Human pheochromocytomas show reduced p27Kip1 expression that is not associated with somatic gene mutations and rarely with deletions.

Abstract:

Pheochromocytomas are neuroendocrine tumors arising in the neural crest-derived chromaffin cells of the adrenal gland or in extra-adrenal sympathetic ganglia (paragangliomas). In a rat model of multiple endocrine neoplasia (MEN), absence of functional p27Kip1 protein predisposes to pheochromocytoma and paraganglioma development. As no data is available regarding the involvement of p27Kip1 in human pheochromocytoma and/or paraganglioma, we set out to determine the expression pattern of p27Kip1 in those tumor types. A panel of 25 pheochromocytomas and 23 paragangliomas was collected. Two pheochromocytomas were from MEN2 patients. The paragangliomas included 15 tumors that developed at the carotid bifurcation, three in the jugulo-tymppanic area, and five at other sites. Except for the MEN2 cases, all others were apparently sporadic. Immunohistochemistry for p27Kip1 and the proliferation marker Ki67 was performed. We found that p27Kip1 expression is reduced/lost in 56% of pheochromocytomas, but only in 18.1% of paragangliomas. Downregulation of p27Kip1 was not associated with increased proliferation. Cases showing reduced/lost p27Kip1 expression were screened for the presence of somatic mutations in CDKN1B (p27Kip1) and for allelic imbalance at the p27Kip1 locus. Three cases had allelic
imbalance but none had mutations. In conclusion, pheochromocytomas display extreme reduction/loss of p27Kip1 expression at high frequency.