hPG80 (Progastrin)
A Novel Blood-Based Biomarker for Detection of Neuroendocrine Neoplasms

BACKGROUND
Current blood-based biomarkers for neuroendocrine neoplasms (NENs) lack both sensitivity and specificity. This is especially true for high-grade NENs (small and large cell neuroendocrine carcinomas). hPG80, progastrin, is a novel bio-marker which is easily measured in plasma using an ELISA test. Recently discovered to be elevated in colorectal (Fig.1)1, gastro-esophageal, hepatic and pancreatic adenocarcinoma, this study is the first to explore hPG80 in NENs. In a normal physiological state, hPG80 is a precursor protein to hormone gastrin and comprises of 80 amino acid. Overexpression of GAST gene in neoplastic tissue has been implicated in elevated hPG80. Since GAST is a target of Wnt/B-catenin/Tcf4 pathway, it is not surprising that hPG80 is elevated in various solid tumors.

METHODS
hPG80 concentrations were quantified in plasma from 95 patients with mainly stage IV NEN using DxPG80 technology (ECS Progastin, Switzerland) and compared with hPG80 concentrations in 50-80 year old (n=252) and 18-25 year old (n=137) healthy donors.

RESULTS
The median hPG80 in NENs patients was 5.54 pM (IQR 2.07-17.11 pM) as compared to 1.5 pM (IQR 0.60-3.09 pM) for patients in the 50-80 year old control group and 0.29 pM (IQR 0.00-1.27 pM) for patients in the 18-25 year old cohort (p<0.0001, two-tailed Mann-Whitney U-test). A subgroup analysis of NENs revealed a median hPG80 of 3.54 pM (IQR 2.02-19.91 pM) in neuroendocrine carcinoma (NEN n=25) and 5.8 pM (IQR 1.91-16.74 pM) in neuroendocrine tumor (NET n=70). Interestingly, small cell lung cancer sub cohort (n=13) also showed significant elevation of hPG80 with a median at 9.09 pM (IQR 2.66-25.33 pM). All the above-mentioned differences were statistically significant as compared to healthy controls. Diagnosis accuracy estimated by the ROC AUCs is 0.89 for all NENs, 0.97 for NETs and 0.92 for NECs when compared to the young 18-25 yo control group and 0.75 for all NENs, 0.74 for NETs and 0.75 for NECs when compared to the old 50-80 yo control group.

CONCLUSION
Plasma hPG80 in NENs suggests hPG80 may be a diagnostic blood biomarker for both low- and high-grade NENs and further study is warranted. A prospective multicenter clinical trial is ongoing in Neuroendocrine Tumors to evaluate its role in monitoring of disease (NCT04750954).

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