Sample Abstract – *Cancer Biology*

Abstract Title: Identification of novel mutational drivers reveals oncogene dependencies in multiple myeloma

Understanding the profile of oncogene and tumor suppressor gene mutations with their interactions and impact on the prognosis of multiple myeloma (MM) can improve the definition of disease subsets and identify pathways important in disease pathobiology. Using integrated genomics of 1273 newly diagnosed patients with MM, we identified 63 driver genes, some of which are novel, including IDH1, IDH2, HUWE1, KLHL6, and PTPN11. Oncogene mutations are significantly more clonal than tumor suppressor mutations, indicating they may exert a bigger selective pressure. Patients with more driver gene abnormalities are associated with worse outcomes, as are identified mechanisms of genomic instability. Oncogenic dependencies were identified between mutations in driver genes, common regions of copy number change, and primary translocation and hyperdiploidy events. These dependencies included associations with t(4;14) and mutations in FGFR3, DIS3, and PRKD2; t(11;14) with mutations in CCND1 and IRF4; t(14;16) with mutations in MAF, BRAF, DIS3, and ATM; and hyperdiploidy with gain 11q, mutations in FAM46C, and MYC rearrangements. These associations indicate that the genomic landscape of myeloma is predetermined by the primary events upon which further dependencies are built, giving rise to a nonrandom accumulation of genetic hits. Understanding these dependencies may elucidate potential evolutionary patterns and lead to better treatment regimens.

KEY

Abstract contains sufficient background to understand the problem under investigation

Abstract must contain a hypothesis, objective or statement about the problem under investigation

Abstract must contain a brief statement of the experimental methods/methodology used

Essential results must be present in summary form (even if preliminary)

Abstract must contain a conclusion that explains how the work contributes to the hypothesis, objective or statement of problem

Abstract Source: Walker B.A. et. al. (2018). *Blood* 132:587-597. DOI: https://doi.org/10.1182/blood-2018-03-840132.