

hPG80 (Progastrin)

A Novel Blood-Based Biomarker for Detection of Neuroendocrine Neoplasms

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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/ β -catenin/Tcf4 pathway, it is not surprising that hPG80 is elevated in various solid tumors.

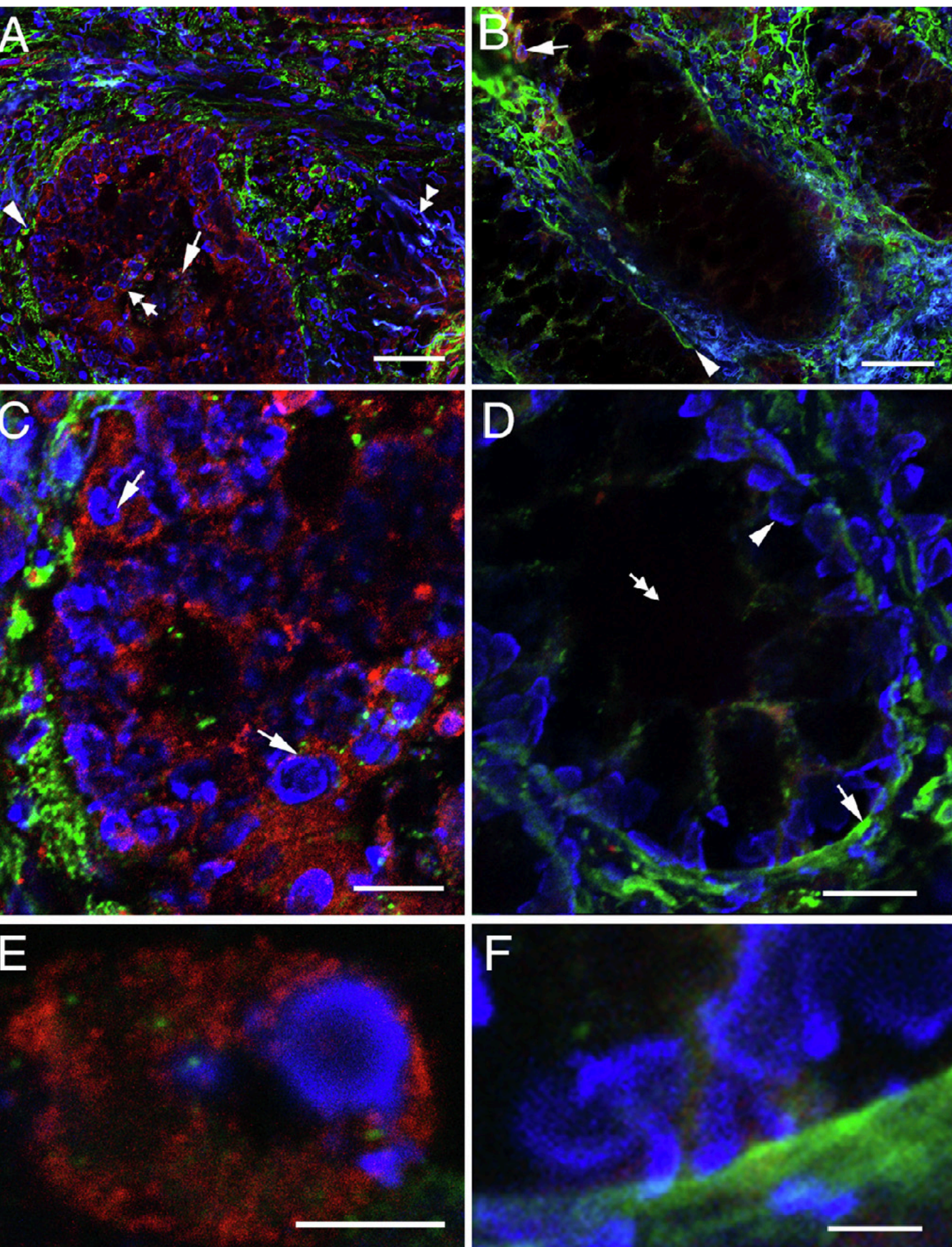


Figure. 1. High expression of hPG80 by tumor cells from colorectal cancer. **(A)** Confocal image of a tumoral mass showing high expression of hPG80 in colon cancer (patient 6607). The tumor cells expressing hPG80 were visualized with IHC for hPG80 (red). The hPG80-immunoreactive cells were often clustered into masses (arrow) into low-differentiated glands surrounded by disrupted basement membranes (arrowhead, HSPG-immunoreactivity, green). The double arrowhead indicates autofluorescence in the connective tissue (blue), which contrasts with cell nuclear counterstaining with bisbenzimidazole (blue, double arrow).

