Abstract #31 | Poster

Understanding the role of cFLIP in the pathogenesis of Diffuse Large B Cell Lymphoma

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Diffuse Large B Cell Lymphoma (DLBCL) is the most common form of Non-Hodgkin Lymphoma (NHL), accounting for ~ 30-40% of all adult cases. It is highly heterogeneous and is classified into two subgroups: ABC-DLBCL and GCB-DLBCL, which are further classified into five clusters.

Over the years, DLBCL therapy has made substantial progress; first-line chemoimmunotherapy upon diagnosis achieves a cure rate of ~ 60% in DLBCL patients. Despite this and other significant advancements in therapy options (e.g., CAR-T cell therapy), refractory and relapsed cases remain a major clinical challenge.

Death receptor-induced cell death (extrinsic apoptosis) is fundamental in the regulation of tissue homeostasis and DLBCL pathogenesis is associated with resistance to cell death or dysregulation of cell survival. The cFLIP/Caspase-8 heterodimer is a crucial checkpoint in this apoptotic pathway because it regulates the biological outcome (survival or death) of death receptor stimulation. cFLIP is an anti-apoptotic protein that hinders the enzymatic activity of Caspase-8 and contributes to increased cell proliferation and tumorigenesis. However, cFLIP’s role in B cell biology and lymphomagenesis is yet to be thoroughly described. Therefore, we hypothesize that cFLIP can contribute to DLBCL pathogenesis by modulating Caspase 8-mediated responses downstream of immune receptors.

Keywords: Diffuse Large B Cell Lymphoma, cFLIP, Cell death, Death receptors