Oncogenic action of PBF in head and neck cancer is associated with poorer overall survival

M L Read, B Modasia, A Fletcher, R J Thompson, K Baker, H Nieto, M J Campbell, K Boelaert, A S Turnell, V E Smith, M Mehanna and C J McCabe
Institute of Metabolism and Systems Research, University of Birmingham, UK

To determine the role of PBF and PTTG in HNSCC by studying:
- Tumour expression levels
- Impact on p53 stability and target genes
- Patient survival

Elevated expression of PBF and PTTG in HNSCC

PBF and PTTG were abundantly overexpressed in HNSCC in (i) Tumour tissue (n = 53) and (ii) TCGA data (n = 497)

(i) PBF and PTTG alone caused a significant increase in p53 protein turnover (~6-fold). Co-expression of both PBF and PTTG resulted in the greatest reduction in p53 protein stability (13-fold).

(ii) PTTG retained the ability to bind p53 in the absence of PBF, but the degree of interaction was attenuated. (iii) Whereas PBF binding to p53 was markedly increased in the absence of PTTG.

High PBF expression is associated with poorer survival

An important transcriptional relationship between PBF and p53 was highlighted by extensive correlation between PBF expression with 129 p53-target genes in wild-type p53 HNSCC (high PBF/PTTG versus low PBF/PTTG expression; left - 60/129 genes). In contrast, fewer p53 target genes were correlated with PBF in different PBF/PTTG expression subgroups (middle - 16/129 genes; right - 21/129 genes).

Summary

This is the first study to show that PBF is of critical relevance to head and neck cancer. HNSCC patients with high tumoural PBF and PTTG have worse outcomes due in part to greater aberration of p53-dependent signalling.

References