(B) The tissue peripheral to the tumor mass showed scarce hPG80-immunoreactive cells in the connective tissue (arrow) and linear basement membranes (arrowhead). **(C)** Magnified field of the area indicated by an arrowhead in (A) showing the perinuclear location of hPG80-immunoreactivity (arrows). **(D)** Magnified field of the peripheral tissue showing the linear basement membrane (arrow), nuclei of epithelial cells (arrowhead) and the lumen of the gland (double arrow). **(E)** Highly-magnified field showing one cell and the cytoplasmic localization of hPG80. **(F)** Absence of hPG80-immunoreactive cells in the peripheral tissue. Scale bars: A and B: 50 mm; C and D: 20 mm; E and F: 5 mm.¹

Reference:
1. B. You, Alexandre Prieur, et al. / EBioMedicine 51 (2020) 102574

METHODS

hPG80 was quantified in the plasma from 31 patients using DxPG80 technology (ECS-Progastrin, Switzerland). Progastrin concentrations in 18-70 YO (n=557) and 18-25 YO (n=137) healthy blood donors were compared to 31 stage IV NEN patients.

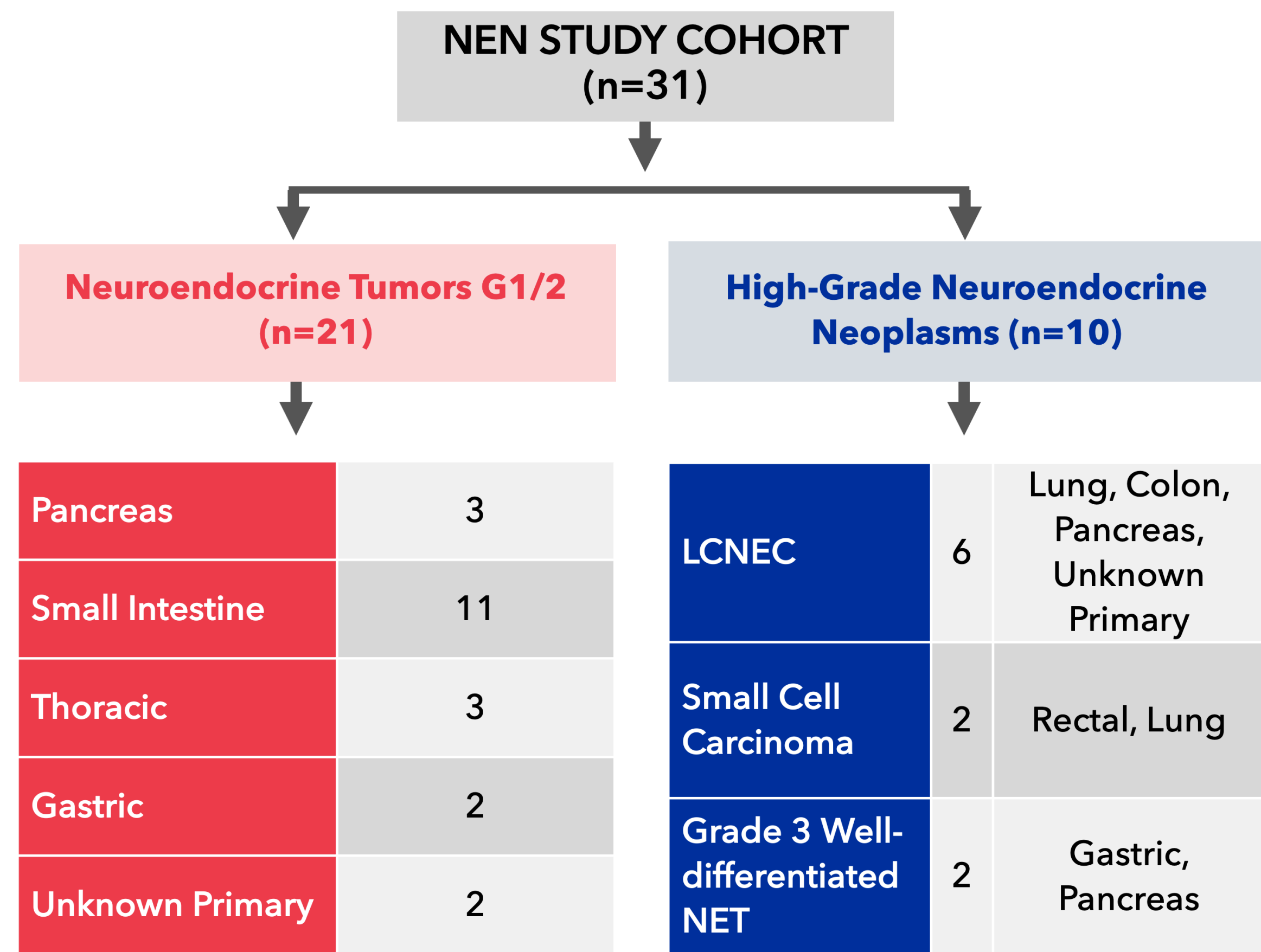


Figure 2. Study cohort demographics.

RESULTS

Mean hPG80 in NENs was 14.17 pM as compared to 2.04 pM and 0.99 pM in 18-70 and 18-25 YO control groups (p<0.0001), respectively. Subgroup analysis of NENs revealed mean hPG80 of 24.61 pM in high-grade NENs (n=10) vs 10.88 pM in G1/2 NETs (n=21).

