

System-Level Integration and Analysis of High-Throughput Molecular Data in the Framework of Cellular Pathways**Bugrim, Andrej****GeneGo Inc., New Buffalo, MI, USA**

This presentation will address a critical problem faced by the biomedical researchers in both industry and academia -- the lack of computational tools for efficient correlation of high-throughput molecular data with functional cellular processes and for computational reconstruction of disease mechanisms. Such reconstruction, based on comprehensive, accurate representation of metabolic and signaling pathways and networks is necessary to correlate the manifestations of a given disease with the vast amounts of relevant high throughput molecular data (HTP) that has been generated over the last ten years in both industry and academia. Much of the value of this HTP data (whether it be gene or protein expression, or metabolomics data) is lost when analyzed in the absence of an accurate functional network thereby complicating even more the complex, expensive process of drug discovery. In the presented work we address the very core of this problem through our Systems Reconstruction™ (SR) technology and MetaCore™ platform for *in silico* reconstruction of disease mechanisms. At the core of this approach is comprehensive database of human cellular functionality consisting of tissue-specific biochemical, regulatory and signaling pathways linked into expert-curated maps (models) and computer-generated networks. These models and networks serve as a framework for system-level integration of diverse HTP molecular and disease-related data invaluable for the understanding of mechanisms of complex human diseases such as cancer, diabetes, immune and CNS diseases. As a demonstration of our technology we present reconstruction of Glaucoma, a complex neurodegenerative disease affecting optic nerve head (ONH). In this study we compare and analyze microarray data obtained in normal and glaucomatous human ONH astrocytes within the systems level of cellular functionality by using MetaCore™ platform. Our results include more than 80 pathways, affected by glaucoma. We propose several novel regulatory pathways that coordinate induction of stress genes, genes controlling cell motility and membrane remodeling in reactive ONH astrocytes.