Complex signaling networks, consisting of receptors, kinases, and transcription factors, are involved in the regulation of metabolism, but how these events are accurately coordinated within a cell is not well known. Molecular scaffolds, such as those belonging to the 14-3-3 protein family, are ideal candidates due to their ability to facilitate protein localization and protein-protein interactions. In general, scaffolds are presumed to have passive signaling roles, and whether they actively contribute to overall metabolism has not been formally examined. Since their discovery in brain extracts, 14-3-3 proteins have been demonstrated to have large interactomes due to their ability to recognize phospho-Ser/Thr proteins, and this suggests that they may participate in diverse metabolic processes. We recently discovered novel roles of 14-3-3 proteins, and specifically the 14-3-3ζ isoform, in the regulation of pancreatic β-cell survival, adipogenesis, and glucose homeostasis. Alterations in the activity of signaling effectors are known to promote the pathogenesis of chronic diseases, such as type 2 diabetes and obesity, but whether similar changes can occur with scaffolds is not known. Thus, the overall objectives of my research group are aimed at exploring how 14-3-3 proteins facilitate signaling events underlying metabolism and to investigate their potential contributions to the development of chronic diseases, in particular obesity and diabetes. The long-term goal is to determine if 14-3-3 proteins or components of their interactomes can one day be targeted for the treatment of chronic diseases.