Background

- Approximately 30% of paragangliomas (PGL) and pheochromocytomas (PCC) have a hereditary basis.
- Multi-gene hereditary cancer panel testing for PGL/PCC has become increasingly more common than single-gene testing algorithms.
- We describe the spectrum of pathogenic and likely pathogenic (PV/LPV) variants identified at a clinical laboratory after a year of offering a PGL/PCC panel.

Methods

- We performed a retrospective review of clinical and molecular data for all PGL/PCC panels ordered between January 2016 and February 2017.
- The PGL/PCC panel includes NGS and/or exon-level deletion/duplication analysis of SDHA, SDHB, SDHC, SDHD, SDHAF2, TMEM127, MAX, VHL, FH, RET, MEN1, and NF1. (NGS only was performed on SDHA and RET.)
- Variants were classified based on the AMP/ACMG guidelines for variant classification (Richards 2015).

Results

- Among 160 probands tested for PGL/PCC panels, 34% (n=55) had a PV/LPV.
- The positive test yield was 46% (40/87) for probands with PGL and 18% (10/56) for probands with PCC. (Figure 1)
- PV/LPV were identified in all genes on the panel except for SDHAF2, FH, or NF1. (Figure 1)
- Average age at tumor diagnosis was lower for probands testing positive than those without PV/LPV for both PGL (39±18 vs 43±16) and PCC (34±14 vs 43±17).

Conclusions

- Our data are consistent with recent estimations that approximately 30% of PGL/PCC are caused by germline PV/LPV.
- This data supports previous recommendations that patients with PGL/PCC undergo testing regardless of age at diagnosis or family history.

References