Chronic diseases such as obesity and diabetes have significant genetic and environmental components. One important environmental component is the lack of physical activity, or physical inactivity. This first part of this dissertation determines how reductions in physical activity contribute to increases in fat mass. Furthermore, how the increase in fat mass changes the energy utilizing pathways within fat tissue itself, in both a normal and obese was examined. Importantly, this work demonstrates that during the first days of inactivity fat mass increases in a healthy manner not associated with what is seen in diabetic or obese animals. In the second part of the dissertation the role of physical activity on DNA methylation was examined. DNA methylation, unlike genetic mutations, does not change the sequence of DNA, indirectly affects how much of a given gene is expressed. This was the first attempt to examine whether physical activity can change DNA methylation of specific genes. Using a technique that looks for differences in DNA methylation throughout the whole genome several genes looked like they may differ in methylation. However, these genes did not differ in expression amount. Thus, although it seems that genes can be more or less methylated in response to physical activity whether this has a functional importance in gene expression requires further study.