NEURO-ONCOLOGY

A microRNA-based mechanism for NF- κ B activation in glioma

The microRNA miR-182 is a key component of a pathway through which transforming growth factor β (TGF- β) signalling induces constitutive activation of nuclear factor κ B (NF- κ B) in glioma cells, new research published in *The Journal of Clinical Investigation* reveals. TGF- β has previously been shown to repress NF- κ B in normal cells but to activate this factor in cancer cells, and a team led by Jun Li at Zhongshan School of Medicine, Guangzhou, China, set out to explore this paradox.

As Li explains, “over the past decade, ubiquitin modification has emerged as a uniquely important mechanism for the regulation of NF- κ B signalling.” In the new study, Li and colleagues found that expression of CYLD, a deubiquitinase that negatively regulates NF- κ B signalling, was downregulated in glioma tissue from 14 patients, and in 15 glioma cell lines. However, *CYLD* mRNA was expressed at similar levels in glioma and normal tissue, suggesting that *CYLD* protein expression was being regulated at the post-transcriptional level.

Through use of the TargetScan algorithm, Li and colleagues identified *CYLD* as a probable target of miR-182—a microRNA that was already known to be

overexpressed in glioma cells. Consistent with this idea, overexpression of miR-182 in glioma cell lines led to reduced *CYLD* levels, whereas inhibition of miR-182 increased the expression of *CYLD*.

To complete the pathway, the researchers examined the relationship between TGF- β signalling and miR-182 activity. They found that TGF- β increased the expression of miR-182 in glioma cells but not in normal human astrocytes.

“We demonstrate that tumour-promoting miR-182 is markedly induced by TGF- β in glioma cells but not in normal cells, suggesting that increased miR-182 levels might be indicative of

the oncogenic arm of the biological effects of TGF- β ,” concludes Li. “Further translational research will be conducted to determine the significance and feasibility of using miR-182 as a biomarker for clinical decision-making on whether to use TGF- β inhibitors in a specific glioma patient.” In addition, the researchers plan to investigate miR-182 itself as a target for glioma therapy.

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Original article Song, L. *et al.* TGF- β induces miR-182 to sustain NF- κ B activation in glioma subsets. *J. Clin. Invest.* 122, 3563–3578 (2012)