

## MS05-7 Impact of glycerol metabolism through aquaporin 7

○Norikazu MAEDA<sup>1</sup>

<sup>1</sup>Department of Metabolic Medicine, Graduate School of Medicine, Osaka University

**Background:** We previously cloned aquaporin 7 (AQP7) belonging to aquaglyceroporin from human adipose tissue cDNA library. AQP7 is abundantly expressed in fat tissue and testis, and is also detected in heart, kidney, and skeletal muscle. The role of AQP7 has not been fully understood in fat and heart. **Materials and methods:** We generated and analyzed AQP7-knockout (AQP7-KO) mice. For *in vitro* experiments, 3T3-L1 adipocytes and H9c2 cardiomyocytes were used. **Results:** 1. AQP7-KO mice showed a disturbed increase of plasma glycerol and rapid reduction of plasma glucose during prolonged fasting at around 8 weeks of age. 2. The body weight and fat mass increased significantly in AQP7-KO mice compared to wild-type (WT) mice after 12 weeks of age. AQP7-KO mice developed obesity and insulin resistance even at a young age after consumption of high-fat/high-sucrose diet. Introduction of AQP7-siRNA resulted in the significant increase of glycerol content, glycerol kinase activity, and triglyceride content in 3T3-L1 adipocytes. 3. Cardiac morphology and function in AQP7-KO mice were similar to those of WT mice under basal conditions, although low glycerol and ATP content were observed in hearts of AQP7-KO mice. In H9c2 cardiomyocytes, glycerol uptake and glycerol-dependent ATP elevation were decreased by AQP7-siRNA. The *ex vivo* heart study showed the impairment of cardiac glycerol consumption levels in AQP7-KO mice. Pressure overload caused severe heart failure in AQP7-KO mice. **Conclusions:** A series of our data may indicate that AQP7 maintains the glycerol homeostasis in fat and heart.