Khadija Rafiq et al., Virol Res J 2018, Volume 2

THE ROLE OF B CELLS IN DIABETIC CARDIOMYOPATHY

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Diabetic cardiomyopathy (DCM) is typified by alterations in cardiac morphology and function, independent of hypertension or coronary disease. The disease is characterized by intramyocardial inflammation, cardiomyocytes apoptosis and cardiac fibrosis. The molecular mechanism that links inflammation to DCM is incompletely understood. This study investigates the role of B cells on the development of DCM. Induction of diabetes in WT mice resulted a significant decrease in B cell infiltration into the left ventricular heart, but not in other organs, during the development of DCM. Interestingly, decreased B cell numbers correlate with the downregulation of the expression of a B cell inflammatory molecule, Allograft Inflammatory Factor-1(AIF-1), which has been reported to enhance lymphocyte activation. However, the molecular mechanism(s) responsible for the decrease of B cell homing and AIF-1 expression in diabetic hearts as well as their relationship during the development of DCM is unknown. Focused on gaining insight into the role of AIF-1 in B cell migration, our *in vitro* study showed that B cell migration to cardiomyocytes is regulated by AIF-1 expression. We observed significant migration of B cells to hyperglycemic GFP-tagged AIF-1 transfected H9C2 cells compared to control cells transfected with an empty vector. Interestingly, Adenovirus AIF-1 overexpression promoted B cell homing to diabetic heart tissues, reduced inflammation and pathological remodeling. These effects of AIF-1 overexpression on the diabetes-induced cardiac dilatation and function are independent of AIF-1 effects on hyperglycemia since blood glucose levels are similar in diabetic WT mice with or without AIF-1 overexpression. This study suggests that diabetes attenuates AIF-1 expression, and this in turn, prevents B cell homing to diabetic heart tissues which in trun results in an increase of cardiac inflammation that leads to DCM.

BIOGRAPHY

Khadija Rafiq has her expertise in Immunology and Cellular Biology. Over the past several years she has been investigating how the immune system affects cardiac myocyte growth and cardiac function with a focus on signaling molecules that are activated by inflammatory proteases. Her research interest focuses on elucidating the role of inflammatory serine proteases in the development of diabetic cardiomyopathy. It is well known that inflammation plays a role in the development of diabetic cardiomyopathy. The goals of her research are to identify novel signaling mechanisms that control cardiac cell growth and apoptosis.

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