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**Susceptibility to Develop Obesity Affects Cardiometabolic Risk Profiles in Female
Obesity-prone Osborne-Mendel and Obesity-resistant S5B/PI Rats**

Obesity and dietary fat intake are important contributors to cardiometabolic disease; however, inherent susceptibility to obesity may independently influence disease risk. Previous studies demonstrated that high-fat diet (HFD) consumption had limited effects on metabolic syndrome-related outcomes in female obesity-prone Osborne-Mendel (OM) and obesity-resistant S5B/PI (S5B) rats. In contrast, strain-dependent differences in cardiometabolic risk factors have been reported in male OM and S5B rats, but not investigated in females. Therefore, the current study investigated cardiometabolic risk factors in female OM and S5B rats. We hypothesized that female OM rats would exhibit greater cardiometabolic risk than female S5B rats and that HFD consumption would further exacerbate these factors in OM rats.

Circulating levels of lipids, adiponectin, glucose and inflammatory markers were assessed following 6 weeks of HFD or LFD intake in female OM and S5B rats. Left ventricle hypertrophy and mRNA expression of markers of cardiovascular health were evaluated.

OM females exhibited greater visceral adiposity, cardiac hypertrophy, and elevated expression of left ventricular inflammatory and vascular remodeling markers compared with S5B females. These strain differences were evident in rats fed the LFD, indicating an inherent predisposition toward increased cardiometabolic risk in OM rats. HFD consumption further increased visceral adiposity in OM rats and differentially altered circulating TNF- α , adiponectin, and cardiac inflammatory gene expression in a strain-dependent manner.

Significance: This study demonstrates that inherent differences associated with obesity susceptibility were a stronger determinant of cardiometabolic risk than short-term HFD intake in female rats, highlighting the importance of underlying individual variability in cardiometabolic disease risk.