Gene	Locus	Associated Syndrome(s)	Inheritance	Penetrance	PCC or PGL	Bilaterality or Multifocality	Metastatic Potential	Biochemical Phenotype	Associated Features
Cluster 1A									
SDHA	5p15.33	PGL5, CSS, 3PA	AD	Less than 5%	PGL	More data needed	Up to 70%	NA or DA	ccRCC, GIST*, PC*, PA**
SDHB	1p36.13	PGL4, CSS, 3PA	AD	30-40%	PGL, sometimes PCC	Commonly multifocal, rarely bilateral adrenal	Up to 75%	NA or DA	ccRCC, GIST*, PC*, PA**, NB
SDHC	1q23.3	PGL3, CSS, 3PA	AD	< 10%	PGL, sometimes PCC	More data needed	Rare	NA or DA	ccRCC, GIST*, PC*, PA**
SDHD	11q23.1	PGL1, CSS, 3PA	AD, paternal	90% if paternal inheritance	PGL, sometimes PCC	More data needed	15-20%, more data needed	NA or DA	ccRCC, GIST*, PC*, PA**
SDHAF2	11q12.2	PGL2	AD, possibly paternal	More data needed	PGL	More data needed	More data needed	NA or DA	
FH	1q43	Also in HLRCC	AD	About 1-3%	Both	Moderate	Moderate/high	NA	HLRCC: cutaneous and uterine leiomyoma, type 2 papillary RCC
IDH1/2	2q34 (IDH1), 15q26.1 (IDH2)	Also in Ollier disease and Maffucci syndrome	Mosaic	Variable by mosaicism	PGL	More data needed	More data needed	More data needed	Enchondromas, chondrosarcomas, spindle cell hemangiomas, many other soft tissue sarcomas
SLC25A11	17p13.2	PGL6	AD	More data needed	PGL	More data needed	High	NA	
DLST	14q24.3	PGL7	AD	More data needed	PGL, sometimes PCC	Likely moderate to high, more data needed	Likely low, more data needed	NA	PA (prolactinoma) and endometrial carcinoma (single reports)
Cluster 1B									
VHL	3p25.3	von Hippel-Lindau syndrome	AD	10-30%	PCC, PGL is rare	50%	5-7%	NA	Retinal angiomas, CNS HB, RCC, PNET, ELST, cystic lesions (pancreatic, uterine broad ligament, or epididymal)
EPAS1 (HIF2A)	2p21	Pacak-Zhuang syndrome	Mosaic, rarely AD (germline)	Variable by mosaicism; unknown (germline)	PGL, sometimes PCC	100% (somatic)	> 50% (somatic)	NA	Polycythemia, duodenal ampullar somatostatinoma, ocular anomalies, CNS venous anomalies, CCHD
Cluster 2									
RET	10q11.21	Multiple endocrine neoplasia, type 2A	AD	50%	PCC, rarely PGL	50-80%	< 5 %	A	MTC, hyperparathyroidism, Hirschsprung disease, and cutaneous lichen amyloidosis
RET	10q11.21	Multiple endocrine neoplasia, type 2B	AD, 75% *de novo*	50%	PCC, rarely PGL	50-80%	< 5 %	A	MTC, marfanoid habitus, (sub)mucosal and other (ganglio)neuromas
NF1	17q11.2	Neurofibromatosis type 1	AD, 50% *de novo*	Up to 13% (may be asymptomatic)	PCC, rarely PGL	16%	7%	A	Cafe-au-lait spots, axillary or inguinal freckling, Lisch nodules, optic pathway glioma, peripheral nerve sheath tumors, neurofibromas, astrocytoma, medullary thyroid cancer, carcinoid tumors, spina bifida, scoliosis
TMEM127	2q11.2		AD	33%	PCC	25% bilateral adrenal	Low	A	
MAX	14q23.3	Some cases of 3PA	AD, possibly paternal	More data needed	PCC, sometimes PGL	Frequently bilateral adrenal as well as multifocal	Around 10%	A	Ganglioneuroma, NB, PA**, parathyroid adenoma, chondrosarcoma, and pulmonary adenocarcinoma
HRAS	11p15.5		Sporadic	More data needed	PCC, rarely PGL	Low	More data needed	S	Ganglioneuroma
H3F3A	1q42.12		Mosaic	More data needed	PCC, PGL	Present, limited reports	More data needed	More data needed	Giant cell tumors of bone

Table 1. Genes and features of pheochromocytoma and paraganglioma-associated syndromes. Genetic and clinical features of genes described for PPGL syndromes, modified from Pacak 2022 (10). CCHD, cyanotic congenital heart disease; CNS, central nervous system; CSS, Carney-Stratakis syndrome; ELST, endolymphatic sac tumor; HB, hemangioblastoma; HLRCC, hereditary leiomyomatosis and renal cell carcinoma; MTC, medullary thyroid carcinoma; NB, neuroblastoma; PA, pituitary adenoma; PC, pulmonary chondroma; PNET, pancreatic neuroendocrine tumor; ccRCC, clear cell renal cell carcinoma; GIST, gastrointestinal stromal tumor; PCC, pheochromocytoma; PGL, paraganglioma; NA, noradrenergic; DA, dopaminergic; A, adrenergic; *Associated with Carney-Stratakis syndrome or Carney triad. **Included in three P Association (3PA).