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When virology and cellular genetics collide: EBNA1, A virally encoded transcription factor, engages cellular host promoters and intervenes with cellular gene expression

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Epstein Barr nuclear antigen 1 (EBNA1) is expressed in all forms of EBV infections and tumors, and plays a key role in EBV transcription and replication. Since EBV is maintained in the nucleus of the infected cell, EBNA1 has access to host genomic DNA as well. We examined if EBNA1 interacted with cellular genomic DNA. Microarray analysis demonstrated changes in global gene expression in response to EBNA1's expression, which was validated by QPCR analysis. Subsequently, we hybridized EBNA1-chromatin immunoprecipitation (ChIP) to human promoter arrays to identify global genomic binding sites. Interestingly, sequence analysis of the 100 promoters most enriched revealed a unique DNA motif which differs from the EBNA1 binding site at the EBV genome. These putative EBNA1-regulated genes were confirmed using QPCR on the ChIP samples. Hence, we demonstrated a direct viral intervention in the genomic activities of its host cell. We speculate direct manipulation of the host genome improves the virus' ability to coexist with the infected cell.The role of EBNA1 in manipulating cellular gene expression and combined with its central role in EBV transcription and replication makes it a promising target of interest for both therapy and diagnostics of EBV associated diseases, including Burkitt's lymphoma (BL), HIV-associated lymphoma, post-transplant lymphoproliferative disorder, and nasopharyngeal carcinoma(NPC) which is very predominant in Asia. The combination of genomics and bio-informatics emerging tools will enable us to identify drugs by their ability to reverse and contradict the cellular gene expression imposed by EBNA1.

Biography

Dr. Allon Canaan received his BSc from Hebrew University (Jerusalem) and his MSc and PhD from the Weismann Institute of Science (Rehovot) in Israel. He moved to the USA for postdoctoral studies at Yale School of Medicine, where he is still conducting his research.

Dr. Canaan was the first to report, in 2002, on cellular gene expression changes inflicted by EBNA1. Subsequently, he demonstrated the direct binding of EBNA1 to the promoters of regulated cellular genes. For these pioneering discoveries Dr. Canaan was an invited speaker in variety of international conferences.