Synopsis of PhD work

The immune system is an interactive network of different lymphoid organs, cells, humoral factors, and cytokines. In many ways, it is like an army equipped with different weapons to provide protection against infection and malignancies. During tumor progression, infected cell releases various immunosuppressive factors that suppress immune system either directly or by activating host's suppressor mechanism in many ways. Therefore, one of the approach of cancer immunotherapy is to restrict the growth of such tumor and tumor mediated immunosuppression by using several immunopotentiator such as Lipopolysaccharide (LPS), Heat shock Protein 70 (Hsp70), Cisplatin and IFN-g. Hsp70-peptide complex are the most abundant soluble intracellular proteins expressed in almost all cells and are expressed at high levels during cell stress including infection and malignancies. They are basically known as molecular chaperone as they assist in correct native folding of a newly synthesized polypeptides. Among different HSPs, Hsp70 is most abundant cytosolic protein, well characterized, and attracts much attention of the immunologists because of its versatile and immunopotentiating function in the immune system. Hsp70 extracted from tumor cells or virus infected cells are capable of eliciting CD8+ CTL response *in vivo* and *in vitro* against a variety of antigen expressed in the cells from which these peptides have been purified. Macrophages are an essential and fundamental part of innate immune system, and acts as first line of defense against infection. They not only induce innate immune response but also induce adaptive immune response through MHC restricted antigen presentation to T cells and B cells. Although, they play pivotal role in eradication of infection and malignancy from the host, their tumor promoting activity has also been observed during tumor progression. It is probably due to fact that normal function and phenotype of macrophages

resides with tumor cells get suppressed due to the continuous exposure with various immunosuppressive cytokines secreted by tumor cells. These phenotypically suppressed macrophages are termed as tumor associated macrophages (TAMs). The presence of TAMs within the tumor microenvironment has been associated with enhanced tumor progression and shown to promote cancer cell metastasia. It is because; TAMs are highly suppressed phenotype or polarized type II macrophages which differ from its normal counterparts in terms of receptor expression, cytokines and various non-specific effector molecules production. Findings shoes that Hsp70 treatment induces F-actin expression in both NMO and TAMs which is responsible for lamellipodia formation that helps the cells to migrate in and out from tumor microenvironment enhanced expression of macrophage fusion receptor (MFR) responsible for fusion of macrophage to make giant cells and expression of CD54 (ICAM-I) responsible for adherence, cell to cell attachment in NMO and TAMs. The present study also shows that autologous Hsp70 stimulation enhances the expression of CD80 and CD86 co responsible for increased T cell activation and CTL response class I (H2Db) expression which provide first signal for T cell. Therefore, the present study expand our knowledge to understand the tumor well as TAMs reactivity with autologous Hsp70 indicate that the immunosuppressive function of TAMs could be revert back towards tumor destruction. It also shows that treatment of autologous Hsp70 can restore the normal function of tumor associated macrophages by enhancing their antigen presenting capacity and expression of various receptor molecules on the surface. However, if no antigen is known for any disease immune response of the host, makes it a better option to use either as an adjuvant or Hsp70 alone for immunization against any disease.

DST Inspire Faculty Award

I awarded DST inspire faculty Award in the year 2016 and the title of the project was Role of Macrophage in the regulation of Bone and Blood forming stem cell and progenitor cells migration and development. In this project, I tried to find the possible mechanism to explore the cross talk between M1 macrophages and MSCs. How these M1 macrophages will impact the progression and migration of TA-MSCs in breast cancer. My unpublished data show that M1 macrophages facilitates to reversion of tumor-promoting function of MSC (T-MSCs) into tumor regressing function.

Details

INSPIRE Faculty Award - Offer letter [DST/INSPIRE/04/2016/001027]

Title of the Project :- Role of Macrophage in the regulation of Bone and Blood forming stem cell and progenitor cells migration and development

Note-

- 2 Ph.D. student registered in this project
- Only a Research grant was utilized because I was appointed as Assistant Professor at the same time when I received this DST Inspire faculty award.