Sylvester researchers develop novel disease model to study multiple myeloma

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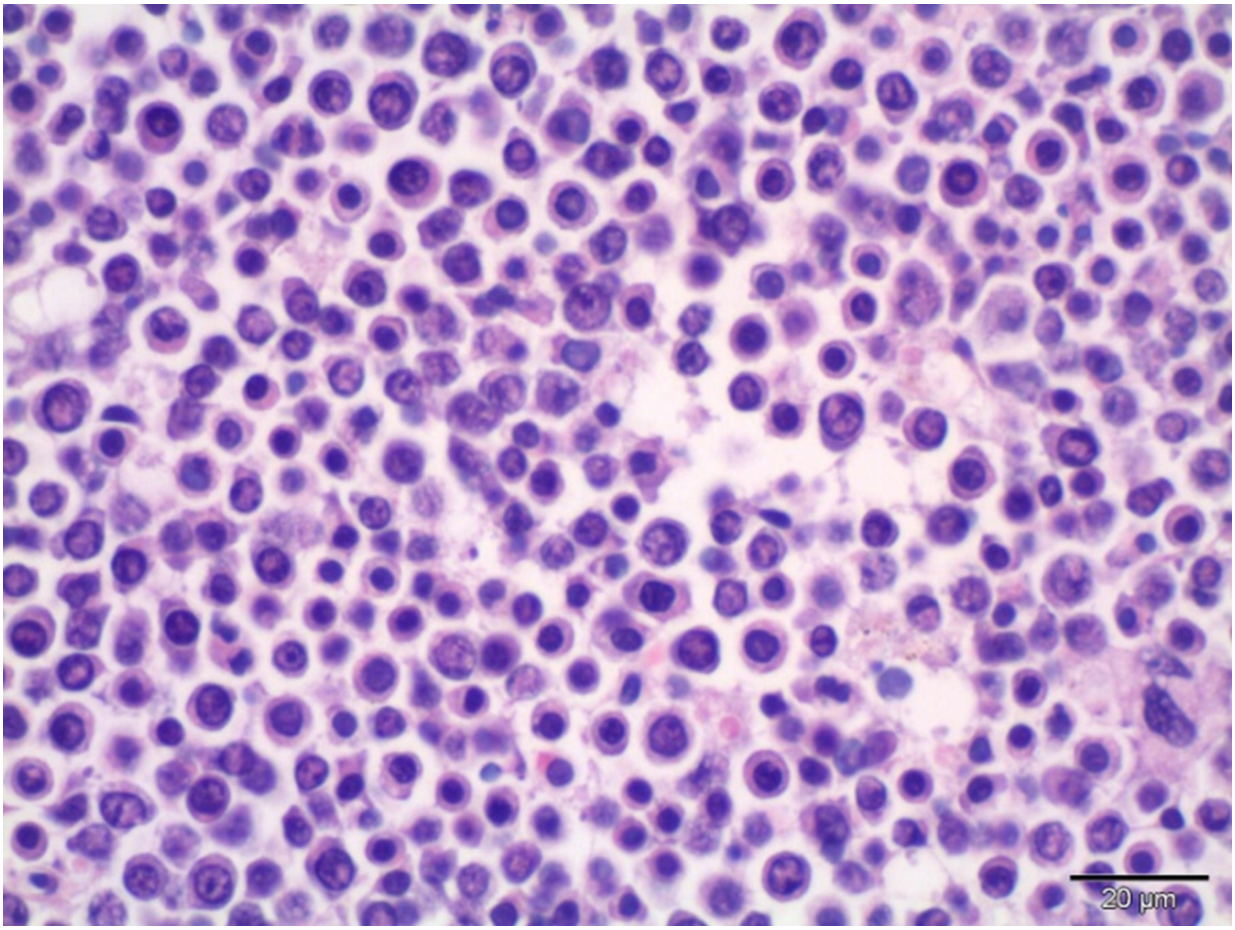

Multiple myeloma cells in the bone marrow. Credit: Sylvester Comprehensive Cancer Center

Researchers at Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine have developed an animal model that allows them to better understand the mechanisms that lead to the development of multiple myeloma, a hematologic cancer of plasma cells, and the amyloidosis that sometimes accompanies it. The study was published in the journal *Scientific Reports*.

"Multiple myeloma is the second most common hematologic malignancy in the U.S. and it is a very complex disease," said Stephen D. Nimer, M.D., director of Sylvester and senior author of the study. "So far, there have not been animal models of malignant plasma-cell diseases that allow us to study their stepwise progression and fully understand the complex cellular mechanisms. Now that we have a proper model of the disease, we'll be able to more effectively study multiple myeloma as well as potential treatments."

Multiple myeloma affects more than 30,000 Americans each year and is slightly more prevalent in men than in women. While considered incurable, multiple myeloma is treatable and the five-year survival rate is approximately 47 percent. In patients with multiple myeloma, abnormal plasma cells accumulate in the bone marrow where they interfere with the production of normal blood cells. Multiple myeloma can also lead to kidney failure, bone destruction, and a predisposition for infection.

The new animal model of multiple myeloma was generated when a team of researchers from Sylvester and Memorial Sloan Kettering Cancer Center in New York crossed two genetically modified mice: mice lacking the Mef gene and mice with a Rad50 gene mutation (Rad50s). Mef, also called Elf4, is a transcription factor—originally cloned in the Nimer lab—that is known to both promote and suppress the formation of cancers. Rad50 is a component of a sensor of DNA damage induced by various stresses and it regulates the DNA damage response pathways in cells.

"In this study, we found that 70 percent of the generated mice died from multiple myeloma or other plasma-cell neoplasms with various symptoms related to multiple myeloma," said Takashi Asai, M.D., Ph.D., associate scientist at Sylvester and first author of the study. "We also found that the phenotype of these mice is not linked to activation of a specific oncogene, or inactivation of a specific tumor suppressor, other than Mef."

"Although outcomes for multiple myeloma patients have greatly improved, it remains an incurable disease, despite the availability of newer treatments," said Nimer. "Several animal models of multiple myeloma have been reported, including models of human myeloma cells. However, these models imperfectly mimic the human disease. Developing more-reliable and accurate animal models that help us better understand myeloma and test new treatments will take us to the next level on the long and challenging road to a cure."

More information: Takashi Asai et al, Generation of a novel, multi-stage, progressive, and transplantable model of plasma cell neoplasms, *Scientific Reports* (2016). DOI: 10.1038/srep22760

Provided by University of Miami Miller School of Medicine

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