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Title: Gene expression analysis of rheumatic heart disease valves using NanoString technology

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Background & Aims: Rheumatic heart disease (RHD) ranks as one of the most serious cardiovascular scourges of the past century and remains a force to be reckoned with in the developing world.

Methods: The nCounter® NanoString® technology is a multiplex analysis system. It is currently the only system capable of quantifying up to 800 nucleic acids of formalin-fixed paraffin-embedded (FFPE) tissue with one single reaction and without amplification step. Avoiding amplification step allow to get rid of typical analysis bias (i.e cross-hybridization, background noise, level of detection...). Despite this difference with others technologies, nCounter® system has been demonstrated to show comparable results between FFPE and fresh frozen samples and in that a sensitivity that is higher than that of microarrays and about equal to that of RT-PCR. Beyond the advantage of being performed on the same sample used for light microscopy, nCounter® offer the opportunity for analysis on large retrospective and longitudinal analyses of archived samples in the setting of decentralized multicenter studies. We have taken advantage of these different characteristics to analyze transcriptomic profiles from FFPE valves of RHD patients.

Results: Using the B-HOT panel, developed in part by our team4, and based on heatmap analysis (data not shown), our first results show two distinct transcriptomic profiles between inflammatory burden region of RHD valves patients (n=13) and control valves (without lesions, n=10).

Our differential gene expression analysis between those 2 groups show several genes overexpressed in RHD group compared to control valves (Fig 1A). Interestingly, and as potential therapeutic targets, genes related to CD20 (MS4A1, MS4A2) and IL-6R are among genes that are differentially expressed.

Box plots gene expression specific to those genes give insights on a strong tendency for an overexpression of CD20-genes related and IL6-R gene (Fig 2B).

Conclusions: Taken together, these preliminary results suggest a potential role for CD20 and IL6-R in inflammatory responses of RHD valves lesions. Rituximab (CD20) and Tocilizumab (IL6-R) could be potential therapeutic molecules to be used on RHD patients. Further investigations remain to be conducted to validated these hypotheses.