Microparticles treatment modify Apoptosis responses in differentiated THP-1 cells Infected with *Mycobacterium tuberculosis*

Awadh Bihari Yadav* and Amit Misra

Pharmaceutics Division, Central Drug Research Institute, Lucknow

**Objective**

To test the hypothesis that microparticles (MP), with or without anti-tubercular drugs, activate a pro-apoptotic response in differentiated THP-1 cells infected with *Mycobacterium tuberculosis* (MtB); in the terms of induction of early and late apoptosis, alteration of mitochondrial membrane potential, caspase-3, 8 & 9 activity, P2R activity.

**Methods**

1. **Experiment 1 (in vitro)**
   - Cytokine production by the cultured murine macrophage cell line J774 A.1 as a function of time after infection and treatment

2. **Experiment 2 (in vitro)**
   - Early apoptosis induction analysis in differentiated THP-1 cell line infected with M. tb H37Rv, stained with annexin V and propidium iodide (PI)

3. **Experiment 3 (in vitro)**
   - Alteration of MMP: Normal+ treated MP, I: infected cells, ISD: infected + treated SD, IMP: infected + MP, IDMP: infected + blank MP

4. **Experiment 4 (in vitro)**
   - Caspase-3, 8 & 9 induction in differentiated THP-1 cells in response to infection and treatment

**Discussion**

We propose that inhaled microparticles evoke a pro-apoptotic response in MtB infected with MtB. In two ways: by providing a direct stimulus to the infected MtB during the event of phagocytosis and indirectly, through the anti-bacterial action of the incorporated drugs, resulting in modifying the pathogen’s immunosuppressive strategy. Apoptosis is a valid and integrative response, since it denies sanctuary to the pathogen which has evolved to survive and replicate within MtB. Further evaluation of the interplay between bactericidal drug action leading to MtB survival and induction of innate bactericidal responses, some of which may lead to apoptosis, is in progress.

**References**


Hannaguth, G.; Lauterbach, Y.; Manfredal, C. and Grosa, A. (2005), Prophylactic BID is an ATN Effector in the DNA-damage reaction. Cell 122: 579-91

**Acknowledgments**

Funded by the NMITLI program of CSIR. ABY is the recipient of a SRF from CSIR. We thank A.L. Vishwakarma for performing flow cytometry.