Mi Wang, Ph.D. candidate [mentor: Dr. Alan Tall]

During atherogenesis, monocyte-derived cells traverse into the subendothelial space where they ingest deposited lipoproteins, accumulate lipids and transform into specialized macrophage foam cells. The subsequent retention of foam cells creates a great challenge in the treatment of atherosclerosis. The emigration of these macrophages in a favorable lipoprotein environment has been reported to contribute to atherosclerosis regression marked by reduced atherosclerotic plaque size and reduced foam cell content in the lesions. Therefore, preventing the retention of foam cells and promoting their emigration from atherosclerotic lesions represents a promising therapeutic strategy.

Although the mechanism of foam cell retention is not fully understood, it has been reported that elevated cholesterol level in the plasma membranes of macrophages inhibits their migration by altering Rho GTPase signaling. It is also known that ABCA1 and ABCG1 are ABC transporters that play an important role in promoting cholesterol efflux in macrophages, contributing to a restored plasma cholesterol level. My preliminary studies in the Tall laboratory have shown that macrophages lacking ABCA1 and ABCG1 show impaired migration in chemotaxis assays, correlating with increased cell membrane ruffling and Rac1 activation.

Based on these findings, I hypothesize that ABCA1 and ABCG1 play an important role during the emigration of macrophages from atherosclerotic lesions by reducing the plasma membrane cholesterol content and restoring their ability to migrate.

I will carry out cellular and molecular studies to gain further insight into the mechanisms of ABCA1 and ABCG1 dependent chemotaxis. *in vivo* studies will be performed to determine the effect of combined deficiency of ABCA1 and ABCG1 on macrophage retention. I will also study the role of ABCA1 and ABCG1 in foam cell emigration using a mouse model of atherosclerosis regression.

The proposed study will improve our understanding of foam cell retention in atherosclerosis and potentially provide guidance for the development of therapeutic approaches that aim to promote atherosclerotic plaque regression.

This study will be carried out in collaboration with Dr. Tamara Pagler and Dr. Marit Westerterp, who are both post-doctoral research scientists in Dr. Alan Tall's laboratory.