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## Novel role of DOCK2 in diet-induced obesity and lung injury

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Obesity is a significant health burden and is involved in the development of various lung diseases. However, little is known about the effects of chronic high-fat and high-fructose (HFHF) diet-induced obesity on lung inflammatory/injury. We previously showed that dedicator of cytokinesis 2 (DOCK2) is critical for high-fat diet (HFD)-induced obesity and adipose tissue inflammation. DOCK2 deficient mice were protected from HFD induced body weight gain, insulin resistance, and increased proinflammatory cytokines in the adipose tissue and peripheral circulation. However, it remains elusive whether DOCK2 plays a role in lung injury associated with chronic HFHF diet-induced obesity. In this study, we showed that chronic HFHF diet (20 weeks) induced lung inflammatory infiltration and collagen expression in the wild-type (WT) C57BL/6 mice. Macrophage marker CD68 and monocyte chemoattractant protein-1 (MCP-1) expression were notably increased in the lungs of WT mice fed a HFHF diet. Importantly, HFHF diet increased lung DOCK2 expression that co-localized with fibroblast marker, fibroblast-specific protein 1. These data suggest a potential role of DOCK2 in regulating proinflammatory phenotype of lung fibroblasts. Further, DOCK2 deficiency attenuated lung inflammation and fibrosis induced by chronic HFHF diet. In primary normal human lung fibroblast cells, TNF- $\alpha$  and IL-1 $\beta$  induced DOCK2 expression concurrent with MCP-1, IL-6, and matrix metalloproteinase-2. DOCK2 knockdown also suppressed TNF- $\alpha$  induced increase of these inflammatory mediators. Taken together, these findings suggest a previously unrecognized role of DOCK2 in mediating diet-induced obesity, and lung inflammation/fibrosis in chronic HFHF diet caused obesity.

### Biography

Dr. Guo completed her PhD in 2014 from the University of Georgia (UGA) where she continued as a postdoc scholar and a research scientist. During her study at UGA, Dr. Guo received both pre-doctoral and postdoctoral fellowships from American Heart Association. She joined the University of Texas Health Science Center at Tyler as an Assistant Professor in 2019 with a NIH K99/R00 grant. She has published more than 30 papers in reputed journals (e.g., Circ. Res., ATVB, J Lipid Res., J. Hepatol., and Am. J. Pathol.). She also serves in the reviewer committee for the American Heart Association.

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