Chronic Hypoxia Stimulates the Susceptibility of Hela Cells to Lymphokine Activated Killer Cell (Lak)

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Background Chronic hypoxia is a common condition in necrotic area of solid tumors and an important determinant for the immune responses in human malignancy. In this study, we have examined whether the sensitivity of HeLa cells to lymphokine activated killer cell (LAK) can be modulated by chronic hypoxia that is relevant to a common microenvironment of many solid tumors.

Methods 1) Generation of LAK effector cells...Human PBMC was activated with recombinant human IL-2 (rhIL-2) for 3 days at a concentration of 1,000U/1×10⁶ cells to utilize as a source of LAK. 2) Hypoxic conditions in HeLa cells...HeLa cells were grown in a complete DMEM and hypoxic condition was generated by placing the cells in a Gas-pak pouch (Becton Dickson, Cockeysville, MD). 3)LAK activity assay...Radioactivity released from the ⁵¹Cr-labeled target (T) tumor cells co-cultured with LAK effector (E) cells in various E:T ratio was measured to calculate the specific cytotoxicity of LAK.

Results The susceptibility of HeLa cells to the LAK-induced killing was significantly increased in cells grown in hypoxic condition compared with that of normoxic controls.

Conclusion Hypoxic HeLa cells were more sensitive to LAK-induced killing. Our data suggest the tumor cells in the hypoxic necrotic area may more susceptible to killing by host immune system. This finding may have important implications for development of therapies to stimulate the patient’s immune response against tumor.