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MicroRNAs may control mRNAs in circulating peripheral blood mononuclear cells during the acute phase of Kawasaki disease

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Introduction------MicroRNAs (miRs) are small noncoding RNAs of 18-25 nucleotides that mediate gene silencing through imperfect hybridization to 3' untranslated regions in target mRNAs. The human genome encodes more than 800 different miRs that modulate a variety of biological activities including immunological reactions. Kawasaki disease (KD) is the most common systemic vasculitis syndrome primarily affecting small and medium-sized arteries, particularly the coronary arteries. Patients are diagnosed with KD if they had 5 or more of the following diagnostic criteria: more than 5 days-lasting fever, conjunctivitis, skin rash, red palms and soles or peelings, and swollen lymph nodes. It was reported that peripheral blood mononuclear cells (PBMCs)-derived vascular endothelial growth factor (VEGF) may contribute to later vascular injury and remodeling in KD, but the etiology of KD is not clear yet. Though KD may be associated with immunological problems, the involvement of miRs in KD has not been reported.

Methods------We performed mRNA and miR microarray analysis of PBMCs isolated from acute KD patients (N=4) who were responsive to intravenous immunoglobulin treatment (2g/kg/24hr), a febrile disease group (viral or bacterial infection, N=6), or healthy controls (N=6). The data were analyzed using GeneSpring GX 11.0 software and Ingenuity Pathways Analysis tools.

Results--------Prior to treatment miR-93 and miR-877 were down-regulated and miR-92b, miR-182 and miR-296-5p were up-regulated by comparison with the febrile group and healthy controls. The levels of these 5 miRs normalized after treatment. The expression of *VEGFA*, which were previously reported to be controlled by miR-93, was up-regulated prior to treatment and normalized upon treatment, negatively correlating with the expression of miR-93.

Conclusions-----We identified 5 miRs, miR-93, miR-877, miR-92b, miR-182, miR-296-5p, which were highly specific to the acute phase of Kawasaki disease suggesting a small number of known miRs play an important role during the acute phase of KD. In particular miR-93 may control the expression of *VEGFA* and have an important role in signaling resulting in the development of coronary artery lesions. We are currently analysing the biological function of the other 4 miRs.