Elastin-Derived Peptides in the Development of Kawasaki Disease

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Kawasaki Disease (KD) is an 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 local weakening of the arterial wall and subsequent ballooning, referred to as aneurysm formation. KD affects young children primarily under the age of five, making it the number one cause of acquired heart disease in Canadian children.

A hallmark feature of aneurysm formation is elastin breakdown. Elastin is an important structural protein found in the middle layer of arteries, including the coronary arteries. The breakdown of elastin generates small fragments that are soluble in the circulation, 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 such as lactose. However, 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.

Preliminary results further demonstrate that EDPs are biologically active. EDPs promote the upregulation of key molecules involved in elastin breakdown and aneurysm formation in KD. More importantly, this effect can be inhibited in the presence of lactose, a common galactosugar. Furthermore, EDPs are 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 how galactosugars can be used to alter heart disease in mice developing KD, and the association of EDPs and children with KD.

There is no laboratory test to definitively diagnose KD, and the symptoms often resemble a non-specific infection. This can result in a delayed diagnosis and necessary treatment, which increases the risk of aneurysm formation. EDPs may be a novel marker of disease activity, and establishing them as such will aid in identifying high-risk children and help direct therapy appropriately. 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, this research will greatly impact both the diagnosis and treatment of children with KD.