Supplement Methods:

A. Vascular Access, Plasma Flow and Sampling.: Catheter sheaths were first placed in the right femoral artery and femoral vein followed by insertion of a catheter into the femoral artery through the femoral artery sheath and insertion of a catheter into the hepatic vein through the femoral vein sheath. Appropriate positioning was confirmed by nonionic contrast injection and patency of the sheaths and catheters was maintained by continuous infusion of normal saline at a rate of 30 mL/hr. The femoral artery sheath was used for infusion of indocyanine green (ICG) to measure plasma flow in the leg and splanchnic region using indicator dye dilution techniques (1; 2). The femoral vein sheath, femoral artery catheter, and hepatic vein catheter were used to collect blood samples. Baseline blood samples (3 sets each 10 minutes apart) were taken from these intravascular catheters after ICG had been infusing for 30 minutes.

B. Analysis of Samples: Plasma [${}^{2}H_{5}$]phenylalanine enrichment was measured by liquid chromatography-tandem mass spectrometry as previously described (3). Blood glucose was measured by the glucose oxidase method while plasma measurements were performed as follows: c-peptide by a 2-site immuno-enzymatic sandwich assay on the Roche Cobas e411 (Roche Diagnostics, Indianapolis, IN 46250), glucagon by a direct, double antibody radioimmunoassay (RIA) (Millipore Corporation, Billerica, MA 01821) and insulin by a two-site immunoenzymatic assay on the DxI 800 automated immunoassay system (Beckman Instruments, Chaska, MN 55318). ICG concentration was measured by spectrophotometry. AAs and their metabolites were measured in duplicate by liquid chromatography-mass spectrometry as described at each three time-points and averages were used for calculations (4; 5). Blood glucose, ICG, and plasma L-(ring- ${}^{2}H_{5}$)-phenylalanine enrichment were measured in triplicate at each of the three time points and averages of these values were used for calculations (3).

References

1. Bradley SE, Ingelfinger FJ, et al.: The estimation of hepatic blood flow in man. J Clin Invest 1945;24:890-897

2. Jorfeldt L, Wahren J: Leg blood flow during exercise in man. Clin Sci 1971;41:459-473

3. Zabielski P, Ford GC, Persson XM, Jaleel A, Dewey JD, Nair KS: Comparison of different mass spectrometry techniques in the measurement of L-[ring-13C6]phenylalanine incorporation into mixed muscle proteins. J Mass Spectrom 2013;48:269-275

4. Lanza IR, Zhang S, Ward LE, Karakelides H, Raftery D, Nair KS: Quantitative metabolomics by H-NMR and LC-MS/MS confirms altered metabolic pathways in diabetes. PLoS ONE 2010;5:e10538

5. Irving BA, Carter RE, Soop M, Weymiller A, Syed H, Karakelides H, Bhagra S, Short KR, Tatpati L, Barazzoni R, Nair KS: Effect of insulin sensitizer therapy on amino acids and their metabolites. Metabolism 2015;64:720-728