Title: Hereditary Paraganglioma-Pheochromocytoma Syndromes *GeneReview* - Mutations in *SDHB*, *SDHC*, and *SDHD*
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Summary of Reports of Mutations in *SDHB*, *SDHC*, and *SDHD* in Different Populations

- Of 56 individuals with familial PGL/PCC or other syndromes discussed in the Differential Diagnosis section (i.e., neurofibromatosis [NF], von Hippel-Lindau disease, and multiple endocrine neoplasia type 2 [MEN2]), 12 (21.4%) had mutations in *SDHB* or *SDHD* [Amar et al 2005]. In central Europe and the US, *SDHD* and *SDHB* mutations occur in roughly equal proportions, whereas SDHC mutations are rare [Baysal et al 2002, Neumann et al 2004, Schiavi et al 2005].
- In a German and Polish registry of individuals with PGL/PCC with either a *SDHD* or *SDHB* mutation, mutations in *SDHB* and *SDHD* were detected in equal proportions [Neumann et al 2004]. Approximately 12% of individuals with pheochromocytoma or paraganglioma from a German and Polish registry, without known family histories or evidence of other syndromes in which PGL/PCC can be seen (i.e., NF, von Hippel-Lindau syndrome, and MEN2), had a germline mutation in *SDHD* or *SDHB*. Mutations in *SDHB* and *SDHD* were detected in equal proportions [Neumann et al 2004]
- In ten US families with skull base and neck paraganglioma, *SDHD* mutations were found in five (50%) and *SDHB* mutations in two (20%); two *SDHD* mutations (5%) and one *SDHB* mutation (3%) were detected among 37 simplex cases [Baysal et al 2002].
- In 445 individuals from a large French registry with PGL/PCC, germline mutations were found in 54.4% of cases (29.2% in *SDHD*, 21.6% in *SDHB* and 3.6% in *SDHC*). Mutations were found in 99% of cases with a positive family history, and in 16.3% of cases that were apparently sporadic [Burnichon et al 2009].
- In a decade-long French study (2001-2010), of 1620 index cases of PGL/PCC, a germline mutation was found in 22.4% of cases (37.7% in *SDHB*, 27.5% in *SDHD*, 17.6% in *VHL*, 8.3% in *SDHC*, 6.3% in *RET*, 1.9% in *TMEM127*, 0.55% in *SDHA* and none in *SDHAF2*. Overall, a germline mutation was found in 44.7% of patients with a suspected hereditary PGL/PCC, and 8% of patients with an apparently sporadic PGL/PCC [Buffet et al 2012]. Among 314 French persons with pheochromocytomas or extra-adrenal sympathetic paragangliomas, 10% had a germline mutation in *SDHD* or *SDHB* [Amar et al 2005].
- In 316 individuals with PGL/PCC, a germline mutation in *SDHA* was found in 1.6% of all, and 3% of apparently sporadic cases [Korpershoek et al 2011].
- Of 242 cases of PCC and 201 cases of skull base & neck PGLs that tested negative for known susceptibility genes, no germline mutations were detected in *SDHAF2* [Bayley et al 2010]. The same group found the *SDHAF2* Gly78Arg mutation in a Spanish kindred with skull base and skull base PGLs, that had also previously been reported in a Dutch kindred [Hao et al 2009].
- Fourteen of 34 (41%) Australian individuals with skull base and neck paragangliomas had mutations in *SDHD* (79%) or *SDHB* (21%), including 10/11 of the familial cases (91%) [Badenhop et al 2004].

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