

**Table S 1: Statistical analyses of COX-2 status with regard to clinical characteristics and genetic background of tumors in two independent series of PPGL samples;** data in parentheses were calculated from low sample numbers ( $n < 7$ ); as Mann-Whitney  $U$  test showed significant sex-related differences in COX-2 immunoreactivity in tissue samples, multiple regression analyses was applied to distinguish whether the trends observed in the genetic subgroups were related to genetic background or different sex ratios only; levels of significance: \*  $P < 0.05$ ; †  $P < 0.01$ , ‡  $P < 0.001$

<b>COX-2 expression levels in RNA samples</b>			
<i>Mann-Whitney U tests</i>			<i>P</i> value
Sex	male vs. female		0.455
Malignancy	benign vs. metastatic		0.825
Tumor location	adrenal vs. others		0.486
	(adrenal + thoracic & abdominal) vs. others		(0.847)
	thoracic & abdominal vs. others		0.767
	(head & neck) vs. others		(0.010*)
<i>Pearson correlation</i>		<i>r</i>	<i>P</i> value
Age at diagnosis		-0.2119	0.088
Tumor diameter		-0.2201	0.197
Mutation	<i>VHL</i>	0.371	0.002†
	<i>SDHx</i>	0.098	0.419
	<i>SDHB</i>	-0.145	0.232
	( <i>SDHD</i> )	(0.252)	(0.035*)
	<i>EPAS1</i>	0.015	0.903
	( <i>NF1</i> )	(-0.207)	(0.086)
	<i>RET</i>	-0.267	0.025
	<i>HRAS</i>	-0.121	0.318
Transcriptional signature	cluster I	0.406	< 0.001‡
Origin of mutations	germline	0.03	0.804
<b>COX-2 immunoreactivity in tissue samples</b>			
<i>Mann-Whitney U tests</i>			<i>P</i> value
Sex	male vs. female		0.030*
Malignancy	benign vs. metastatic		0.775
Tumor location	adrenal vs. others		0.587
	thoracic & abdominal vs. others		0.673
	head & neck vs. others		0.273
<i>Pearson correlation</i>		<i>r</i>	<i>P</i> value
Age at diagnosis		-0.1606	0.124
Tumor diameter		-0.1677	0.127
<i>Multiple linear regression considering sex of the patients</i>		<i>r</i>	<i>P</i> value
Mutation	<i>VHL</i> ; male	0.328; 0.307	0.144; 0.053
	<i>SDHx</i> ; male	0.032; 0.318	0.842; 0.048*
	( <i>SDHA</i> ); male	(0.135); 0.317	(0.706); 0.049*
	<i>SDHB</i> ; male	0.081; 0.311	0.771; 0.056
	( <i>SDHC</i> ); male	(0.221); 0.324	(0.630); 0.044*
	<i>SDHD</i> ; male	0.867; 0.398	< 0.001‡; 0.007†
	( <i>SDHAF2</i> ); male	(0.253); 0.330	(0.528); 0.041*
	<i>EPAS1</i> ; male	-0.175; 0.300	0.576; 0.067*
	<i>NF1</i> ; male	0.298; 0.303	0.120; 0.056
	<i>RET</i> ; male	-0.948; 0.335	< 0.001‡; 0.026*
	( <i>HRAS</i> ); male	-0.130; 0.313	0.694; 0.052
Transcriptional signature	cluster I; male	0.159; 0.323	0.332; 0.043*
Origin of mutations	germline; male	-0.014; 0.319	0.928; 0.047*
<b>COX-2 histologic pattern in tissue samples</b>			
<i>Pearson correlation</i>		<i>r</i>	<i>P</i> value
Mutation	<i>VHL</i>	0.040	0.700
	<i>SDHx</i>	0.266	0.009†
	( <i>SDHA</i> )	(-0.057)	(0.582)
	<i>SDHB</i>	0.092	0.375
	( <i>SDHC</i> )	(0.137)	(0.182)
	<i>SDHD</i>	0.194	0.058
	( <i>SDHAF2</i> )	(0.084)	(0.414)
	<i>NF1</i>	-0.031	0.767
	( <i>HRAS</i> )	(-0.081)	(0.431)
	( <i>EPAS</i> )	(-0.190)	(0.065)
Transcriptional signature	cluster I	0.197	0.054
Origin of mutations	germline	0.242	0.018*