Abstract:

Diabetes and insulin resistance are associated with significantly accelerated rates of cardiovascular disease. Inflammatory gene mediated activation of circulating monocytes has been implicated in this pathology but the underlying molecular mechanisms are not fully understood. We have examined the nature of key inflammatory chemokines and cytokines involved in monocyte activation under diabetic conditions in vitro, macrophages from diabetic mice as well as in peripheral blood monocytes isolated from diabetic patients. We investigated specific molecular, transcriptional and post transcriptional mechanisms involved in the enhanced expression of these genes by high glucose and advanced glycation end products. We have also examined nuclear transcriptomic mechanisms and chromatin remodeling events triggered by diabetic conditions in cultured monocytes and in cells from diabetic patients. We have recently developed a systems biology procedure to profile and compare chromatin histone modifications between multiple groups using chromatin immunoprecipitation (ChIP) linked with microarrays (ChIP-on-chip). Our results provide new insights into the mechanisms responsible for the accelerated rates of vascular inflammation and cardiovascular complications observed in diabetes.