Year III: Development of M. mercenaria Neoplastic Hemocytes as a Novel Alternative Experimental Model for BCL-2 Interactions in Blood Cancers: An Application for Targeted Drug Studies

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Anti-apoptotic B-cell leukemia/lymphoma (Bcl-2) proteins are overexpressed in around half of human cancers, linked to tumorigenesis, chemotherapy resistance, and poor prognosis. Effectively modeling this complex molecular interaction is essential for its progression as a therapeutic target, yet the costliness and time-intensive nature of current models limit study. However, disseminated neoplasia (DN), a transmissible cancer naturally occurring in the hemocyte "blood" cells of bivalve mollusks, shares notable similarities to human leukemia. To develop M. mercenaria as an effective model, this study examined neoplasia transmission between bivalves. Cohabitation yielded increased tumor cell fraction in healthy clams after 3 months. Exposure to hypoxic conditions promoted DN progression after 7 days, and cancer cell inoculation elevated transmission in healthy clams ($p=0.0409$). Excess lipid accumulation in tissue was characterized as a new potential DN biomarker, aiding in future disease identification. M. mercenaria were evaluated for functional similarities between human and bivalve Bcl-2 after exposure to inhibitors at varying concentrations. Significant changes ($p=0.0209$) in relative protein expression were observed in SDS-PAGE, suggesting Bcl-2 inhibitors downregulate Bcl-2 expression in M. mercenaria. Clams treated with concentrations >0.3 mg/kg maintained suppressed tumor progression in the months following exposure. Results show promise for M. mercenaria as naturally occurring in vivo cancer models for Bcl-2 interactions, with analogous biomarkers and physiological responses identified. Applications include high-throughput drug screening, minimizing vertebrate testing, and reducing cost per specimen >50-fold for early novel drug candidate screening.

Awards Won:
Third Award of $1,200