

Identification of subtype-specific glycoproteins from ovarian tumors

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ABSTRACT

Ovarian cancer is the most lethal gynecologic malignancy with epithelial ovarian tumors comprising ninety percent of ovarian tumors in adult women. The origin of epithelial ovarian tumors are heterogeneous and can be subclassified histologically into serous, mucinous, endometrioid, clear-cell, transitional-cell types, squamous cell, mixed, and undifferentiated subtypes. Different subtypes of ovarian tumors have differences in clinical outcome and response to chemotherapy. Understanding the molecular basis of these subtypes of ovarian tumors is increasingly important in understanding and predicting responses to targeted biological therapeutic agents. Therefore, the direction of ovarian cancer biomarkers discovery for therapy would be toward the subtypes with early stage diagnosed cancers.

In this study, we identified glycoproteins specific for different subtypes of ovarian tumors and determined their tissue-specificity. The glycoproteins from seven subtypes of ovarian tumors and normal control ovarian tissues were isolated from three individuals separately using solid-phase extraction of glycopeptides isolation method. The isolated glycopeptides were analyzed by quantitative proteomic analysis method using the LC-MS and LC-MS/MS data generated by ESI-QSTAR. In addition, spectral count quantitation from LC-MS/MS data generated by multiple analyses using LTQ was also employed to increase the confidence of identification and quantification. The results were validated by targeted quantitative proteomic approach, selected reaction monitoring (SRM), which has high sensitivity and selectivity.

The results from this study allowed us to determine around 1000 *N*-linked glycosylation sites from cancer tissues and identify subtype-specific glycoproteins for ovarian tumor. This will facilitate the understanding of molecular mechanism of ovarian cancer subtypes and differentiate them in molecular level. The results also provide the candidate glycoproteins as molecular basis for detection and treatment of different ovarian tumors and further development and validation are required for clinical usage.