Evaluation of Antitumor Effects Of VEGFR-2 Inhibitor F16 In A Colorectal Xenograft Model	
Authors	**Khalid Alhazzani, Thiagarajan Venkatesan, Umamaheswari Natarajan, Mohammad Algahtani, Ali Alaseem, Saad Alobid & Appu Rathinavelu**
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Objectives

Colorectal cancer (CRC) is the third most prevalent type of cancer in the United States. The treatment options for cancer include surgery, chemotherapy, radiation, and/or targeted therapy, which show significant improvement in overall survival. Among the various available treatments, antagonizing VEGF/VEGFR-2 pathways have shown effectiveness in limiting colorectal cancer growth and improving clinical outcomes. In this regard, we hypothesized that F16, a novel VEGFR-2 inhibitor, would control colorectal cancer growth by blocking the VEGFR-2 singling pathway in both in vitro and in vivo conditions. Therefore, the current study was aimed to analyze the efficacy of F16 on the growth of Colo 320DM cells under in vitro and in vivo conditions.

Results

Human RT^2 profiler PCR array analysis results clearly showed that angiogenesis and anti-apoptosis-related gene expressions were significantly reduced in HUVEC cells after F16 (5 µM) treatment. In addition, Western blot results revealed that F16 attenuated the downstream signaling of the VEGFR-2 pathway in HUVEC cells by up-regulating the p53 and p21 levels and down-regulating the p-AKT and p-FAK levels. Accordingly, F16 confirmed potent cytotoxic effects against the cell viability of Colo 320DM tumors, with an IC_{50} value of 9.52 ± 1.49 µM. Furthermore, treatment of mice implanted with Colo 320DM xenograft tumors showed a significant reduction in tumor growth and increases in survival rate compared to controls. Immunohistochemistry analysis of tumor tissues showed a reduction in CD31 levels also in F16 treated groups.

Conclusions

These results justify further evaluation of F16 as a potential new therapeutic agent for treating colorectal cancers.