The Role of Vascular Adhesion Protein-1 in the Pathogenesis of Diabetes and Its Complications

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Vascular adhesion protein-1 (VAP-1) is a dual-function protein. It participates in inflammation and can catalyze the breakdown of amines through its semicarbazide-sensitive amine oxidase activity, to produce oxidative stress and advanced glycation end products (AGEs).

Obesity up-regulates VAP-1 expression in adipose tissue. Adipose VAP-1 can then up-regulate the secretion of monocyte chemotactic protein-1, which propagates inflammation and results in insulin resistance. Plasma VAP-1, a marker of adipose inflammation and insulin resistance in human, can predict the development of diabetes in the future. Besides, serum VAP-1 can predicts diabetic complications. VAP-1 is a source of systemic oxidative stress and AGEs in human subjects. Serum VAP-1 correlates positively with fasting plasma glucose and hemoglobin A1c, and is higher in subjects with diabetes. Serum VAP-1 is higher in subjects with chronic kidney diseases and is positively associated with the extend of albuminuria. Moreover, serum VAP-1 can predict the development of end-stage renal disease in subjects with type 2 diabetes. There is an association between serum VAP-1 and carotid intima-medial thickness, a surrogate marker for stroke in the future. Most importantly, serum VAP-1 can predict cardiovascular mortality, cancer-related mortality, and all-cause mortality independent to all traditional risk factors in subjects with type 2 diabetes. Serum VAP-1 can enhance mortality prediction over and above established risk factors, the extend of which is comparable to the performance of age, smoking, serum creatinine, and proteinuria.

In summary, VAP-1 is involved in the pathogenesis of diabetes and its complications. Our findings suggest that serum VAP-1 is a novel biomarker to predict the development of diabetes and its complications.