

## **VEGF<sub>165b</sub> CAN INHIBIT COLORECTAL CANCER GROWTH *IN VIVO***

Alexander H.R. Varey, Emma S. Rennel, Anthony R. Dixon<sup>§</sup>, Steven J. Harper,  
David O. Bates

MVRL, Department of Physiology, University of Bristol, Preclinical Veterinary  
School, Southwell Street, Bristol BS2 8EJ

<sup>§</sup> Department of Surgery, Frenchay Hospital, North Bristol NHS Trust, Frenchay  
Park Road, Frenchay, Bristol BS16 1LE

**INTRODUCTION.** VEGF-A has been shown by Bates et al.(1) to comprise both pro-angiogenic (VEGF<sub>165</sub> etc) and anti-angiogenic (VEGF<sub>165b</sub>) isoforms. Furthermore, VEGF<sub>165b</sub> has previously been shown by Woolard et al.(2) to be able to reduce VEGF<sub>165</sub> mediated growth of malignant melanomas *in vivo*. In this study we aimed to show that we could reduce the growth of human colon carcinoma *in vivo* by VEGF<sub>165b</sub> overexpression.

**METHODS.** Using the LS174t human colon carcinoma cell line, which forms highly vascularised tumours in nude mice(3), cells were transfected with a pcDNA3 vector to overexpress VEGF<sub>165</sub>, VEGF<sub>165b</sub>, both or neither (empty vector). Selection was then carried out using Geneticin and expression levels verified *in vitro* prior to implantation of the cells. 6 mice were used per group and 2 million cells injected subcutaneously per mouse in the lumbar region, close to the midline. Tumour length and width were then measured every 2-3 days, until the first tumour reached 16mm maximum diameter, when the experiment was terminated. Analysis of the results was then performed using a 2 way ANOVA in Prism 3, with post hoc Bonferroni comparisons between groups at 15 days.

**RESULTS.** The experiment had an overall p value of 0.035. Results of post hoc comparisons were as follows, given as mean±SEM. VEGF<sub>165b</sub> expressing tumours (326±210 mm<sup>3</sup>) were smaller than VEGF<sub>165</sub> tumours (1610±570 mm<sup>3</sup>, p<0.0001) and control (pcDNA3) tumours (1134±770 mm<sup>3</sup> p<0.05). Expression of both isoforms resulted in smaller tumours (736±273 mm<sup>3</sup>) than VEGF<sub>165</sub> alone (p<0.001), but significantly greater than VEGF<sub>165b</sub> alone (p<0.05). See Figure 1.

**DISCUSSION.** The results of this experiment confirm that not only can VEGF<sub>165</sub> overexpression accelerate colon carcinoma tumour growth *in vivo*, but VEGF<sub>165b</sub> overexpression can inhibit tumour growth. Moreover, VEGF<sub>165b</sub> overexpression can mediate escape from VEGF<sub>165</sub> accelerated tumour growth, as shown by the co-expression group. These results suggest a potential role of VEGF<sub>165b</sub> as a chemotherapeutic agent in treatment of colorectal cancer.

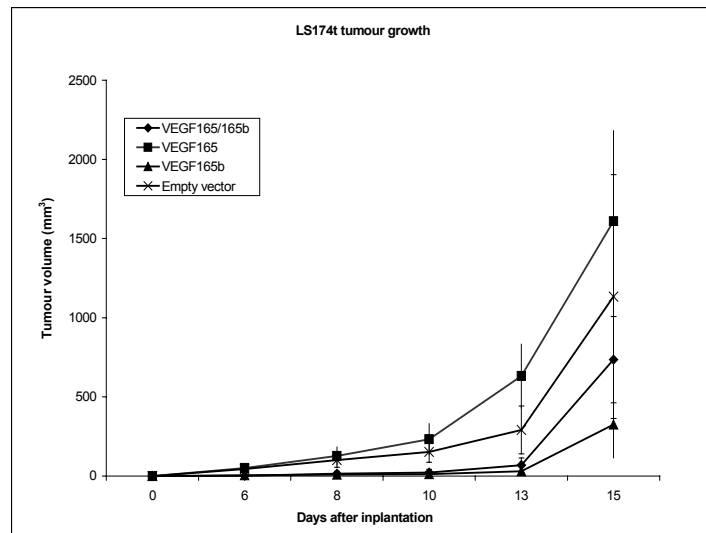


Figure 1. Tumour growth curves of LS174t cells over-expressing VEGF isoforms.

**REFERENCES.**

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