中文題目:從動物實驗到臨床研究尋找與食道癌的臨床診斷和分期相關之創新基因

英文題目: Identification of novel genes associated with the diagnosis and staging of esophageal cancer through in-vivo and human studies

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Background: This study aims to identify the novel and potential upregulated genes related to secretionary or membranous proteins for the clinical diagnosis and staging of esophageal squamous cell carcinoma (ESCC).

Methods: By combining microarray-based screening, which contained at least 25,000 DNA oligonucleotide probes, of esophageal tumors from both N-nitrosomethylbenzylamine- and arecoline-induced F344 rats and 17 human ESCC specimens, we further confirmed the potential candidate genes by tissue arrays in 243 cancer tissues and 126 normal tissues of esophagus from Taiwan, Korea, and USA and by ELISA in 78 serum specimens of ESCC patients from Taiwan.

Results: Four candidate genes, including *ATP1A1*, *SPINT2*, *CMTM8*, and *AGR2*, were chosen due to their up-regulation in more than half of 17 paired tissues from 17 ESCC patients in the microarray-based screening. The four genes were verified by RT-PCR and immunohistochemical (IHC) staining in ESCC tissue specimens and only ATP1A1 (ATPase Na+/K+ transporting alpha 1 polypeptide) expression was consistent and further studied. Among the 243 cancer tissues and 126 normal tissues of esophagus, we found that the positive expressions of ATP1A1 by IHC staining were 207 (85%) of 243 in cancer tissues and 88 (70%) of 126 in normal tissues. After adjusted for age and sex, ATP1A1 overexpression had a 3.2-time (95% CI = 1.8-5.6) to be likely in cancer tissues than in normal tissues. ATP1A1 expression was also correlated to the tumor stage by IHC staining. Using the median level of 1,465.0 pg/mL of serum ATP1A1 protein expression as the cut-off point, we found that patients with stage III-IV had a 2.91-fold (1.12-7.36) likely to have high serum ATP1A1 levels than those with stage I-II after adjusting for age and sex.

Conclusion: ATP1A1 overexpression may serve as a potential noninvasive marker of the clinical diagnosis and staging for ESCC patients.