List of figures and tables

Chapter 1

Figure 1.1. Schematic representation of TLR signaling pathways 15
Figure 1.2. Schematic representation of cooperation between innate and adaptive immunity 18
Figure 1.3. Schematic representation of different population of macrophage, exhibiting distinct physiologies 24
Figure 1.4. Three signals from macrophages are important for T cell priming responses and effector commitment 26
Figure 1.5. Schematic representation of MHC class I and MHC class II antigen presentation pathways 29

Table 1. Distinguishing features of the innate and adaptive immune system 4
Table 2. TLRs and their ligands 10

Chapter 3

Figure 3.1. Purification of recombinant Mtbhsp60 69
Figure 3.2. Mtbhsp60 induces IL-10 production in THP-1 macrophages 70
Figure 3.3. Mtbhsp60 induces IL-10 production in THP-1 macrophages as analysed at transcript level 71
Figure 3.4. Mtbhsp60 binds efficiently to both TLR2 and TLR4 receptors 73
Figure 3.5. Semi-quantitative RT-PCR data indicated that IL-10 activation by Mtbhsp60 is TLR2 dependent 75
Figure 3.6. IL-10 induction by Mtbhsp60 is inhibited in THP-1 macrophages when both TLR2 and TLR4 receptors are blocked 76
Figure 3.7. Anti-TLR2 mAb inhibits Mtbhsp60-induced IL-10 production in THP-1 macrophages. 77
Figure 3.8. Mtbhsp60 induces IL-10 in peritoneal macrophages during its interaction with TLR2 78
Figure 3.9. The anti-TLR2 or the anti-TLR4 neutralizing mAb or the isotype control antibody is not cytotoxic to THP-1 macrophages 79
Figure 3.10. siRNA mediated gene silencing of TLR2 and TLR4 receptors 81
Figure 3.11. Silencing of TLR2 expression by siRNA down-regulates Mtbhsp60-induced IL-10 in THP-1 macrophages 82
Figure 3.12. Mtbhsp60 colocalizes with Early Endosome Antigen 1 (EEA1) in endosomes

Figure 3.13. Monodansylcadaverine (MDC) inhibits endocytosis of Mtbhsp60 in THP-1 macrophages

Figure 3.14. MDC increased cell-surface accumulation of Mtbhsp60

Figure 3.15. Monodansylcadaverine (MDC) inhibits Mtbhsp60-mediated induction of IL-10 in THP-1 macrophages

Figure 3.16. MDC does not affect viability of cells treated with Mtbhsp60

Figure 3.17. Mtbhsp60 undergoes receptor-mediated endocytosis through interaction with TLR2

Figure 3.18. Mtbhsp60 colocalizes with TLR2 receptors

Figure 3.19. IL-10 activation by Mtbhsp60 is dependent on TLR2-mediated endocytosis of Mtbhsp60 in macrophages

Figure 3.20. Interaction of Mtbhsp60 with TLR4 or TLR2 plus MDC triggers TNF-α production

Figure 3.21. Mtbhsp60 fails to induce IL-10 in macrophages harvested from TLR2 KO mice and TNF-α in macrophages harvested from TLR4 KO mice

Figure 3.22. Ecolihsp60 binds to both TLR2 and TLR4 receptors

Figure 3.23. Ecolihsp60 is retained at the surface of cells treated with either anti-TLR2 or anti-TLR4 mAb

Figure 3.24. TNF-α production by Ecolihsp60 is inhibited in THP-1 macrophages treated with either anti-TLR2 or anti-TLR4 mAb

Figure 3.25. Secondary structure comparison of Mtbhsp60 with Ecolihsp60

Figure 3.26. Comparison of phosphorylation status of p38 MAPK and ERK 1/2 mediated by Mtbhsp60 between the TLR2 receptor that undergoes endocytosis against TLR4 that does not undergo endocytosis

Figure 3.27. Mtbhsp60 activates p38 MAPK when it interacts with TLR2 while its interaction with TLR4 predominantly induces ERK 1/2 activation

Figure 3.28. Blocking TLR2 mediated endocytosis of Mtbhsp60 results in inhibition of p38 MAPK phosphorylation but cause an increase in ERK 1/2 phosphorylation

Figure 3.29. Mtbhsp60 activates NF-κB transcription factors mainly through TLR4.

Figure 3.30. The NF-κB inhibitors, BAY11-7082 and PDTC prevents TNF-α induction in THP-1 macrophages by Mtbhsp60 during its interaction with TLR4

Figure 3.31. DNA-binding activity of p50 and p65 NF-κB complex in THP-1 macrophages treated with Mtbhsp60 in the presence of isotype control antibody or anti-TLR2 mAb or anti-TLR4 mAb