Modeling The Bone Marrow Microenvironment’s Influence on Leukemic Disease

The bone marrow microenvironment serves as both the site of initiation of the majority of hematopoietic malignancies and also contributes to maintenance of minimal residual disease by promoting biologically relevant changes in tumor cells. These functional alterations of leukemic cells include, but are not limited to modulation of cell cycle [1,2], regulation of anti-apoptotic signaling cascades [3-6], and influence on metabolic activity [7-9]. Of clinical relevance, these pathways impact on therapeutic response, making it critical to have robust in vitro systems to interrogate tumor cell interactions with stromal elements of the microenvironment to screen chemotherapeutic agents and inform the in vivo model design.

To generate a model of the marrow microenvironment niche, human leukemic cells were co-cultured with human primary bone marrow stromal cells (BMSC). Frequently, applications require separation of tumor cells and stromal components for subsequent western blot, PCR, DNA or RNA based analysis. However, confocal microscopy provides the unique opportunity to study critical tumor:stromal cell interactions in vitro without physically detaching the tumor population prior to evaluation. This approach is valuable given the transient nature of cell signaling that may be immediately altered upon physical removal of leukemic cells from niche derived stroma. With this approach, a variety of targets are amendable to evaluation, with Ki67 shown in Figure 1 as just one example.

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References