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IMPACT OF FUNCTIONAL POLYMORPHISMS OF VEGF ON BREAST CANCER RISK IN NORTH-WEST INDIANS

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Angiogenesis is an essential process in tumor growth, provides potential routes for tumor dissemination and metastasis. Vascular endothelial growth factor (*VEGF*) is a potent regulator of angiogenesis and is involved in the development and progression of solid tumors. Cancers use lymphangiogenesis and *VEGF* has been described as major mediator of breast cancer angiogenesis. The aim of the present study was to investigate the potential association of thirteen [ten promoter (-2578C/A, -2549I/D, -460T/C, -417T/C, -172C/A, -165C/T, -160C/T, -152G/A, -141A/C and -116G/A), two 5'-UTR (+405C/G, -7C/T) and one 3'-UTR (+936C/T)] *VEGF* polymorphisms with breast cancer risk in patients from Punjab, North-west India. In this study, DNA samples of 250 pathologically confirmed breast cancer patients and 250 ages and gender matched unrelated healthy individuals were screened for thirteen selected *VEGF* polymorphisms using direct PCR, PCR-RFLP and Sanger sequencing methods. Of 250 breast cancer patients, 7 were males and 243 were females. About 73.6% of patients developed breast cancer after 40 years of age. A significant association of *VEGF* -2578AA, -2549II, -460CC, +405GG, -152AA and -116AA genotypes with increased breast cancer risk were observed. *VEGF* -165CT and -141AC genotypes were associated with decreased risk for breast cancer. A strong linkage was observed between *VEGF* -2578C/A and -2549I/D, -2578C/A and -460T/C, -2549I/D and -460T/C and -165C/T and -141A/C polymorphisms. Haplotype analyses indicated that *VEGF* -2578A/-2549I/-460C/+405G/-7C/+936C and -417T/-172C/-165C/-160C/-152A/-141A/-116A combination was associated with increased risk while combination of -2578C/-2549D/-460T/+405G/-7C/+936C was associated with decreased risk for breast cancer. Analysis using TFSEARCH software revealed that *VEGF* -2578C/A, -417T/C, -172C/A and +405C/G polymorphisms altered the binding site of specific transcription factors. In this case-control study, *VEGF* -2578C/A, -2549I/D, -460T/C, +405C/G, -165C/T, -152G/A, -141A/C and -116G/A polymorphisms were associated with susceptibility to breast cancer in patients from Punjab, North-west India. *VEGF* is an important target in anti-cancer therapy, and findings about polymorphisms influencing *VEGF*-targeted therapies will help physicians to tailor therapy in individual manner.

Biography

Kamlesh Guleria has completed his PhD from Guru Nanak Dev University, Amritsar, Punjab, India and Postdoctoral studies from Institute of Genetic Medicine, Newcastle University, Newcastle upon Tyne (UK). He also worked as Research Scientist at Sir Ganga Ram Hospital, New Delhi, India. Since 2009, he is working as Assistant Professor, at Department of Human Genetics Guru Nanak Dev University, Amritsar. He has published more than 20 papers in reputed journals and has been serving as an Editorial Board Member of repute and he has secured extramural research grants from various funding agencies in India.

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