Bose Institute

A new insight into tumor immune-evasion: Crosstalk between cancer stem cells and T regulatory cells

A. Dutta, D. Sengupta, S. Paul, S. Chakraborty, S. Mukherjee, T. Das; Division of Molecular Medicine, Bose Institute,

P 1/12, C.I.T Scheme VIIM Kolkata- 700054

* For correspondence: Email id: tanya@jcbose.ac.in

INTRODUCTION

Cancer stem cells (CSCs) are considered as the major cause for tumor initiation, progression and relapse. Updating the conventional paradigm, that tumor cells themselves are capable of driving the disease it has more recently become apparent that the interaction between the tumor cells and its microenvironment, especially the immune cells plays an important role in disease progression. But our understanding of these complex interactions remain restricted. Given the current understanding of tumor microenvironment where CSCs are responsible for tumor progression we are trying to understand the contribution of CSCs in modulating the host immune system.

OBJECTIVE

- To investigate the mechanism of immune evasion by tumor-initiating CSCs
- Deciphering the role of CSC in generation of immunosuppressive Treg cells
- Unraveling the mechanism behind the same
- To understand whether the mechanism is equally effective *in-vivo*

METHODS

- Isolation of tumor-initiating CSCs using MACS™ bead, and characterization of the same using flow cytometry and in-vivo tumor formation assay.
- Co-culture of isolated tumor-initiating CSCs in contact-dependent as well as contact-independent manner with activated T naïve cells and analyze the induction of immunosuppressive regulatory T cells (Treg cells) in both the culture condition.
- Identification of CSC-secreted factors involved in Treg generation using MALDI-TOF.

RESULTS

Figure 1- Tumor-initiating CSCs are positively correlated with Treg cells

Figure 2- Tumor-initiating CSCs are responsible for the expansion of Treg cells

Figure 3- CSC-secreted exosomes are responsible for Treg generation.

Figure 4-CDE-induced Treg cells are suppressive in nature

Figure 5- FoxP3 governs CDE-mediated Treg generation

Figure 6- Exosomal-FoxP3 utilizes cellular transcriptional and translational machinery to induce the expression of CD25 gene and maintain self expression

GRAPHICAL REPRESENTATION

FUTURE PROSPECTS

REFERENCES

- Thomas W. Owens, Matthew J. Naylor. Breast cancer stem cells. Front Physiol. 2013; 4: 225.
- Canter RJ, Grossenbacher SK, Ames E, Murphy WJ. Immune targeting of cancer stem cells in gastrointestinal oncology. JGastrointestOncol. 2016; 7:S1-S10.
- Garcia-Rubiño ME, Lozano-López C, Campos JM. Inhibitors of Cancer Stem Cells. Anticancer Agents Med Chem. 2016; 16(10):1230-9.
- Gao M, Kong Y, Yang G, Gao L, Shi J. Multiple myeloma cancer stem cells. Oncotarget. 2016; 7(23):35466-77.

ABBREVIATIONS

CSC- Cancer stem cells; NSCCs- Non-stem cancer cells; CDE-CSC- derived exosomes; CM- Conditioned Media; Exo-Exosome; A-Actinomycin-D; C-Cycloheximide; Tn-T naïve cells; MCP2- Methyl CpG binding protein 2; CNS2- Conserved non-coding sequence 2