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Cameron Johnstone

Peter MacCallum Cancer Ctr.

Nathanial Harris

University of Wollongong, nlh28@uowmail.edu.au

Marie Ranson

University of Wollongong, mranson@uow.edu.au

Anil K. Rustgi

University of Pennsylvania

Robin L. Anderson

Peter MacCallum Cancer Ctr.

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Abstract

Abstract of a poster presentation at the AACR 106th Annual Meeting, 18-22 April, 2015, Philadelphia, PA.

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Serglycin proteoglycan promotes progression and metastasis of triple-negative breast cancers

Cameron N. Johnstone¹, Nathaniel Harris², Marie Ranson², Anil K. Rustgi³, and

Robin L. Anderson¹

¹*Peter MacCallum Cancer Ctr., East Melbourne, Australia;*

²*University of Wollongong, Wollongong, Australia;*

³*University of Pennsylvania, Philadelphia, PA.*

Poster Presentation

Introduction

Triple-negative breast cancers have a propensity to metastasize and a poor outcome relative to other breast cancer subtypes. No molecularly targeted therapies exist for triple-negative disease and the standard of care for remains surgery followed by adjuvant radiotherapy and/or chemotherapy. Therefore, new therapies that target the molecular alterations present in triple-negative tumors are needed to either prevent metastatic dissemination or kill micrometastatic lesions at distant sites. The serglycin gene encodes a large secreted proteoglycan decorated with chondroitin sulfate modifications and expressed primarily by the hematopoietic system.¹ While serglycin was recently shown to be expressed by mammary epithelial cells², its role in breast oncogenesis is unclear.

Methods

Serglycin expression was analyzed by RNA-based (qRT-PCR) and protein-based (immunohistochemistry) methods³. Serglycin expression was specifically knocked down in triple-negative breast cancer lines (MDA-MB-231_HM4, SUM159) by shRNA technology using the pGIPZ lentiviral system. Genetically engineered cells were assessed in vitro using standard assays. Tumor growth and spontaneous metastasis to lung, liver and spleen was analyzed in vivo by orthotopic inoculation of cells into Nod.Scid.IL-2Rgamma-null (NSG)⁵ immuno-deficient mice.

Results

Serglycin was found to over-expressed in a subset of triple-negative breast cancers as well as in several metastatic triple-negative/claudin-low breast cancer cell lines including MDA-MB-231, SUM159 and Hs578T. Knockdown of serglycin was engineered in highly-metastatic MDA-MB-231_HM (231_HM) cells and in a metastatic variant of SUM159 cells. In vivo experiments showed that knockdown of serglycin reduced the growth rate of primary 231_HM tumours implanted in the mammary fat pads of mice. Moreover, following resection of the primary tumours, spontaneous metastasis to lung, liver and spleen was reduced in serglycin-depleted 231_HM cells.

Conclusions

The hematopoietic proteoglycan serglycin is over-expressed in a subset of triple-negative breast cancers and may represent a novel target for anti-cancer therapy.

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