

How EGFR promotes skin cancer

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A study to be published in Cell Biology reveals how Scientists have pinpointed the molecular mechanisms underlying tumour response to EGFR — a protein that boosts the development of skin cancer, and an important target for cancer therapy.

Epidermal growth factor receptors (EGFR) stimulate skin cells called keratinocytes to multiply while simultaneously stopping them from becoming more specialised. The overall effect encourages tumours in skin cancer to develop. The research reveals that EGFR wields these functions in skin cancer by preventing expression of Notch1, a gene essential for tumour development.

Notch1 gene expression and activity are significantly lower in keratinocyte cancer cell lines and tumours. When looking for small molecules that may activate Notch protein signalling, G. Paolo Dotto, Massachusetts General Hospital, Charlestown, USA and co-authors found that EGFR is a major negative regulator of Notch1 gene expression in human keratinocytes and skin cancers. By analysing this mechanism in a mouse model of EGFR-dependent skin cancer, they also showed that EGFR stops expression of Notch1 by blocking the tumour suppressor gene p53.

EGFR is an important target of cancer therapy and several selective EGFR inhibitors have now been approved for clinical use. These findings provide further understanding of the molecular mechanisms underlying the tumour response to EGFR inhibition.