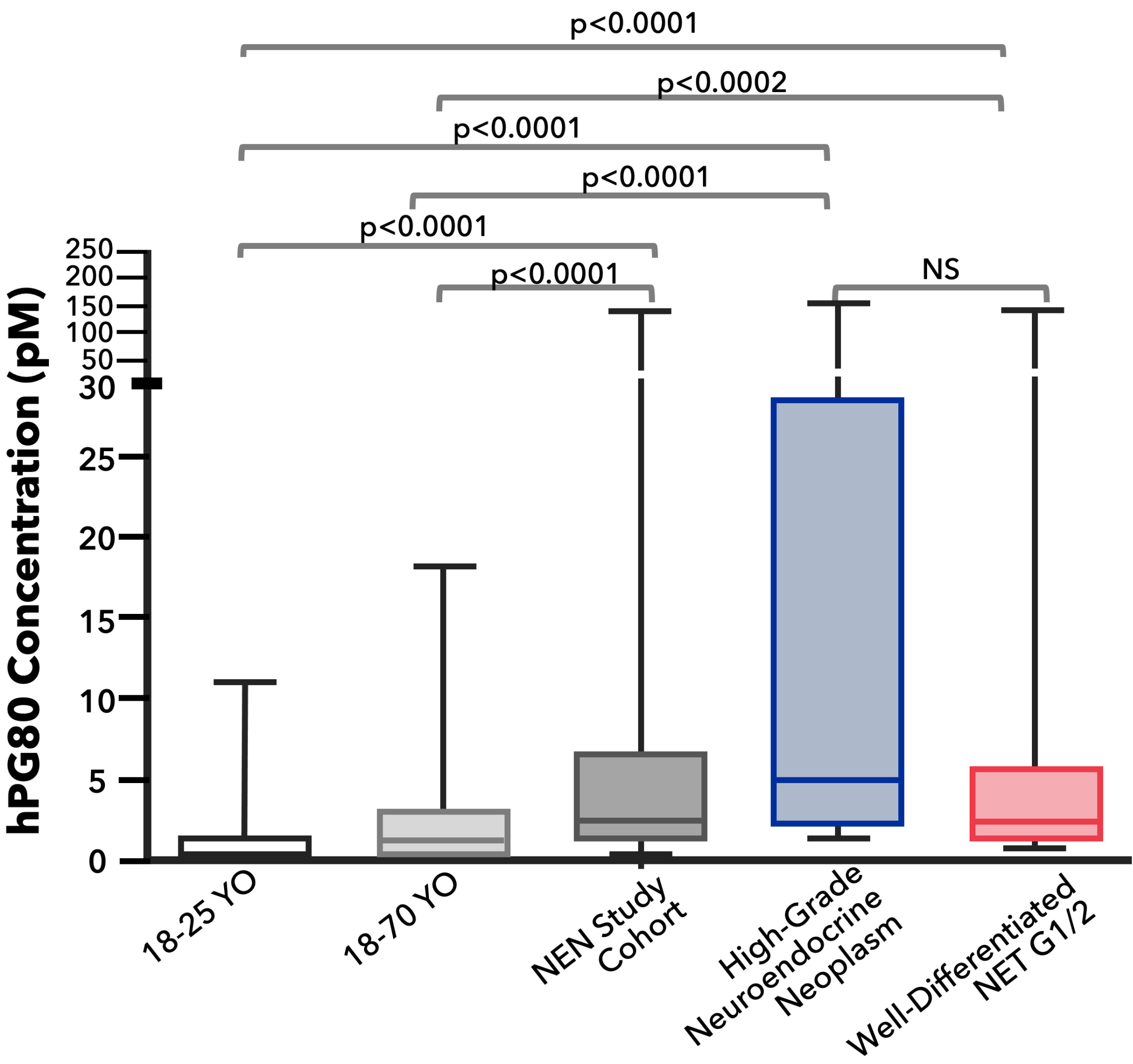


Figure 3. Box-Whisker plots comparing progastrin in neuroendocrine neoplasm patients vs. healthy cohorts (18-25 YO, 18-70 YO). (p<0.0001)

	18-25 YO	18-70 YO	NEN Study Cohort	High-Grade Neuroendocrine Neoplasm	NET G1/2
N=	137	557	31	10	21
Minimum	0.000	0.000	0.050000	1.360	0.5300
25 Percentile	0.000	0.000	1.250	2.210	1.130
Median	0.2000	1.050	2.450	4.765	1.970
75 Percentile	1.070	2.925	6.300	28.69	5.440
Maximum	11.06	18.10	142.1	154.1	142.1
Range	11.06	18.10	142.0	152.7	141.6
Mean	0.9931	2.043	14.17	24.61	10.88
Std. Deviation	1.876	2.695	33.02	46.96	30.76
Std. Error of Mean	0.1603	0.1142	5.931	14.85	6.713

Table 1. Data Table of progastrin in neuroendocrine neoplasm patients vs. healthy cohorts

CONCLUSION

This first-ever study of plasma hPG80 in NENs suggests hPG80 may be a diagnostic blood-based biomarker in both low and high-grade NENs and further study is warranted. A prospective trial is ongoing in small cell lung cancer to evaluate its role in monitoring of disease (NCT03958045) and further studies in low-grade NETs are underway.

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