

Proteomic Analysis of Skin from Mice with Type 2 Diabetes

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The C57BL/6J strain of mice has been well documented to develop obesity and type 2 diabetes when exposed to a high-fat diet. Thus, they represent a useful animal model to mimic several aspects of disease progression seen in humans. While other models of obesity linked diabetes exist, such as db/db and ob/ob mice, the majority of these models are monogenic meaning that they are the result of a single mutated gene. In the case of ob/ob and db/db mice, the mutated genes are leptin and the leptin receptor, respectively. Since in humans, type 2 diabetes is thought to be a polygenic disease as well as the result of poor diet and sedentary life style, we used C57BL/6J mice to study changes in a variety of organs as the mice progress from a normal to obese to diabetic phenotype. In this study, the skin proteome of mice in the diabetic state is presented. Comparative proteomic analysis on skin from type 2 diabetic C57BL/6J mice fed a high-fat diet was performed. Non-diabetic mice fed a regular chow diet served as controls. Indicators of type 2 diabetes including body weight as well as circulating concentrations of leptin, FFA, insulin and glucose were measured at multiple time points to track the progression of the disease. Once all 5 of these indicators of diabetes were significantly elevated in the high fat fed mice as compared to controls, the skin samples were taken. Two-dimensional gel electrophoresis 2-D GE was performed on proteins isolated from these samples. The 2-D gels were then stained with Sypro Orange and images were captured using a CCD camera. Using PDQuest 7.0 software, proteomic profiles from the skin samples of both control and diabetic mice were established. Of the more than 850 distinct protein spots that were detected by the software, 29 were shown to be consistently altered with 7 showing a decrease and 22 an increase in the diabetic state compared to controls. The 28 differential protein spots were then removed from the gels and analyzed by MALDI-TOF and MS/MS analyses. Peak data were used to determine the identities of the proteins that were altered in the diabetic state. These results help establish a specific proteomic profile for intact skin in the diabetic state. Moreover, since skin is one of the easiest tissues to biopsy, human skin biopsies coupled with proteomic analysis have the potential to be useful for a non evasive method for the early diagnosis and perhaps prevention of hyperinsulinemia and diabetes.

This work was supported in part by the State of Ohio's Eminent Scholar Program that includes a gift from Milton and Lawrence Goll, by a grant from the AMVETS organization, by funds from the National Institute of Diabetes and Digestive and Kidney Disease (grant DK064905) and by a grant from DiAtheGen LLC.