KIDNEY CANCER

Stearoyl-CoA desaturase: a novel therapeutic target for RCC

Outcomes for patients with advanced clear cell renal cell carcinoma (ccRCC) are discouraging. The currently available therapeutic options for these patients have not been shown to improve long-term survival, and although medications have recently been approved for use in patients with advanced disease, so far none have proven curative and combination protocols are problematic owing to toxicity caused by the non-tumour-specific effects of the drugs.

Now, a team based at the Mayo Clinic in Florida, USA, have identified a novel therapeutic target for ccRCC and show that inhibition of this target results in tumour inhibition *in vitro* and *in vivo*.

The team used quantitative real-time PCR to determine the expression of *SCD1*, which encodes stearoyl-CoA desaturase (SCD1), a constituent of lipid metabolism. They observed that SCD1 expression was abnormally high in ccRCC samples compared with patient-matched normal tissue at both the transcriptional and protein

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levels. With this in mind, the team then investigated the effect of SCD1 inhibition in ccRCC cell lines, using both genetic knockdown and pharmacological techniques. Lentiviral constructs were used to knockdown *SCD1* expression by >80%, which resulted in a >80% decrease in tumour proliferation. When SCD1 was blocked using the small molecule inhibitor A939572, they also observed significantly reduced cell proliferation and induction of apoptosis.

Finally, the researchers investigated whether A939572 might have the potential to be used in combination

with a currently available treatment option, temsirolimus, using cell-line and mouse models. Each of the drugs reduced tumour growth alone, but a marked improvement was noted when the two were used in combination. A 20–30% reduction in tumour volume was observed in xenografted mice treated with each monotherapy, which rose to >60% in those receiving combination treatment, compared with placebo-treated controls. “Targeting metabolic pathway components, such as SCD1, may be the key to success in developing novel combinatorial therapies that lead to enhanced survival, or potentially cure, for patients with cancer,” author Christina von Roemeling told *Nature Reviews Urology*.

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Original article von Roemeling, C. A. *et al.* Stearoyl-CoA desaturase 1 is a novel molecular therapeutic target for clear cell renal cell carcinoma. *Clin. Cancer Res.* doi:10.1158/1078-0432.CCR-12-3249