

# INNATE LYMPHOID CELLS IN ALL DEVELOPMENTAL STAGES OF ATHEROSCLEROSIS

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## ABSTRACT

Atherothrombotic diseases such as coronary artery disease (acute myocardial infarction), cerebral ischemia (stroke), and peripheral arterial disease are still major contributors to global mortality and morbidity (1). Inflammation (inflammation) is an important process in the development of atherosclerosis and thrombosis (2). Natural lymphoid cells/innate lymphoid cells (ILCs) are partners of T lymphocytes, which are involved mainly in the early stages of the disease. They are divided into groups 1, 2 and 3 based on the specific transcription factors (TF) and the expression of the cytokines they produce (3). Recent studies in mice assume the involvement of ILC in atherogenesis (4). Nonetheless, there have been no studies on the presence and role of ILCs in human atherosclerotic tissue. Our review of the literature found that finding ILCs in human tissues was challenging because there were no unique markers to specifically identify ILCs (5). This study aims to find a combination of markers that can detect the presence of ILC and findings with the course of atherosclerosis in humans. This study is expected to provide information on whether ILC as a strong immunomodulator can be an important alternative target in the prevention and/or treatment of atherosclerosis. This study is an ex vivo experiment, using a human atherosclerotic plaque specimen obtained anonymously from a clinical autopsy at UMC Amsterdam, the Netherlands. Permission was obtained from the UMC Amsterdam Ethics Council. Selected specimens were fixed in formalin and stored as tissue paraffin blocks, and classified according to the degree of atherosclerosis progression (5). Specimens were cut and made into microscope slides to be painted with multiple sequential staining immunohistochemistry technique. Multiple antibodies will be combined as markers for ILC1 (T-bet), ILC2 (GATA3) and ILC3 (ROR $\gamma$ T) with exclusion markers for T and B cells. ILCs are identified by creating stacks of overlapping slides that have been painted with combination markers using the DigiPath server. . Each specimen was selected three observation areas measuring 0.5mm<sup>2</sup> to identify and count the number of ILC1, ILC2 and ILC3 expressed as the number of cells per mm<sup>2</sup> and as a ratio to all lymphocytes. All data will be presented as scatter plots and statistically analyzed using SPSS 24.0. The output targets of this study are articles published in a database of internationally reputed indexed journals, namely Atherosclerosis (SJR Q1), and one reference book and/or internationally indexed proceedings (ICRIEMS) as additional outputs. Currently, this basic research is at the technology readiness level at TKT 1 and is expected to reach TKT 2 eventually. The University of Amsterdam is ranked 55 according to the QS World University Rankings, therefore this collaborative research will certainly contribute to UNY's "IKU", boost UNY World rankings and support the internationalization of UNY.

Kata Kunci: *atherosclerosis, inflammation, innate immunity, lymphoid cells*