JOURNAL CLUB

A novel mechanism for MET and EGFR axis regulation in non-small cell lung cancer involving microRNA-27a and Sprouty2

Epidermal growth factor receptor (EGFR) and hepatocyte growth factor receptor (MET) are tyrosine kinase receptors that have been implicated in the pathogenesis of non-small cell lung cancer (NSLC). Sprouty2, a ubiquitously expressed protein, has been shown to upregulate EGFR and MET in several types of cancers. Conversely, microRNAs are small non-coding RNA molecules that regulate gene expression negatively, and microRNA-27a (miR-27a) is thought to function as a tumour suppressor in NSLC. However, the regulatory pathways between MET, EGFR, Sprouty2 and miR-27a have not been fully elucidated in lung cancer.

Using gene expression analysis in A549 lung cancer cells, Acunzo *et al*[1] show that miR-27a overexpression results in reduced levels of EGFR and MET. In addition, they found that overexpression of miR-27a caused a reduction of Sprouty2 levels in the same cell line.

To investigate the relationship between Sprouty2, EGFR and MET, RNA interference was used to silence Sprouty2. This resulted in a downregulation of both MET and EGFR levels. Finally, the authors demonstrated that, in cells with a combination of both miR-27a overexpression and Sprouty2 silencing, downregulation of EGFR and MET was greater than when miR-27a was not overexpressed.

From these findings, Acunzo *et al* propose that miR-27a downregulates MET and EGFR via two different pathways: (1) directly by negatively regulating gene expression; and (2) indirectly through Sprouty2 downregulation. This study suggests a novel mechanism through which the EGFR and MET signalling pathways are regulated in NSLC and may provide a unique strategy for targeted lung cancer therapies in the future.

▶ Acunzo M, Romano G, Palmieri D, *et al*. Cross-talk between MET and EGFR in non-small cell lung cancer involves miR-27a and Sprouty2. *Proc Natl Acad Sci USA* 2013;110:8573–8.

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