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2.1. Aims

The overall objective of this thesis was to identify and demonstrate the fate of heavy metal cadmium on the suppression of the immune system and its contribution on the development of carcinogenesis or malignancy. As cadmium is one of the essential constituent of the advanced technological article of our daily life; therefore its exposure to the society brings an unfortunate fate. However, proper understanding of the mechanisms of how it starts to suppress immune system sheds a new light on the understanding of the mechanisms behind neoplastic growth. In this study, the following mechanistic approach of the cadmium induced immune suppression has gained importance.

* The dose dependent study of toxicity of cadmium in the mouse spleen and lymphocytes both *in vivo* and *in vitro*.

* Mechanism and influence of death proteins in the cell death process of spleen and thymus lymphocytes.

* The exact role and regulation of reactive oxygen species (ROS) in these signaling pathways and in the damage.

2.2. Motivation

Cadmium is such a material whose necessity in physiological system is nil or at least still unknown; this makes cadmium a potential toxic elements for living being. However, due to its chemical and physical properties it occupies an important position in some industries. Not only that as a consequences of that the exposure to this toxic element becomes a fatal risk for living beings. Obviously a question comes on that perspective; whether cadmium itself is responsible
for the fatal effects of the toxicity or in combination? Definitively, the answer has two perspectives; within in vivo conditions the effects are due to combined effects of several factors and an organism in a true environment always exposed to a combination of chemical or physical agents. Moreover, the study provides a view at least what will be the possibilities of contribution of the cadmium on those aspects. In addition to that several researches were carried out on the toxic effects of cadmium on the liver and kidney at the tissue level and as well as in cells. Recently, some approach was coming out in respiratory tissues and cells; besides some approaches were coming out on different models like fate of cadmium on breast cancer or pancreas etc. But whatever is the approach of model; till date research was carried out on some focused objectives:

A) To track out the cellular mechanisms that plays the pivotal role in the fate of the cells or tissues,

B) Probable involvement of the signaling cascades in these events.

In this research focus is on the fate, behavior, development of the immune cells in response to cadmium. This study helps to understand not only the fate of the immune cells in the cadmium toxicity, but how immune system fails to evoke a successful immune reaction and failure of which how the conditions deteriorate. Moreover, there is also possible to validate or get an idea how modulation of immune systems involves in the process of neoplastic growths.

2.3. Approach

To achieve these goals several approaches has been taken. To study the mechanistic approach of cadmium induced immune cell fate both in vivo and in vitro studies were carried out. The experimental importance of these two approaches is many folded. There are so many limitations to track out every event that take place in an in vivo model. Therefore, an in vitro
study was carried out to find out the eventual consequences of the in vivo findings. In the in vitro model several consequent events were tracked out by modulation of the activity of the various signaling molecules. These above mentioned approaches were clearly described in the manuscript-1 and manuscript-2 of the chapter-3.

Modification of approach: Besides these, in the later part of the study, some conceptual changes have been made in the objective of the study depending upon the experimental need and previous studies. In the objective, it was stated that the fate of the cadmium also to be studied in the cells of the thymus. But later it was found that several groups demonstrate the atrophic and degenerative changes that have been takes place in the thymus, which means cell death. Therefore, it was necessary to study the fate on the aspects of antigen presenting cells; particularly focusing on dendritic cell subsets called mDCs, which are derived from the bone marrow. Next, it was decided that focus should be on the lymph nodes. Lymph nodes (LNs) are the home of APCs where each and every aspects of life of a true APC occurs; starting from maturation, Ag presentation and the communication with T-cells. On the other hand, LNs are such a basin which drains the tissue derived-Ag to itself. However, in manuscript-3 of chapter-3 the fate of the LNs residents’ mDCs (CD11c+) are demonstrated in response to cadmium that are originally bone marrow derived.