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Epstein-barr virus in Malaysian classical Hodgkin's lymphoma

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Summary

There is a clear realation between classical Hodgkin's lymphoma and infection with the Epstein-Barr virus, the causative agent of infectious mononucleosis. However, remarkable differences have been observed between different populations and different geographic localisations. The most frequent type of EBV, type A, can be found in the tumor cells all over the world, including Malaysia, according to this thesis. One of the virally induced proteins, the so called Latent Membrane Protein 1 (LMP-1) plays an important role in the transformation of the tumor cells, the so called Reed-Sternberg cells. This thesis demonstrates that a mutated form of LMP-1 is more frequent in the tumor cells of Hodgkin's lymphoma than in reactive lymphoid tissues and in other EBV associated tumors. Analysis of single tumor cells captureed from tissue sections indicates that the mutations probably occur in the tumor cells, since in individual cells mutated as well as unmutated LMP-1 DNA can be found. It is not known whether EBV or another virus is involved in cases of Hodgkin's lymphoma where no EBV DNA or RNA can be detected.

Hodgkin's lymphoma is a special tumor because it contains such a small proportion of tumor cells, generally less than 1%, and is made up of more than 99% of reactive cells, including lymphocytes, histiocytes, eosinophils and plasma cells.

The tumor cells exhibit a remarkable combination of high cell cycle activity with low proliferative activity and a low degree of apoptosis. It appears that the initial steps towards apoptosis have been made but that the process has been halted at some point. Stimulation through NF-kB seems to play an important role, but also anti-apoptotic proteins like bcl-2 and cell cycle regulators like P53 and PRb appear to be important actors. The rel;ation between EBV and these proteins is not clear. In this thesis a significant, inverted, realation is foiund between EBV and Bcl-2 expression. Further research is necessary to identify the mechanisms that are responsible for the disturbance of normal cell cycle regulation in Reed-Sternberg cells