List of figures

Chapter 2: Review of Literature

Figure 2.1: Variation of estrogen levels during menstrual cycle in humans 8
Figure 2.2: Domain structure of ER-α and ER-β 9
Figure 2.3: Sex-based incidence of various autoimmune diseases 13
Figure 2.4: Pathways of apoptosis 23
Figure 2.5: Domain architecture of Bcl-2 family of proteins 25

Chapter 4: Characterization of estrogen receptor expression in human macrophages

Figure 4.1. Human THP-1 macrophages express transcripts for both ER-α and β 58
Figure 4.2: Sub-cellular localization of estrogen receptors in THP-1 macrophages 58
Figure 4.3. Immunocytochemistry for estrogen receptor expression 59
Figure 4.4: Surface binding of E2-BSA-FITC 60
Figure 4.5. Human peripheral blood monocyte derived macrophages express both ER-α and ER-β 61
Figure 4.6. Microscopic analysis of sub-cellular localization of estrogen receptors in hPBMDM 62

Chapter 5: Study of the role of estrogen in human macrophage survival

Figure 5.1. Effect of estrogen on human macrophage viability 65
Figure 5.2. Estrogen protects human macrophages against LPS-induced cell death 66
Figure 5.3. Estrogen modulates Bcl-2 family of proteins in THP-1 macrophages 67
Figure 5.4. Bcl-2 and Bax are modulated via signaling through the estrogen receptor 68
Figure 5.5. siRNA mediated knockdown of ER-α and ER-β 70
Figure 5.6. A differential role for ER-α and ER-β in modulation of Bcl-2 and Bax 71
Figure 5.7. Nuclear translocation of estrogen receptor upon ligand binding 72
Figure 5.8. Membranous estrogen receptor signals for Bcl-2 up-regulation but not Bax translocation 73
Figure 5.9. Role of ERK phosphorylation in Bcl-2 up-regulation

Figure 5.10. E2 induces a rapid intracellular Ca^{2+} flux

Figure 5.11. Bcl-2 up-regulation is mediated by ERK phosphorylation

Figure 5.12. Estrogen-induced Bax translocation is independent of Ca^{2+} influx and ERK phosphorylation

Figure 5.13. Estrogen induces intracellular alkalinization

Figure 5.14. Estrogen-induced intracellular alkalinization mediates Bax translocation

Figure 5.15. Estrogen activates NHE to mediate intracellular alkalinization

Figure 5.16. Estrogen maintains the ratio of Bax and Bcl-2 on the mitochondria

Figure 5.17. Inhibition of Bcl-2 up-regulation results in macrophage death upon exposure to E2

Figure 5.18. Estrogen treatment of Bcl-2 knockdown macrophages leads to cell death

Figure 5.19. Estrogen induces Bcl-2 up-regulation in hPBMDM

Chapter 6: Estrogen modulation of macrophage function

Figure 6.1. Estrogen enhances macrophage phagocytosis

Figure 6.2. Estrogen does not affect ROS generation

Figure 6.3. Estrogen increases NO generation via an iNOS dependent mechanism

Figure 6.4. Estrogen inhibits secretion of IL-1, IL-8 and IL-12

Figure 6.5. Estrogen does not affect the secretion of IL-4, IL-6, IFN-γ and TNF

Figure 6.6. L. major infection in THP-1 macrophages

Figure 6.7. Effect of estrogen on L. major infection in macrophages

Figure 6.8. Histopathology of footpad of BALB/c mice infected with L. major

Figure 6.9. Progression of leishmanial infection in oophorectomized mice

Chapter 7: Discussion

Figure 7.1. Schematic showing intracellular signaling pathways involved in estrogen action on human macrophages