XVI International Symposium on Atherosclerosis
25–29 March 2012, Sydney Convention and Exhibition Centre, Sydney, Australia

- WEDNESDAY 28th March, 2012

Plenary 3: Infection, immunity and atherosclerosis

Future hope for immunisation against atherosclerosis?

Adaptive immunity plays a key role in the development atherosclerosis. As T cells are present at all stages of atherosclerotic disease, it is likely that they are relevant to both the initiation and progression of atherosclerosis. Targeting T cells is an attractive strategy because of the antigen-specific, clonal nature of these cells. Recent evidence supporting immunotherapy as potential strategy for preventing atherosclerosis was overviewed by Professor Göran Hansson, Karolinska Institute, Stockholm, Sweden in the opening lecture of the third plenary session.

Work using a transgenic mouse model has shown that native apolipoprotein B100 (apoB100), but not oxidised apoB100, acts as an antigenic epitope in triggering T cell activation. Once triggered, T cells provide antibodies to a wide range of epitopes, and also play a cytokine-mediated role in activation of macrophages, leading to an increase in inflammation and decrease in plaque stability. This response involves TRBV31+ TCR; immunisation against this T cell receptor significantly reduces atherosclerosis. These data therefore imply that a subset of T cells that recognise ApoB100 epitopes regulate the development of atherosclerosis. Blocking recognition of apoB100 by T cells substantially reduces atherosclerosis. ‘However, there is a window of immunoreactivity between achieving sufficient uptake of oxidised apoB100 by scavenger receptors but not enough to destroy the epitope.’

Among the T cell population, Th1 cells have been shown to promote atherosclerosis, whereas Treg cells suppress atherosclerosis. Dendritic cells play a key role in regulating this process. The dendritic cells patrol the artery, pick up antigens and then move to the lymph node where they then instruct naïve T cells, and this process is successively repeated.

However, it is possible to train dendritic cells to behave better. In hypercholesterolemic mice, apoB loaded tolerogenic dendritic cells have been shown to reduce atherosclerosis, by suppressing the Th1 response to ApoB100 and instead inducing fox3p3+ Treg cells. This can be regarded as an antigen-specific strategy to reduce atherosclerotic disease.

Clearly, atherosclerosis appears to be highly dependent on the type of T cell response within the arterial wall. Research has focused on investigating immunisation as a potential strategy for reducing atherosclerosis. Passive immunisation is the most advanced with some agents already in phase 2 trials. Active immunisation (i.e. vaccination) is at an earlier stage, with ongoing work aimed at identifying suitable peptides for activation of T cells. Other strategies under investigation include immunomodulation (i.e. by blocking co-stimulatory factors or blocking cytokine signalling) and
tolerogenic approaches. ‘Although at early stages, the possibility of immunisation against atherosclerosis is an exciting prospect for the future.’

*Medical writing for ISA2012 reportage was funded by an unrestricted educational grant from AstraZeneca.*