招請講演

# 招聘講演2（ III-IL02）

# Coronary Microvascular Disease in Diabetes : Role of HuR-Cx40-EDH Axis

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## [III-IL02-01]Coronary Microvascular Disease in Diabetes : Role of HuR-Cx40-EDH Axis

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Diabetes is a global epidemic, and many people with diabetes suffer from heart disease. Diabetic heart disease includes obstructive coronary artery disease (CAD) and coronary microvascular disease (CMD = non-obstructive CAD). Recent reports alert the importance of CMD in diabetes as a risk factor for cardiac mortality; however, the molecular mechanism by which diabetes promotes CMD is poorly understood. At the meeting, I will talk about the role of HuR in the development of CMD in diabetes. HuR is an RNA-binding protein: a key regulator of mRNA stability and translation. Diabetic mice exhibited decreases in coronary flow velocity reserve (CFVR, a determinant of coronary microvascular function), accompanied by capillary rarefaction and attenuated endothelium-dependent relaxation (EDR) in small coronary arteries: the causes of CMD. HuR levels in cardiac endothelial cells (CECs) were significantly lower in diabetic mice and diabetic patients than the controls. EC-specific HuR-KO mice showed significant reductions in capillary density, EDR, and CFVR. The results from a PCR array revealed that HuR, Cx40, and Nox4 levels were decreased in CECs from diabetic and HuR-KO mice compared to control mice. Cx40 expression and HuR binding to Cx40 mRNA were reduced in CECs from diabetic mice. Cx40-KO mice exhibited decreased capillary density, EDR, and CFVR, whereas EC-specific Cx40-overexpression restored CFVR by increasing capillary density and EDR in diabetic mice. These data suggest that decreased HuR contributes to the development of CMD in diabetes via downregulating Cx40 in CECs, and Cx40 is a promising therapeutic target for CMD in diabetic patients.