Non-neuronal cholinergic system prevents coronary vascular dysfunction in diabetic heart

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Background: Diabetic individuals suffer extensive myocardial damage during ischemia due to impaired ATP production and coronary vascular dysfunction. The cardiomyocytes possess a non-neuronal cholinergic system (NNCS) as it has choline acetyltransferase (ChAT) to synthesize acetylcholine (ACh). ACh released from cardiomyocytes activates hypoxia-inducible factor-1 pathway in an auto/paracrine manner under non-hypoxic condition. Activation of this pathway via NNCS promotes angiogenesis and is a promising mechanism to target ischemia in diabetes.

Aim: To investigate if activation of NNCS could improve the coronary vasculature in diabetic heart.

Methods: Type-2 diabetic db/db mice with ventricle-specific ChAT transgene (db/db-ChAT-tg) and control db/db mice of 12- and 24-weeks old were used. Catheterization of the jugular vein and carotid artery was performed in combination with synchrotron radiation microangiography to visualize the in-vivo coronary circulation. Changes of the coronary circulation to ACh (10µg/kg/min) and sodium nitroprusside (SNP, 10µg/kg/min) were assessed. Immunofluorescence analysis was performed to measure the density of arterioles and capillaries ex-vivo.

Results: In comparison to db/db mice, the number of second and third order vessels was higher in the db/db-ChAT-tg mice of 12- and 24-weeks old under baseline condition. In response to ACh and SNP, number of third order vessels were further increased in the db/db-ChAT-tg mice of both ages. However, the magnitude of the diameter changes in db/db-ChAT-tg mice was comparable to that in db/db mice of both ages. Besides, the db/db-ChAT-tg mice had increased density of arterioles and capillaries compared to the db/db mice of both ages.

Conclusion: NNCS-induced angiogenesis prevents coronary vascular dysfunction in diabetic heart.