New Tools To Detect, Track And Target Cancer Cells In Vivo

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TECHNOLOGY DESCRIPTION

Detection of drug resistant residual oncologic disease is a major technical challenge since the cells can hide in low numbers at any spatial location and may not always be detected in blood draws or aspirates. Residual tumor cells can lie dormant for long periods and can reinitiate tumor growth leading to disease relapse. There is no way to visualize and track cancer stem cells in vivo. Moreover, there is a critical need for the development of methods to specifically target drug resistant residual disease, and to detect cancers at earlier stages. The researcher has focused on the role of Musashi (Msi), a highly conserved RNA binding protein originally identified in drosophila, since Msi is expressed in stem and progenitor cells across many tissues, and long been used as a marker of undifferentiated cells.

BACKGROUND

The researcher has developed a novel fluorescent reporter mouse in which fluorescent signals reflected endogenous Msi expression (*Msi1*^{eYFP}, *Msi2*^{eGFP}, Msi1 reporter mice (Reporter for Musashi1, or REM1) showed expression in the stem cell enriched adult subventricular zone, and Msi1^{+} cells were Nestin+ and CD133+ consistent with Msi1 marking neural stem/progenitor cells. Msi2 reporters (REM2) reflected endogenous expression of Msi2, being highest in hematopoietic stem cells and declining with maturation.

The Msi reporters described here represent exciting new tools that could be broadly useful for studying cancer. Because Msi reporter activity can be visualized through live imaging these reporter mice can be uniquely used to image and track cancer stem cells *in vivo*, and can provide a dynamic view of endogenous cancer growth, tumor dissemination and metastasis in its native microenvironment. The fact that reporter positive cells are preferentially gemcitabine resistant, raises the exciting possibility that this could serve as a new platform to identify therapy resistance *in vivo*. The integration of such reporters in drug development may provide a powerful and sophisticated complement to traditional

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OTHER INFORMATION

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- Medical
  - Disease: Cancer
  - Screening
  - Stem Cell

RELATED CASES
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screens, by allowing the identification of therapies that are better able to target tumor propagating cells, and drug resistant residual disease. In addition, the spatially restricted distribution of Msi+ cells could have important implications for loco regional, aggressive targeting of driver cells that mediate resistance and disease relapse.

APPLICATIONS

This invention could provide a new and unique platform for drug discovery. In addition to its application in cancer drug development, the model may also allow for development of diagnostic and prognostic kits for these diseases. The model could be used to identify and screen compounds that expand stem cell populations and trigger improved regeneration in a variety of tissues.

STATE OF DEVELOPMENT

The reporter mice have been developed and tested in pancreatic cancer. These reporters allowed functional and image based tracking of stem cell signals within cancers *in vivo*, revealing that Msi expression rises as premalignant lesions progress to adenocarcinoma, and that Msi reporter+ tumor cells are the key drivers of pancreatic cancer: they preferentially harbor capacity to propagate adenocarcinoma, are enriched in circulating tumor cells, and are markedly drug resistant.

INTELLECTUAL PROPERTY INFO

A provisional patent application has been filed.

RELATED MATERIALS

► Fox RG, Lytle NK, Jaquish DV, Park FD, Ito T, Bajaj J, Koechlein CS, Zimdahl B, Yano M, Kopp J, Kritzik M, Sicklick J, Sander M, Grandgenett PM, Hollingsworth MA, Shibata S, Pizzo D, Valasek M, Sasik R, Scadeng M, Okano H, Kim Y, MacLeod AR, Lowy AM, Reya T. Image-based detection and targeting of therapy resistance in pancreatic adenocarcinoma. Nature 2016 Jun 16;534(7607):407-411. doi: 10.1038/nature17988. Epub 2016 Jun 6. - 06/06/2016

PATENT STATUS

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United States Of America	Issued Patent	10,578,608	03/03/2020	2016-095

Additional Patent Pending

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