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## Biomarkers of paraganglioma metastatic potential identified

Overexpression of both vascular endothelial growth factor (*VEGF*) and a natural antisense form of hypoxia-inducible factor 1 $\alpha$  (*aHIF*) is associated with decreased metastasis-free survival in patients with paraganglioma (PGL), according to a study conducted at Radboud University Nijmegen Medical Centre, The Netherlands.

Paul Span and his research team set out to investigate the role of hypoxia-induced gene expression, in particular *aHIF*, on disease progression. Frozen tumor tissue collected from 87 patients with PGL enabled Span and colleagues to correlate the expression of *aHIF* and *VEGF*, as assessed by quantitative RT-PCR, with tumor subtypes characterized by specific germline mutations and with disease prognosis, after a follow-up period of up to 21 years. The results indicated that *aHIF* and *VEGF* are overexpressed in PGLs with a hypoxic-like phenotype that results from mutations in *SDH* and/or *VHL*.

Patients with increased *VEGF* and *aHIF* expression had significantly reduced metastasis-free survival, indicating that overexpression of these genes could be a marker of PGL virulence. As Span explains, metastases develop in 10–15% of PGLs and often occur decades after primary treatment, which requires long-term indiscriminate patient follow-up. The identification of biomarkers of PGL aggressiveness could facilitate targeted selection of patients for intensive follow-up. “Identifying the mechanisms associated with or involved in disease progression could offer new targets for therapy or metastasis prevention,” he adds.

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**Original article** Span, P. N. *et al.* Overexpression of the natural antisense hypoxia-inducible factor-1 $\alpha$  transcript is associated with malignant pheochromocytoma/paraganglioma. *Endocr. Relat. Cancer* **18**, 323–331 (2011)