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Increased T-cell activation and Th1 cytokine concentrations prior to the diagnosis of B-cell lymphoma in HIV infected patients

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Background: Despite the use of combined antiretroviral therapy, HIV-infected individuals have a higher risk of developing B-cell lymphoma compared to the general population. We aim to explore whether lymphocyte activation, increase in Th1 response as well as markers of EBV reactivation, may precede lymphoma diagnosis.

Methods: Thirteen cases and 26 controls matched on $CD4^+$ T-cell count and HIV plasma viral load were identified. Samples were collected 0 to 5 years prior to B-cell lymphoma diagnosis. Seven out of thirteen (54%) and 16/26 (61.5%) of cases and controls were receiving antiretroviral therapy at the time of sampling, respectively. $CD8^+$ T-cell activation and Th1 cytokine concentrations were measured before lymphoma onset, together with IgG antibodies directed against viral capsid antigen (VCA) and serum levels of EBV DNA.

Results: A higher level of $CD8^+$ T-cell activation was observed in patients developing lymphoma. Four out of seven Th1 cytokine serum concentrations were significantly higher in patients with lymphoma than in the control group: IL-2R, IL-12 p40/70, IFN-γ-inducible protein 10 (IP-10) and monokine induced by IFN-γ (MIG). Anti-VCA IgG level were significantly higher in cases than in controls. Four cases (30%) but no controls had detectable EBV DNA in serum.

Conclusion: A higher level of T-cell activation, Th1 cytokine serum concentration and markers of EBV replication, preceded B-cell lymphoma diagnosis. This may suggest that viral antigen stimulation is associated with the genesis of lymphoma in HIV-infected patients.

New approaches to cancer therapeutics: Incorporating noncoding sequences into the development pipeline

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This lecture will address topics related to the recent development of pipelines for analysis of non-coding sequences in whole-genome NGS data. The decreasing costs of NGS patient and individual full-genome analysis now makes it economically feasible to gather genotypic information for non-coding sequences as well as coding sequences. In many cases, the primary effects of variants presumed to exert their effects at the coding sequence level may in fact be from gene expression alterations, either directly through transcription factor interactions, through miRNA interactions, or through pathway disruptions. The use of bioinformatics resources for large cancer genome datasets for will also be discussed. These approaches can be applied to pharma development processes, as well as for diagnostics and decision support systems in clinical applications.

Biography

David Ghosh has developed data resources for gene expression analysis for over 20 years. As the founder of IFTI, he developed the first transcription factors database (TFD), which is still in current use. IFTI has worked with academic and commercial partners in the US and in Japan in bioinformatics development related to transcription factors and gene expression. He has published numerous reviews and primary research publications in the areas of molecular biology, gene expression and bioinformatics, and has previously served on an NIH review panel.

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