THERAPY

FGFR3 is key

Overexpression of fibroblast growth factor receptor 3 (FGFR3) has been shown to drive oncogenesis in a subset of patients with multiple myeloma. However, epithelial cancers — such as bladder cancer — also exhibit deregulation and mutation of FGFR3, but whether this contributes to tumorigenesis *in vivo* has remained unclear.

To address this, Avi Ashkenazi and colleagues specifically knocked down *FGFR3* expression and found that this suppressed the growth of bladder cancer cell lines and established xenografts in nude mice. Using phage display, they generated an FGFR3-specific monoclonal antibody (R3Mab) that had a similar affinity for human and mouse FGFR3. R3Mab blocked the activity of wild-type and mutant FGFR3 in bladder cancer cell lines.

Furthermore, treatment of mice with 5 or 50 mg per kg R3Mab significantly suppressed the growth of established RT112 (wild-type FGFR3) bladder cancer xenografts. In addition, they showed that treatment with R3Mab reduced the phosphorylation of FGFR substrate 2 α and mitogen-activated protein kinase, indicating that FGFR3-mediated signalling was suppressed. Moreover, R3Mab significantly inhibited the growth and progression of UMUC-14 xenograft tumours expressing the most common FGFR3 mutation found in bladder cancer. Importantly, R3Mab specifically targets FGFR3, rather than other members of the Fgfr family; this is

likely to be important for anticancer therapy given that signalling by another family member, FGFR2, is often context specific and hence associated with opposing roles in the oncogenesis of different tissues.

Therefore, Jing Qing *et al.* have established that FGFR3 is an oncogenic driver of bladder cancer, raising the possibility that FGFR3 has important roles in the oncogenesis of other epithelial cancers.

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ORIGINAL RESEARCH PAPER Qing, J. *et al.* Antibody-based targeting of FGFR3 in bladder carcinoma and t(4;14)-positive multiple myeloma in mice. *J. Clin. Invest.* **119**, 1216–1229 (2009)