scientific awards.

ken@ibms.sinica.edu.tw