Poster Presentation

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Structural characterization of Retinoic Acid Receptor-α (RARA)

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Acute promyelocytic leukemia (APL) is a hematological malignancy characterized by the presence of balanced reciprocal translocation between promyelocytic leukemia (PML) gene on chromosome 15 and the retinoic acid receptor-alpha (RARA) gene on chromosome 17. This translocation leads to a fusion transcript known as PML-RARA which is present in 98% cases of APL [1]. It is well established that PML-RARA associated APL is sensitive to both all-trans-retinoic acid (ATRA) and arsenic trioxide (ATO) [2]. It promotes the degradation of chimeric oncogenic protein through a series of molecular events leading to differentiation of promyelocytes. The mutations identified in RARA moiety such as Val218Asp, Arg72Gln, Thr278Ala, Thr291Ile, Asn299Asp, Arg294Trp, Ala300Gly and Gly391Glu affect the binding of ATRA which in turn result the non-degradation of chimeric oncoprotein [3]. Considering the importance of RARA, the RARA region comprising 60-462 amino acids was cloned, expressed and purified in bacterial system. Further purified by size exclusion chromatography using FPLC to get active protein in native conditions. Secondary structure and folding pattern of protein was characterised by Circular-Dicroism (CD) and Fluorimetry. It has been concluded that purified protein has correctly folded secondary and tertiary structures. We have observed the melting temperature (Tm) using Thermal denaturation by CD spectroscopy.

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