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γ -retroviral mediated NPM-ALK transfer in polyclonal T cells causes loss of surface markers with monoclonal cancerous transformation

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Background & Study Design: Mature T cell lymphomas are rare cancers with a very poor prognosis due to less research on its pathogenesis and the targeted therapy. They have a chronic course of disease development, which could be due to a control mechanism, exerted by other normal polyclonal T cells to compete a cancerous T cell to get a survival stimulation from MHC (major histocompatibility complex), present on APCs (antigen presenting cells). To investigate the pathogenesis, we transferred a T cell oncogene (NPM-ALK) through γ -retroviral vector into polyclonal T cells, which were isolated from wild type Black 6 mice, and subsequently transfused these cells in Rag 1 deficient mice.

Results: After a period of 6 months, 2 out of 5 mice developed lymphoma (large spleen and mesenteric lymph nodes), confirmed by histopathology. The surface marker analysis was done by using FACS (fluorescence activated cell sorting). The lymphoma cells did not express any T cell markers (CD3/TCR). None of the 5 mice from control group (transplanted with control γ -retroviral vector) developed any cancer. We further analyzed the tumor masses for the pattern of clonality of the tumor cells by performing LM-PCR (ligation mediated- polymerase chain reaction). The tumors were found to be of monoclonal pattern, which indicates that among 2×10^5 transfused NPM-ALK-carrying polyclonal T cells, only one T cell got transformed into a cancerous cell to give rise to a full-blown tumor of the same clonality (monoclonality).

Conclusion: γ -retroviral mediated NPM-ALK transfer into polyclonal T cells caused loss of T cell markers and resulted in the development of same types of monoclonal tumors in both mice. A more specific molecular pathway is likely to be involved in polyclonal mature T cells to give rise to similar lymphomas. These mature tumor cells need to be further investigated for the downstream signaling pathways to explore that specific molecular target, which could help to cure these tumors.

Biography

Ashok Kumar has completed his MBBS (MD) and Postgraduate diploma from Liaquat University of Medical & Health Science Jamshoro, and PhD and Post Doctorate from University of Frankfurt, Germany. He is an Associate Professor at AIMST University, Malaysia. He has over 15 publications in peer-reviewed reputed journals.

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