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The combined effects of the functional variants in cell death pathway genes influence herpes simplex virus type-2 infection but not cervical cancer

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Background: Cervical cancer is one of the most important cancers worldwide with a high incident and mortality rate. Even though many sexually active women get infected with human papillomavirus (HPV), only a small fraction of them progress to cervical cancer suggesting the important roles of the additional risk factors in development of the disease including host genetic factors and other infections such as HSV-2. Since cellular apoptosis plays a crucial role in controlling the spread of virus-infections in cells, functional variations in cell death pathway genes might alter the apoptotic mechanism, thereby influencing its ability to clear virus-infections. Functional polymorphisms in FasR (-1377G>A and -670A>G), FasL (-844T>C) and CASP8 (-652 6N ins/del) genes are all know to alter the mechanism of apoptosis by modifying the level of expression of their correspondent proteins. These polymorphisms have been investigated in cervical cancer by different groups including our lab previously.

Objective: In the present study, we attempted to investigate the combined effects of CASP8 polymorphism with any (and all) of the FasR/FasL polymorphisms in cervical cancer, pre-cancerous lesions, HPV infection and HSV-2 infection.

Materials and Methods: Participants were 442 South African women of black African and mixed-ancestry origin with invasive cervical cancer and 278 control women matched by age, ethnicity and domicile status. FasR and FasL polymorphisms were genotyped by TaqMan and CASP8 polymorphism by PCR-RFLP. The results were analysed using haplo.stats software version 1.5.2. All results were adjusted for ethnicity and smoking.

Results: No significant association with any of the combinations of the polymorphisms was found with cervical cancer. However, when compared only among the control group a statistically significant association ($P=0.023$, $CPS=-2.275$) with CASP8 -652 6N ins+FasR-1377A allele was observed with HSV-2 infection.

Conclusion: Our results show that the combined effect of CASP8 -652 6N ins and FasR-1377A allele exerts a protective effect on HSV-2 infection suggesting an important role of the combined effects of the functional variants of cell death pathway genes in infectious diseases and related disorders.

Biography

Koushik Chattopadhyay after completing his Masters in Biotechnology from India moved to University of Cape Town in Cape Town, South Africa to pursue his PhD in human genetics, cancer biology and infectious diseases. He completed his PhD in 2010 and worked as a Researcher at Stellenbosch University and University of KwaZulu-Natal (South Africa) on neurogenetics, pharmacogenetics and extremophiles. After working briefly as a faculty member in genetics at University of KwaZulu-Natal he moved to the USA. Currently he is a Researcher at University of Pittsburgh in Pennsylvania, USA. His expertise is in molecular genetics. He has published several papers in reputed journals and also on the editorial board for several journals.

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