

Lymphomas as Estrogen-Regulated Cancers

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Abstract : Lymphomas are generally not considered as endocrine-related cancers. However, most lymphoid malignancies show gender differences in incidence and show prognosis with males being more affected. Furthermore, some epidemiological data indicate a protective role of estrogens against Non-Hodgkin lymphomas. Recent studies have demonstrated estrogen receptor β (ER β) to be the major ER expressed in normal and malignant cells of lymphoid origin. We have analyzed the effects of estradiol and selective ER α and ER β agonists on lymphoma growth in culture and in vivo. Treating lymphoma cells with estradiol or ER α selective agonist had minor or no effect on cell growth while selective ER β agonist treatment showed an antiproliferative effect. When grafting mice with murine T lymphoma cells, male mice developed larger tumors compared to female mice, a difference that was abolished following ovariectomy, demonstrating estrogen-dependent growth in vivo. When subcutaneously grafting lymphoma cells to mice, so far growth of all tested human B lymphoma tumors (Raji and Ramos Burkitt lymphoma, SU.DHL4 (GC) and U2932 (ABC) DLBCL, Granta-519, Maver1 and Z138 MCL cells), were reduced following treatment with ER β selective agonist (ref. 2 and unpublished). Moreover, the number and size of liver foci of disseminating Raji cells was reduced. We have identified target genes and mechanism that could explain the above effects of ER β agonists. This included effects on angio and lymphangiogenesis. Now we have further analyzed effects of ER β agonists on Ibrutinib-sensitive and -insensitive MCL cells in xenograft experiments as well as ER β expression in primary lymphoma material (DLBCL). Preliminary statistical analysis has been done correlating ER β expression to other biomarkers and clinical data.

Keywords : lymphomas, estrogen receptors, cancer, liver foci

Conference Title : ICSRD 2020 : International Conference on Scientific Research and Development

Conference Location : Chicago, United States

Conference Dates : December 12-13, 2020