

## Affinity Proteomic Plasma Analysis of Small Intestinal Neuroendocrine Tumors

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**Background:** Small intestine neuroendocrine tumor (SI-NET) patients mainly receive diagnosis at the metastatic stage of disease, which lacks curative treatment. An antibody suspension bead array, utilizing the large repertoire of antibodies developed within the Human Protein Atlas (HPA), was used to profile proteomic signatures in blood of SI-NET patients and healthy individuals aiming at utilizing such profiles as diagnostic signatures for SI-NETs.

**Methods:** After an initial screening for putative biomarkers using 184 different HPA antibodies in an initial patient cohort, 20 antigens were selected for validation in a second independent cohort. Selection was based on two criteria, statistical significance, using different univariate and multivariate methods and consistency between experiments. The second cohort consisted of 36 healthy cancer-matched controls, 30 primary-tumors, 42 lymph-node-metastases and 42 liver-metastases. In addition, the study included 34 healthy inflammatory-bowel-diseases- (IBD)-matched controls and 31 IBD patient samples.

**Results:** The first cohort was assayed thrice using an SBA targeting 184 antigens. Proteins that could consistently distinguish healthy individuals and cancer patients using Mann-Whitney U tests as well as Between Group (BGA) and Random Forest Analysis (RF) were selected. Following the initial screening, an independent sample cohort was assayed for 20 different proteins that emerged as significant.

Our findings demonstrated that four targets, insulin-like growth factor 1 (IGF1), interleukin-1 alpha (IL1a), mastermind-like protein 3 (MAML3) and SH3KBP1-binding protein 1 (SHKBP1) were able to distinguish between controls and cancer patients at different stages as well as IBD patients. When proteins were combined in a multivariate classification model they were able to perform with 80% classification accuracy.

**Conclusion:** With the identification of 4 novel targets our future goal is to further evaluate the selected proteins as novel blood biomarkers for SI-NETs and IBDs. Immunohistochemistry and ELISA analyses are currently ongoing to clarify the proteins' function in SI-NETs at different stage of disease.