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Conference Details

Communication Type:Poster	Date:3/15/2019
Total Expense (USD):500	Location:Florence, Italy

Conference Title:Cancer Metastasis: The Role of Metabolism, Immunity and the Microenvironment

Communication Title: Sialic acid metabolism as a key driver of breast cancer metastasis

ABSTRACT

Metastasis, the spread of cancer cells from the original tumor site to other parts of the body, is responsible for ~90% of cancer deaths and is currently incurable. Changes in metabolism – the biochemical processes that convert nutrients into energy and building blocks of life within the cell – occur as cancer cells alter their behavior and spread to new environments during metastasis. Preventing the specific biochemical processes (metabolic pathways) that fuel metastatic spread is therefore a promising approach to stop metastasis. To identify metabolic pathways important for breast cancer metastasis, we measured the levels of intracellular biochemical compounds (metabolites) in two groups of mouse tumors with significantly different metastatic propensities. We found that highly metastatic tumors had elevated levels of sialic acid, a sugar-derived molecule commonly found on cell surfaces. Although elevated levels of cell surface sialic acid was previously associated with tumor malignancy, the importance of its biosynthetic process has not been studied. Based on our results, we hypothesized that metabolism is rewired to increase sialic acid biosynthesis in breast cancer cells; this drives increased sialic acid presentation on the cell surface (through a process known as sialylation) and ultimately promotes metastasis. To confirm this, we measured metabolic flux (the rate of flow through the pathway) in mouse breast cancer cell lines and observed that highly-metastatic cells indeed had increased sialic acid pathway flux. Analysis of gene expression data from human breast cancer patients further revealed that high expression of sialic acid metabolic genes strongly correlated with decreased patient survival, highlighting the clinical relevance of this metabolic pathway. To confirm that sialic acid metabolism plays a causative role in metastasis (as opposed to simply being correlated with metastasis), we then knocked out a key gene of this pathway in two different highly-metastatic cell lines. Following injection of either wild-type or knockout cells into mice, all cell lines formed tumors that grew rapidly; however, tumors originating from knockout cells had an average of ~86% reduction in metastatic spread compared to wild-type tumors. In conclusion, our study revealed the importance of sialic acid pathway for breast cancer metastasis and demonstrated the efficacy of targeting the sialic acid metabolism to stop metastasis. These results have been published in Frontiers in Oncology, May 2018 (doi: 10.3389/fonc.2018.00174).

COMMUNICATION OUTCOMES

The Keystone Symposia on Molecular and Cellular Biology are a series of tightly-focused academic conferences that bring together experts in their field to discuss specific topics in great detail. The Keystone Symposium on Cancer Metastasis focuses on current 'hot topics' of cancer research – metabolism, the immune system, and the tumor cell microenvironment – that in are attracting increasing attention due to their roles in either facilitating or controlling tumor growth and metastatic spread. Many internationally-renowned researchers with decades of experience in the field of cancer research will be speak at this conference; it will be an excellent chance update my knowledge on the latest developments in the field. I will be able to meet these experts in person and discuss their work in depth, gaining deeper insight than can be obtained from simply reading their publications. Importantly, this will be an excellent opportunity to gain international visibility by presenting my work in front of a diverse and highly-experienced audience. I will also obtain valuable feedback and ideas for future directions, and potentially form new collaborations with researchers who possess complementary skillsets and/or infrastructure (for example, since my lab specializes in studies of metabolism, and metabolism has been implicated in modifying the behavior of antitumor immune response, it would be extremely productive to establish collaborative relationships with groups specializing in cancer immunology).

Many of my supervisor Prof. Sophia Lunt's former advisors and colleagues will be present, such as Prof. Matthew Vander Heiden (MIT, USA) and Prof. Sarah-Maria Fendt (VIB Leuven, Belgium), who also study cancer metabolism; my supervisor who is also attending the conference will be able to introduce me and facilitate both my networking with these current and rising stars in the field. Since experts from not only the United States but also many European countries will be attending this conference, this will also be an excellent opportunity for international networking with researchers from other parts of the world. For example, we have been collaborating with a cancer immunology group in University of Laussane (Switzerland) for the past two years; this will be my first opportunity to meet the principal investigator of that group, Dr. Ping-Chih Ho, and discuss our collaborative project in person.

In summary, attending this conference will enable me to update myself on the most current research in the field, gain valuable feedback on my own research, increase my international visibility, network with current and upcoming foremost researchers, form international partnerships and discuss projects in detail with existing collaborators.