Cancer is MAD(2L2); Regulation of Rev7 on Survival and Chemoresistance in Multiple Myeloma

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Multiple myeloma (MM) is a devastating B-cell malignancy occurring in hyperproliferative plasma cells originating from bone marrow. Current therapeutic treatments include non-targeted chemotherapy and the administration of bisphosphonates, which have no particular specificity on their molecular effects. Rev7 is a protein involved in DNA damage and repair tolerance in cells, with overexpression being implicated in poor prognosis for patients with MM. This project aims to understand the underlying properties of Rev7 and its chemotherapeutic effects involved in MM. Protein expressions were measured via western blot analysis, and doxorubicin was serially diluted to measure MM chemoresistance through cell viability assays (IC50 assay) in order to quantify dose-dependent responses. Class-switch recombinations (CSR) were observed through fluorescence-activated cell sorting (FACS) to study myeloma (M) protein diversification. Compared to a variety of B-cell malignancies, Rev7 was upregulated in MM. Half-maximal inhibitory concentrations were directly correlated to Rev7 expression in MM. With increased concentrations of chemotherapeutics, MM remained relatively resistant to doxorubicin in contrast to a non-malignant control. Rev7's non-homologous end joining (NHEJ) pathway counteracts doxorubicin's DNA intercalation processes; thus, inducing increased chemoresistance. Rev7 bypassing the damage produced by doxorubicin suggests that Rev7 attenuates the chemotherapeutic effects of this drug. Subsequently, a retroviral vector inducing Rev7 overexpression will infect the MM cells in order to validate Rev7's chemoresistant role. Using gene therapy, this protein can serve as a novel chemotherapeutic target for MM patients by downregulating its expression.

Awards Won:
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