Hereditary paraganglioma (PGL)

Anne-Paule Gimenez-Roqueplo

Département de Génétique Moléculaire, Hôpital Européen Georges Pompidou, 20-40, rue Leblanc, 75908 Paris cedex 15, France (APGR)

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Identity

Alias
Familial nonchromaffin paragangliomas; Familial glomus tumors; Chemodectomas; Carotid body tumors; Glomus jugulare tumors

Inheritance
Follows an autosomal dominant pattern. This pattern is associated with a maternal genomic imprinting for SDHD gene 35% of head and neck paragangliomas are inherited.

Clinics

Phenotype and clinics
Paragangliomas are highly vascularized tumors derived from neuroectodermal cells. In the familial forms, they are preferentially localized in the head and neck, in the carotid body (80%) and in the glomus jugulare (20%). They may be associated with other neural-crest-derived tumors such as pheochromocytomas. Individuals with familial paragangliomas have a more severe presentation (early age at onset and tumors at multiple sites) than do those with sporadic disease.

Neoplastic risk
Tumors are usually benign. Their gravity result of local invasion and important vascularisation. Among 10% of paraganglioma have a malignant evolution.

Treatment
Early detection and surgery.

Prognosis
Depends on extent of the disease at the time of diagnosis.

Genes involved and proteins

SDHD
Alias
SDH4
Location
11q23
DNA/RNA
Description: 4 exons
Protein
Description: The corresponding protein has 159 amino acids (17 kDa). The 1 to 56 amino acids encode the transit peptide and the 57 to 159 amino acids the mature protein.
Expression: Wide.
Function: SDHD encodes a mitochondrial respiratory-chain protein of complex II called "cybS"or small subunit of cytochrome b in succinate-ubiquinone oxidoreductase.
Mutations
Germinal: Germ-line mutations in PGL patients are heterozygous and lead to protein truncation (false-sense mutations, insertions and deletions). Missense mutations are also described.
Somatic: Loss of wild type allele was usually observed in accordance with the two-hit model for neoplasia.

SDHC
Alias
SDH3
Location
1q21
**DNA/RNA**

**Description:** 7 exons

**Protein**

**Description:** 140 amino acids (15 kDa)

**Expression:** Wide

**Function:** SDHC encodes a mitochondrial respiratory-chain protein of complex II called "cybL" or large subunit of cytochrome b in succinate-ubiquinone oxidoreductase. This protein participates with cybS to the anchorage of the complex II in the inner mitochondrial membrane.

**Mutations**

**Germinal:** Destruction of start codon ATG by a G-to-A transition in exon 1 of SDHC.

**Somatic:** Loss of wild type allele in tumor DNA.

**SDHB**

**Alias**

SDH1

**Location**

1p36.1-p35

**DNA/RNA**

**Description:** 8 exons

**Protein**

**Description:** 252 amino acids (27 kDa)

**Expression:** Wide

**Function:** SDHB encodes a mitochondrial respiratory-chain protein of complex II called iron-sulfur protein. This protein participates with the flavoprotein, encoded by SDHA gene, to the enzymatic reaction which proceed to the oxydation of succinate in fumarate coupled with the reduction of ubiquinone to ubiquinol.

**Mutations**

**Germinal:** Missense mutation leading to protein truncation.

**Somatic:** Not determined.

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**References**


This article should be referenced as such: