

MKR mice were maintained as homozygous and the hyperglycemia conditions (fast glucose level above 350mg/dl) were confirmed by tail vein bleeding glucose test using OneTouch® Ultra Blood Glucose Monitoring System. FVB background wildtype (WT) breeders were ordered from JAX Lab. Twelve-week-old male WT and MKR mice were randomly assigned to two groups (n=4 in each group) and received daily intraperitoneal (I.P) injections of vehicle (PBS) or metformin (Met, 200mg/kg BW) in 50ul volume for 14-days. After euthanization, long bones from hind limbs were dissected. Total bone marrow cells were immediately flushed out with PBS into Eppendorf Protein LoBind tubes. Samples were flash frozen and only thawed at the time of metabolite extraction.