Role of miR-146a in the Regulation of Inflammation in an In Vitro Model of Graves’ Orbitopathy

We have read with great interest the article published by Jang et al. We congratulate the authors for their study and their efforts to explore the potential role of miR-146a in the pathogenesis of Grave’s orbitopathy (GO). The results in the article are displayed elegantly with convincing data. However, we believe that some results presented in their article deserve further discussion.

First, the authors found that the level of miR-146a expression was significantly higher in GO orbital adipose tissue compared with the non-GO normal controls. What we are most interested in is the source of the increased level of miR-146a. It is well known that the spectrum of organism miRNAs is mainly influenced by the complexity of the organism structure and the miRNA expression is tissue-specific. Therefore, what would the possible origin of miR-146a? Is it secreted by orbital adipocytes or from fibroblast cells or other cells? Here, we propose one possibility that the peripheral blood CD$^+$ T cells may be one source of the increased miR-146a in the GO orbital adipose tissues. The reasons are as follows: (1) miRNAs are known to work not only inside the cells, but are also capable of being secreted into the bloodstream to affect other target cells, (2) upregulated miR-146a expression has been detected in the peripheral blood CD$^+$ T cells from patients diagnosed with rheumatoid arthritis, and (3) GO is characterized by orbital T cell infiltration. We think it is very necessary to identify the exact source of miR-146a, which will determine the way of future microRNA immunotherapy.

Second, the authors detected 45 total differentially expressed microRNAs using microarray analyses. In addition to miR-146a, we also noted miR-155, another well-known microRNA in inflammatory autoimmune diseases. Both of them are immune-specific miRNAs and increasingly growing evidence indicates that miR-146a and miR-155 are both indispensable in the adaptive and the innate immune system. MI-146a and miR-155 were significantly upregulated in GO orbital adipose tissue. We want to discuss with Jang and colleagues—what do they think the interrelation between miR-146a and miR-155? Will miR-155 play a similar role in the regulation of inflammation in orbital fibroblasts? Will miR-155 participate in the pathogenesis of GO?

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References

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