Residual feed intake (RFI) is calculated using DMI as the dependent variable and metabolic body weight (BW 0.75) and ADG as independent variables. Mitochondria complex I (mitochondrial NADH: ubiquinone oxidoreductase) is one of the least understood membrane-bound protein complexes. Insulin resistance has been reported in calves, dairy cows, horses, and swine. For all four mitochondria experiments, there was a significant difference (P < 0.05) between RFI and DMI but no difference (P > 0.05) was reported for ADG and MMBW. For experiments one, two, and three, CI was greater (P < 0.05) for -RFI compared to other treatments. The correlation between CI and RFI was -0.37 (P = 0.02), -0.48 (P = 0.034), and -0.84 (P = 0.015) for experiment one, two, and three, respectively. For experiment 4, animals with -RFI had a trend for greater concentration (P = 0.07) of Band I (protein S1) than +RFI. Correlation between RFI and Band I was -0.72 (P = 0.04). A regression was developed using Band I and RFI with RFI = 6.1715 -0.00015BandI, R2 = 0.85, RMSE = 0.62. No significant difference (P > 0.05) was reported in any variable measured during both the glucose and epinephrine tolerance test. We concluded that mitochondrial function was at least in part responsible for differences among animals in metabolic efficiency. In addition, insulin resistance is not responsible for RFI classification in feedlot animals.