Kawasaki Disease Canada – Research Update

Elastin-Derived Peptides in the Development of Kawasaki Disease

By: Alicia Fisch

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Kawasaki Disease (KD) is a paediatric inflammatory disease of the blood vessels in multiple organ systems throughout the body. The most commonly damaged vessels are the coronary arteries that supply blood to the heart. This leads to weakening of the arterial wall and aneurysm formation. A hallmark feature of aneurysm formation is elastin breakdown. Elastin is an important structural protein found the middle layer of arteries, including the coronary arteries. The breakdown of elastin generates small fragments that circulate in the bloodstream, called elastin-derived peptides (EDPs). Interestingly, EDPs are not just mere by-products but are in-fact active. EDPs bind to the elastin receptor to induce several biological events, notably, the upregulation of elastin-degrading molecules. This leads to further elastin breakdown and EDP production, thus, creating a vicious cycle that promotes aneurysm formation in children with KD. In addition to EDPs, the elastin receptor can also bind to galactosugars. However, unlike EDPs, the binding of these sugars induces a change in the shape of the elastin receptor that causes it to fall apart. Accordingly; the overall research objective is to examine the role of EDPs in the development of KD and whether it can be inhibited by galactosugars.

Previous results demonstrated the biological activity of EDPs, including the ability to upregulate key molecules involved in elastin breakdown and aneurysm formation in KD. More importantly, this effect was shown to be inhibited in the presence of galactosugars. EDPs were also found to be increased in the blood of diseased mice with coronary artery inflammation compared to non-diseased mice during disease development. Continued work is underway to examine the association of EDPs and children with KD. There is no single laboratory test to definitively diagnose KD, and the symptoms often resemble a non-specific infection. This can result in a delay in diagnosis and necessary treatment, which increases the risk of aneurysm formation. Greater EDPs in the blood of diseased mice suggests that EDPs may be a novel predictor of disease development, and establishing them as such will aid in identifying high-risk children and help direct therapy appropriately. Furthermore, recent data suggests that galactosugars can be used to alter heart disease in mice developing KD. Diseased mice fed galactosugar-supplemented water developed less severe disease compared to those fed non-galactosugar-supplemented water. Research is ongoing to examine the ability of galactosugars to attenuate disease severity. Arterial lesions develop in up to 25% of appropriately treated children with KD. The potential of galactosugars to inhibit EDPs provides an alternative approach to therapy and opens the door for new drug targets. Thus – the outcomes of this research will affect both the diagnosis and treatment of children with KD.