Aims and Objectives:

Inflammation is a consequence of disease and the body’s defense against infection or injury. When effective, the inflammatory response ensures successful resolution of the condition and forms part of the normal healing process. Regulation of this response is centrally controlled by cytokine-driven communication, which governs both innate and adaptive immunity. The hallmark characteristics of inflammation is recognized by redness, heat, swelling, loss of function, and pain, and has gained recognition as an underlying contributor to virtually every chronic disease including cancer. Several pro-inflammatory molecules have been identified that play a critical role in suppression of apoptosis, proliferation, angiogenesis, invasion and metastasis. Accordingly, a new paradigm is becoming widely accepted, that chronic inflammation, driven in part by chemokines, cytokines and prostaglandins at the site of a tumor, may facilitate tumor progression instead of promoting antitumor immunity. Chronic inflammation is characterized by infiltration of mononuclear immune cells (including macrophages, lymphocytes, and plasma cells), tissue destruction, fibrosis, and increased angiogenesis. Together, these processes provide a favorable microenvironment for the exponential growth of malignant cells. Thus, inflammation may provide both the key mutations and the proper environment needed to foster the growth of cancer cells.

The control of inflammatory progress and induction of apoptosis in the hyper inflamed cells may therefore constitute a therapeutic approach to cancer treatment. The use of anti-inflammatory agents may decrease the incidence and occurrence of various cancers, and improve the prognosis for patients. Moreover, the induction of apoptosis with regulation of cellular growth is also essential for hyper proliferating cells, i.e. in course of cancer treatment.

The successful treatment of inflammatory conditions with the involvement of biologics that may contribute to the relief of autoimmunity, chronic inflammation, and associated tissue damage can be a possible way out for cancer therapy. Leishmania is an eukaryotic protozoan parasite, so its component(s) is expected to be compatible for human host. In the light of recent findings, it seems that LPG (Lipophosphoglycan), a conserved major glycolipid molecule on the surface of
all *Leishmania* species and an evolutionarily perfected molecule, represents a new class of compounds that may be exploited for clinical use as an antiinflammatory agent for overt vascular cell-activation states. Leishmanial lipid is a strong immunosuppressor of host cells and inhibition of the inflammatory responses of synovial cells through induction of apoptosis is one of the main targets of therapeutic intervention in rheumatoid arthritis. In previous investigations, we have shown that a lipid fraction from an attenuated strain of *Leishmania donovani* promastigote (MHO/IN/1978/UR6), developed by long-term *in vitro* culture, suppresses the proliferation of cells obtained from the synovial fluid of rheumatoid arthritis patients by inducing apoptosis. These evidences encouraged us to evaluate the role of the leishmanial lipid(s) (MHOM/IN/1983/AG83) as a mediator of inflammatory responses. It appeared that the leishmanial lipid(s) may be effective in regulating the inflammatory responses concurring with the modulation of cancer cell growth, especially reducing their viability and inducing apoptosis.
Objectives:

- To isolate and identify the lipid(s) from *Leishmania donovani* (MHOM/IN/1983/AG83) and evaluate its bioactive potential on stimulated macrophage cells in respect to its anti-inflammatory role.
- To evaluate the role of leishmanial lipid(s) involving the different key factor(s) in the transcriptional regulation of diverse anti-oxidative enzymes and anti-inflammatory mediator(s).
- To ascertain the molecular mechanisms of leishmanial lipid(s) underlying the regulation of cancer cell survival and apoptosis of host candidate.
- To find out if leishmanial lipid(s) can differentially modulate anti-inflammatory and anti-cancer signal transduction cascade(s) in a concerted manner towards the ultimate prevention of cancer development.

Thus, the objectives of the present research proposal were to develop a potent anti-inflammatory agent from leishmanial lipid(s) that can modulate the inflamed and stressed microenvironment of *in vitro* as well as *in vivo* systems for therapeutic purposes, viz. for regulating cancer cell growth. The success of this investigation would be up new avenues in the medical science in fighting against inflammatory response and cancer cell growth and of use in cancer chemotherapy.