Cleveland Clinic Innovations

Short-Latency Multiple Myeloma Mouse Model and Cell Lines

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PRODUCT

Multiple myeloma mouse model and cell lines that overcome limitations of other disease models

INDICATIONS

Multiple myeloma is an incurable, genetically variable disease that is in need of improved disease models for precision therapeutics

VALUE PROPOSITION

- Model developed based on most common genetic drivers of MM
- AEY-PKM mice develop MM in 81 days with 100% incidence
- Transferable to SCID and wild type mice; related cell lines are available for drug development studies

DEVELOPMENT STAGE

Preclinical studies complete; mice and cell lines available

CONTACT INFORMATION

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IDF 2020-220

OPPORTUNITY

Multiple myeloma (MM) is an incurable cancer of the plasma cells that involves a variety of complex genetic changes. Many mutated genes of interest in MM cause other cancers or are lethal to mouse embryos prior to development of the disease. To date, no pertinent, high penetrance/short latency MM mouse models exist in which multiple genes can be studied at the same time. Therefore, research using MM transgenic models has lagged behind other cancers.

A mouse model of MM with high penetrance and short latency has been a long-sought goal of researchers and industry working in this field. The availability of such a model would enable *in vivo* pre-clinical testing, facilitate the identification of new targets, and allow testing of novel therapeutic approaches that might improve the prognosis of this disease. Lastly, the field does not have a mouse model for MM exhibiting multiple complex mutations that can help advance research.

SOLUTION

Based on strong data indicating the most common genetic drivers of MM in humans, which include Kras mutation, P53 loss of function, and overexpression/translocation of *c-MYC* after initial different chromosomal translocation to IgH domain, Cleveland Clinic researchers have developed a hypermutated, short-latency mouse model of MM for use in preclinical studies. The AEY-PKM (AIDCreERT2$^{+/-}$, EYFP$^{LSL/-}$, P53$^{L/L}$, KrasG12D$^{LSL/-}$, c-MYC$^{LSL/-}$) mouse model is the first to recapitulate the clinical evolution of human MM with short latency (median survival 81 days after tamoxifen injection in 23 days old mice) and 100% incidence. The disease model is also transplantable to SCID and wild type mice, and cell lines APY-PM and AEY-PKM were subsequently generated from the model for preclinical drug development. Moreover, cell lines available from the current mouse model can also be used for *in vitro* studies.

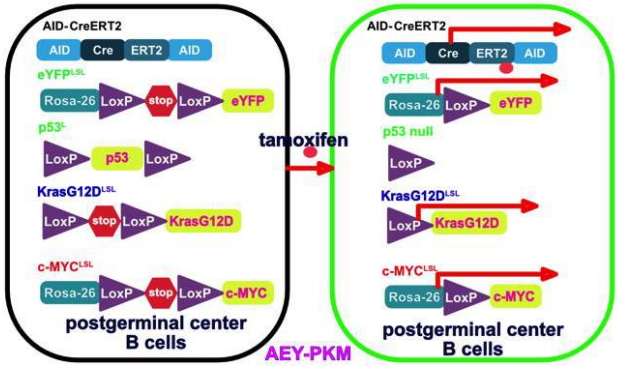

Fig 1: Schematic representation of AEY-PKM conditional transgenic mouse model.