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# Comprehensive Longitudinal Multi-omic Profiling in Weight Gain and Insulin Resistance

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**Abstract :** Three million deaths worldwide are attributed to obesity. However, the biomolecular mechanisms that describe the link between adiposity and subsequent disease states are poorly understood. Insulin resistance characterizes approximately half of obese individuals and is a major cause of obesity-mediated diseases such as Type II diabetes, hypertension and other cardiovascular diseases. This study makes use of longitudinal quantitative and high-throughput multi-omics (genomics, epigenomics, transcriptomics, glycoproteomics etc.) methodologies on blood samples to develop multigenic and multi-analyte signatures associated with weight gain and insulin resistance. Participants of this study underwent a 30-day period of weight gain via excessive caloric intake followed by a 60-day period of restricted dieting and return to baseline weight. Blood samples were taken at three different time points per patient: baseline, peak-weight and post weight loss. Patients were characterized as either insulin resistant (IR) or insulin sensitive (IS) before having their samples processed via longitudinal multi-omic technologies. This comparative study revealed a wealth of biomolecular changes associated with weight gain after using methods in machine learning, clustering, network analysis etc. Pathways of interest included those involved in lipid remodeling, acute inflammatory response and glucose metabolism. Some of these biomolecules returned to baseline levels as the patient returned to normal weight whilst some remained elevated. IR patients exhibited key differences in inflammatory response regulation in comparison to IS patients at all time points. These signatures suggest differential metabolism and inflammatory pathways between IR and IS patients. Biomolecular differences associated with weight gain and insulin resistance were identified on various levels: in gene expression, epigenetic change, transcriptional regulation and glycosylation. This study was not only able to contribute to new biology that could be of use in preventing or predicting obesity-mediated diseases, but also matured novel biomedical informatics technologies to produce and process data on many comprehensive omics levels.

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