Supplemental Discussion

Based on their daily food consumption on high fat diet (1), total energetic expenditure per 35-45 gram mouse is conservatively on the order of 13-14 kcal/day. The relatively low measured RER (0.72-0.80) demonstrated in these studies indicates that the majority of energy disposal of these mice originates from lipid oxidation. An RER of 0.76 predicts that three-quarters of the energy is from lipid oxidation, this would correspond to 9.8 kcal/day of lipid clearance. So, if oxidative muscle accounts for 30% of daily bodily lipid oxidation, then a 25% defect in lipid disposal would produce a $9.8 \times 0.25 \times 0.30 = 0.7$ kcal/day deficit in energy expenditure. This is equivalent to 0.08 grams of excess fat storage per day, which is very close to the measured 0.06 grams per day of excess weight gain.

The change in RER for MuPPARγKO mice can likewise be estimated from the measured defect in fatty acid uptake. Using the above calculations, lipid oxidation accounts for 9.8 kcal/day of the total 13 kcal/day energy expenditure. This would produce an RER of 0.7616, assuming oxidation of one mole of glucose or fatty acid requires 6 or 23 moles of O_2 and produces 6 or 16 moles of CO_2 respectively. As above, in MuPPARγKO mice there is a 25% defect in fatty acid oxidation present in soleus-like muscle, which can be conservatively estimated to represent 25% of the total lipid oxidative tissues. Thus, lipid oxidation and total energy expenditure are reduced by 0.7 kcal/day, predicting an RER of 0.7657. The RER for MuPPARγKO is thus expected to be roughly increased by 0.004, comparing favorably to the measured change of 0.005±0.0005 (Figure 2A).

References

1. **Norris AW, Chen L, Fisher SJ, Szanto I, Ristow M, Jozsi AC, Hirshman MF, Rosen ED, Goodyear LJ, Gonzalez FJ, Spiegelman BM, Kahn CR** 2003 Muscle-specific ppargamma-deficient mice develop increased adiposity and insulin resistance but respond to thiazolidinediones. J Clin Invest 112:608-618