

# 9<sup>th</sup> Biotechnology Congress

August 31-September 02, 2015 Orlando, Florida, USA

## Role of macrophage polarization in tumor metastasis

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Tumor metastasis is affected by dynamic changes in the specific phenotypes of macrophage subpopulations; however, the mechanisms by which tumor cell modulates macrophage polarization remain unclear. Here, we investigated the molecular basis and signaling pathways between tumor cells and macrophage polarization and explored the underlying mechanism how to regulate cancer metastasis. We reported CARD9, a central adaptor protein of innate immune responses, which can contribute to tumor metastasis, associated with poor cancer prognosis via induction of metastasis-associated macrophages. Tumor cell secreted VEGF facilitates activation of the Syk signaling pathway in macrophages, leading to induction of the assembly of the CARD9-BCL10-MALT1 complex, following to activation of NF- $\kappa$ B pathway that mediated metastasis-associated macrophage polarization. Moreover, autophagic activity is a critical factor in tumor development that enhances cellular fitness and survival in the hostile tumor microenvironment. We demonstrated that Cat S-mediated autophagic flux is an important mechanism for inducing M2-type polarization of tumor-associated macrophages (TAMs), which leads to tumor development. Furthermore, efficient clearance of apoptotic cells (efferocytosis) can profoundly influence tumor-specific immunity. Our results suggest a novel mechanism by which ICAM-1 in the tumor microenvironment, via restraining efferocytosis of apoptotic tumor cells, can block M2 macrophage polarization through regulation of PI3K/AKT activation, which leads to prevention of tumor metastasis. Together with experimental and clinical findings, we propose a strategy to selectively target macrophage polarization in combination with the adaptor molecule of innate immune responses, autophagy, or efferocytosis, the novel approaches that could have significant therapeutic potential for cancer metastasis.

### Biography

Min Yang is an Associate Professor of Beijing Anzhen Hospital, Capital Medical University. She received the PhD degree in Peking University in 2007. She is currently a Senior Visiting Scholar in the School of Medicine, University of Pittsburgh. She has published thirteen scientific papers in journals including *Cell Death & Differentiation*, *Cell Death & Disease*, *Cell reports*, *ATVB* and *Molecular Cancer*. Her projects have been continually supported by National or Beijing Science Foundation of China since 2010. She is a Reviewer of Cardiovascular Toxicology, Cardiovascular Therapeutics and Wound Repair and Regeneration. She is interested in identifying mechanisms of macrophage polarization in tumor microenvironment.

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