一般口演 | 心血管発生・基礎研究

一般口演26（ II-OR26）
心血管発生・基礎研究

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[II-OR26-01]非同期を伴った心不全におけるリン酸化キナーゼの活性化の解析ー新開発の長期間ネズミペーシングモデルを用いて

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Purpose) Dyssynchrony (Dys) plays an important role in clinical heart failure. The purpose of this study was to characterize the effect of Dys on phospho-kinase activation in mice failing hearts. Methods) Heart failure (HF) was induced in wild type (C57/Bl6) mice by ischemia-reperfusion (I/R). An ECG-lead and a right ventricular pacing (RVP) lead was implanted and the mouse was connected to a custom made pacemaker/ECG-monitoring system. Mice were then divided into two groups: DysHF (4 weeks of continuous RVP) and Synchronous HF (no pacing). Non- failing/instrumented wild type mice served as additional control (WT-CON). Fractional shortening (FS) was measured using echocardiography after pacemaker surgery and after 4 weeks. Mice hearts were analyzed for relative levels of phosphorylation/activation of 46 kinase phosphorylationsites. Results) After 4 weeks, FS was unchanged in the SyncHF group (36±6%) but decreased in the DysHF group (24±6, $p < 0.01$ vs. both others). 11 of 46 kinase phosphorylation sites had significantly higher level of phosphorylation/activation in the DysHF compared to SyncHF groups. Conclusion) RVP induces left ventricular Dys in mice that when applied for four weeks accelerates heart failure remodeling in infarcted hearts. This is associated with phosphorylation/activation of kinases that regulate a range of cellular processes including cell survival, energy homeostasis and hypertrophy. This novel model can now be used to study the effect Dys on cellular signaling pathways in a genetically modifiable animal for the first time.