

# **Focal adhesion kinase splicing and protein activation in papillary thyroid carcinoma progression**

## **Abstract**

Papillary thyroid carcinoma (PTC), a common endocrine malignancy, presents a challenge from a prognostic standpoint. Molecular alterations underlying PTC progression include deregulation of focal adhesion kinase (FAK) at post-transcriptional and post-translational levels. Searching for candidate markers of PTC progression, we investigated the prognostic significance of FAK alterations on mRNA/protein level. The expression levels and subcellular localisation of auto-phosphorylated FAK (pY397-FAK) were determined by western blot (WB) and immunohistochemistry. The quantity of total FAK mRNA, alternatively spliced FAK-Del26 and FAK-Del33 variants were analysed by RT-qPCR and related to pY397-FAK expression and subcellular distribution. The results were correlated with clinicopathological parameters of the patients. The expression of pY397-FAK was significantly elevated in malignant samples. Active FAK showed predominant cytoplasmic distribution with co-occurrence along the membrane, while nuclear staining was found less frequently. Expression of pY397-FAK in separate cellular compartments correlated with adverse clinicopathological parameters, but the strongest association was found when their mean scores were calculated. Alternatively spliced FAK-Del33 and total FAK transcripts positively correlated to pY397-FAK protein levels as well as to characteristics of PTC advancement. Over-expression of FAK on mRNA (total and Del-33) and activated protein (pY397-FAK) levels is a feature of PTC advanced stages. Of the analysed alterations, the mean pY397-FAK IHC score showed the best predictive performance. Correlation between mRNA FAK-Del33 and pY397-FAK expression implies a regulatory role of alternative splicing in PTC patients.