Abstract Title: Profiling Multiple Myeloma Engraftment Phenomena via an in-vivo SCID Mouse Model and RNA-seq

Abstract: Multiple myeloma (MM) is a cancer of the bone marrow characterized by a malignant transformation of plasma cells (PCs). It is currently incurable but patient overall survival has improved dramatically over the past 15 years. Animal models and molecular profiling have both played critical and complementary roles in these advances. An animal model that provides a human-like bone marrow microenvironment is a valuable tool for growing and studying MM cells. The severe combined immune deficient (SCID) mouse model system allows for the growth of primary MM cells in a human-like bone marrow microenvironment. Regarding molecular profiling, recently our program has begun to transition from microarrays to RNA-seq due to its discovery-based nature, base level resolution, and vastly improved dynamic range, which all facilitates potential for biological insights via the identification of new genes, isoforms, gene fusions, etc.

In this study we aimed to explore MM PC engraftment phenomena using a SCID mouse model and RNA-seq by comparing “before” and “after” time points. A patient’s bone marrow aspirate derived PCs were evenly divided (i.e., before/baseline, and after animal model engraftment). One half of the cells were then injected into a rabbit bone grafted to a SCID mouse (SCID-rab model) and later harvested (aka “after”). mRNA were separately isolated from both “before” and “after” specimens, two cDNA libraries built, and all experiments were run on an Illumina HiSeq-2000 in an identical manner utilizing 101 bp PE sequencing. The Tuxedo suite was utilized for RNA-seq data analysis and all experiments were processed in an identical manner using a standard pipeline protocol. Results will be reported concerning computational strategies for analyses and visualization, as well as biological insights on genes and isoforms with a particular focus on eight key MM genes, CCND1, CCND3, DKK1, FGFR3, MAF, MAFB, NFKB, and WHSC1.