

Epigenetic and metabolic rewiring in metastatic pheochromocytomas and paragangliomas driven by *SDHB* mutations

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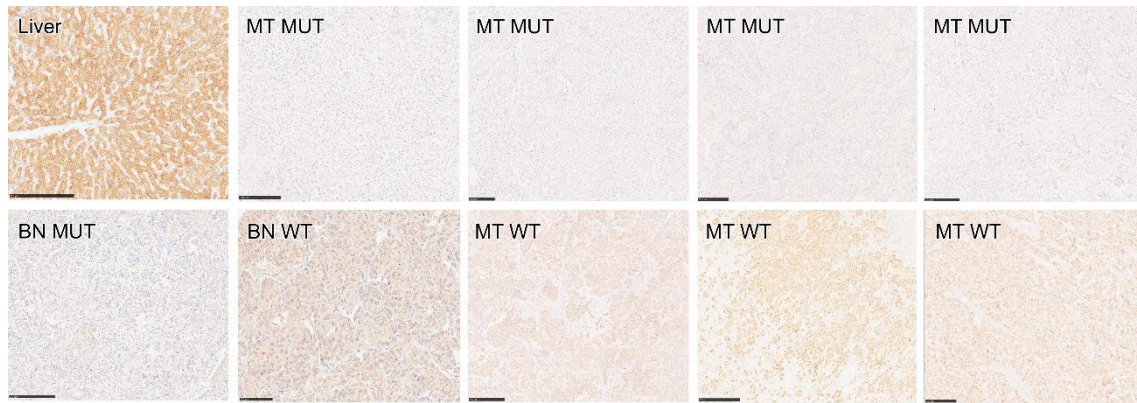
Supplementary data

Supplementary Table S1. Clinical features of PPGL samples for cell line derivation

ID	Age	Sex (F/M)	Tumor location	Mutation *	Additional tumors	Metastasis
PGLa	71	F	vagal paraganglia	none	NET # (pancreas)	no
PCC	46	F	adrenal gland	none	no	no
PGLb	15	F	carotid body	SDHD	no	no
AG	63	M	none	not studied	no	no

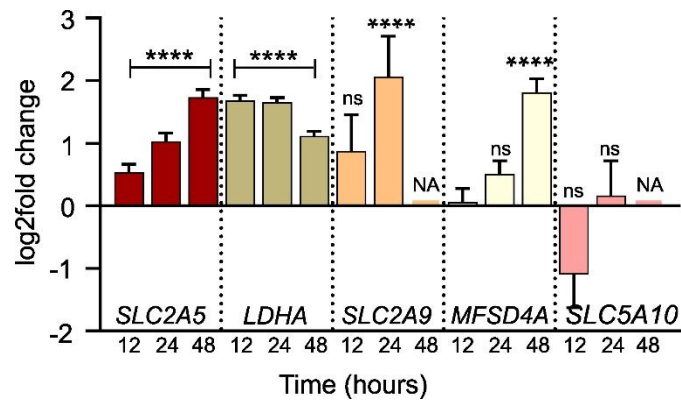
*PPGL susceptibility genes

#Neuroendocrine tumor



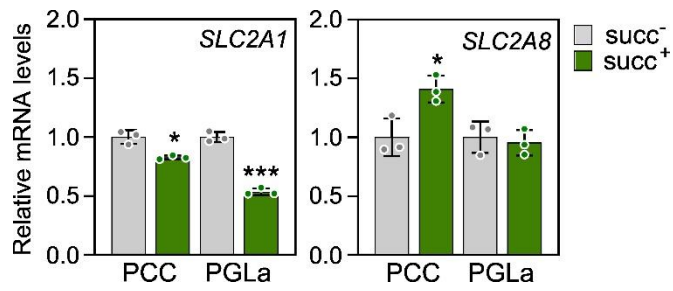
Supplementary Figure S1. Immunohistochemical staining of SDHB in PPGL samples.

Representative SDHB immunohistochemistry in PPGL tissue sections. Loss of SDHB protein expression is observed in *SDHB*-mutated metastatic tumors (MT MUT) and benign tumors (BN MUT), while *SDHB*-wild-type tumors (MT WT and BN WT) show preserved cytoplasmic granular staining. Normal liver tissue was included as a positive control. Scale bars = 100 μ m.



Supplementary Figure S2. Time-course induction of carbohydrate transport-related genes in response to hypoxia in PC12 cells (RNA-seq).

PC12 cells were exposed to hypoxia (1% O₂) and RNA-seq data from a previously published dataset were re-analyzed to quantify temporal changes in the expression of *SLC2A5* and related metabolic transporters. Bars represent log₂-fold change relative to normoxic control. Statistical significance: ****P < 0.0001; ns, not significant; NA, expression not detected.



Supplementary Figure S3. Differential expression of glucose/fructose transporters in succinate-exposed PCC and PGL cell models.

Relative mRNA levels of *SLC2A1* (GLUT1) and *SLC2A8* (GLUT8) measured by qRT-PCR in pheochromocytoma (PCC) and paraganglioma (PGL) primary cultures incubated with or without 1 mM succinate for 24 h. Data are shown as mean $\pm$ SEM. Data are shown as mean $\pm$ SEM; *P < 0.05, ***P < 0.001 (unpaired two-tailed t-test).