Volume 12

Washington University
Undergraduate Research Digest

Spring 2017

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The Potential Role of ER-Associated Degradation Protein DERL3 in Multiple Myeloma

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Multiple myeloma (MM) accounts for 13% of hematologic cancers and is characterized by a diversity of genetic lesions—translocations, copy number alterations, and single nucleotide variants. We designed a single-platform targeted sequencing approach capable of detecting all three variant types. Here, we focused on the translocations. We performed targeted sequencing of myeloma cells from MM patients (n=96) and detected novel IgH translocations with partners near *DERL3* (n=2) and observed outlying expression of *DERL3* from RNA-seq data. Since DERL3 regulates protein misfolding, we hypothesized that knockdown of DERL3 in MM would lead to increased apoptosis. After validating the translocation via PCR, we knocked down DERL3 with shRNA constructs in MM cell lines and observed increased cell death in one of two MM cell lines. This study provided some evidence suggesting DERL3 may play a role in regulating MM progression and may be a target of IgH-induced overexpression. Identifying *DERL3* as a tumor suppressor gene for MM could lead to increased understanding of MM development and potential use for therapy.