

2008 AACR Annual Meeting**April 12-16, 2008****San Diego, CA**[Print this Page for Your Records](#)[Close Window](#)

Abstract Number: 3957

Session Title: Proteomic Tumor Profiling 2

Presentation Title: Protein assessment upon premetastatic niches of NSCLC by both FFPE direct tissue proteomics and SRM MS-based validation assay

Presentation Start/End Time: Tuesday, Apr 15, 2008, 8:00 AM -12:00 PM

Location: Exhibit Hall B-F, San Diego Convention Center

Poster Section: 27

Poster Board Number: 10

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A retrospective clinical proteomic analysis was conducted using formalin-fixed paraffin-embedded (FFPE) tissues in order to investigate molecular profiles of NSCLC stages IA and IIIA, and to assess key proteins relating to premetastatic niches at mediastinal lymph nodes and the disease progression.

Archived FFPE samples were obtained from 13 patients received excision operations for lung cancer patients (during 2003 ~ 2004 at Tokyo Medical Univ. Hospital). FFPE tissues were placed on DIRECTOR™ slides followed by de-paraffin with xylene, and were stained only by hematoxylin. Tumor cells were collected by laser microdissection. Proteins were extracted with the Liquid Tissue® technology and digested with trypsin. The samples were subjected to LC-MS based proteomic analysis. LC-MS data were then processed by label-free semi-quantitative comparison with both the spectral counting method and ion-signal based statistical approaches. Candidate molecules of interest were subjected to their verification and validation using MS-based biomarker assays by selected reaction monitoring (SRM) mass spectrometry.

Semi-quantitative analyses led to candidates of about 40 molecules distinguishing IA and IIIA stages. Secretory proteins up-regulated are especially interesting, which include S100A9, A100A8, Secreted cement gland protein XAG-2 homolog (AGR2), and Dermcidin (DCD), Neutrophil defensin 1 (HNP-1), Mesotrypsinogen, and α -1 protease inhibitor.

Verification was performed using SRM quantitative mass spectrometry (MS-based assay). DCD and AGR2 were found to increase at the IIIA stage, and S100A9 has a quite high expression at metastatic tumors at lymph nodes although it is low at both IA and IIIA primary tumors. SRM assay for Napsin-A (NAPSA) revealed that its expression considerably drops at IIIA stage and was found to be surprisingly low for the IIIA patients known to be already dead when the prognosis was checked.

A tentative diagnostic model was constructed using the multiplex SRM MS-based assays for S100A9, DCD, AGR2, and NAPSA, and showed 83.3% sensitivity, 85.7% specificity, and positive predictive value 83.3%. A receiver operating curve (ROC) of this model demonstrated a good performance. .

Survival rates were tentatively calculated for 34 months with and without expression of S100A9, DCD, AGR2, and NAPSA. NAPSA (+) patients were found to be survived at almost 100% in contrast that the survival rate of NAPSA (-) patients dramatically dropped to 0% in 22 months.

Clinical proteomics using FFPE tissues with already known clinical outcomes is a promising approach to

investigate molecular profiles of cancer, and to capture molecular candidates for diagnostic biomarkers. MS-based assay is the powerful tool along a proof-of-concept strategy and MS-based assays would be of major use at the clinical stage.

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