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].
References


