Description of the PPAR-δ transgenic mouse (marathon mouse)

The PPAR-δ transgenic mouse, also known as the "marathon mouse,",was built based upon the expression of an activated PPAR-δ human receptor with targeted expression in skeletal muscle. Details of the construct are described in "Regulation of Muscle Fiber Type and Running Endurance by PPAR-δ" (*PLoS Biology* 2(10/e294) October 2004). Relative expression levels in various skeletal muscle groups is virtually the same as that of endogenous PPAR-δ in wildtype littermates. In the original mixed genetic background, transgenic and wildtype littermates are born at standard Mendelian ratios, mature at the same rate and are fertile. In the heterogeneous background, transgenic and wildtype littermates show the same total body weight, but the transgenics show a resistance to weight gain on a high fat, high caloric diet. It is this set of age and weight matched male mice that were compared for metabolic properties as well as endurance as measured on a continuous treadmill study. As detailed in the *PLoSB* paper, lipid parameters in the transgenic mice are generally improved, insulin sensitivity is enhanced, and running capacity is tremendously augmented. Specifically, normal mice were able to run approximately 90 minutes in their first run; the transgenic animals run an additional hour longer. The total distance covered by wildtype littermates is approximately 900 meters whereas the transgenic mice run 1800 meters in the first treadmill test. Background activity in cages is identical between wildtype and transgenic mice, therefore distance and running behavior is attributed to increased presence of non-fatiguing Type I muscle fiber. This is confirmed by histologic and genetic analysis. Interestingly, as we move the transgene into the C57BL/6 background, the transgenic littermates show progressive decrease in weight due to a reduction in adiposity. Therefore, most exercise studies are conducted in the outbred background so that littermates can be age, sex and weight matched.