NLRP3 Inflammasome Expression and Activation in Human Atherosclerosis - DTU Orbit

30/01/2019

NLRP3 Inflammasome Expression and Activation in Human Atherosclerosis

Background The NLR family, pyrin domain containing 3 (NLRP3) inflammasome is an interleukin (IL)-1β and IL-18 cytokine processing complex that is activated in inflammatory conditions. The role of the NLRP3 inflammasome in the pathogenesis of atherosclerosis and myocardial infarction is not fully understood.

Methods and Results Atherosclerotic plaques were analyzed for transcripts of the NLRP3 inflammasome, and for IL-1β release. The Swedish First-ever myocardial Infarction study in Ac-county (FIA) cohort consisting of DNA from 556 myocardial infarction patients and 1016 healthy individuals was used to determine the frequency of 4 single nucleotide polymorphisms (SNPs) from the downstream regulatory region of NLRP3. Expression of NLRP3, Apoptosis-associated speck-like protein containing a CARD (ASC), caspase-1 (CASP1), IL1B, and IL18 mRNA was significantly increased in atherosclerotic plaques compared to normal arteries. The expression of NLRP3 mRNA was significantly higher in plaques of symptomatic patients when compared to asymptomatic ones. CD68-positive macrophages were observed in the same areas of atherosclerotic lesions as NLRP3 and ASC expression. Occasionally, expression of NLRP3 and ASC was also present in smooth muscle cells. Cholesterol crystals and ATP induced IL-1β release from lipopolysaccharide-primed human atherosclerotic lesion plaques. The minor alleles of the variants rs4266924, rs6672995, and rs10733113 were associated with NLRP3 mRNA levels in peripheral blood mononuclear cells but not with the risk of myocardial infarction.

Conclusions Our results indicate a possible role of the NLRP3 inflammasome and its genetic variants in the pathogenesis of atherosclerosis.

General information
State: Published
Organisations: Örebro University, Karolinska Institutet, Oslo University Hospital, Norwegian University of Science and Technology, Karolinska University Hospital, Umeå University
Number of pages: 14
Publication date: 2016
Peer-reviewed: Yes

Publication information
Journal: Journal of the American Heart Association
Volume: 5
Issue number: 5
Article number: e003031
ISSN (Print): 2047-9980
Ratings:
Web of Science (2019): Indexed yes
Web of Science (2018): Indexed yes
Scopus rating (2017): CiteScore 4.42 SJR 2.674 SNIP 1.412
Web of Science (2017): Impact factor 4.45
Web of Science (2017): Indexed yes
Scopus rating (2016): CiteScore 3.31 SJR 2.705 SNIP 1.244
Web of Science (2016): Impact factor 4.425
Web of Science (2016): Indexed yes
Scopus rating (2015): CiteScore 4.31 SJR 2.787 SNIP 1.097
Web of Science (2015): Impact factor 5.117
Scopus rating (2014): CiteScore 3.44 SJR 2.391 SNIP 1.362
Web of Science (2014): Impact factor 4.306
Scopus rating (2013): CiteScore 2.07 SJR 1.359 SNIP 5.162
Web of Science (2013): Impact factor 2.882
Original language: English
Keywords: Inflammasome, Interleukin-1β, Myocardial infarction, NLRP3, Polymorphism
Electronic versions:
NLRP3_Inflammasome_Expression_and_Activation_in_Human.pdf
DOI:
10.1161/JAHA.115.003031

Bibliographical note
This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.