Systems biology of gene and metabolic regulation by estrogen receptors and kinases in breast cancer

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The importance of kinases in diseased physiology is well known, as increased kinase activity through phosphorylation, mutations or increased expression is often observed in clinical samples and is associated with a poorer prognosis. However, the mechanisms underlying the interplay between ERα and protein kinase pathways in cancer and metabolic disease, and the processes by which ERα influences these pathways are poorly understood. The main aim of our study is to elucidate the crosstalk and interrelationships between ERα and extranuclear initiated and direct nuclear pathways using integrated OMICs approaches, including RNASeq, ChIPSeq, metabolomics, microbiome analysis and biomarker panel analysis. We will discuss about our recent findings on how these kinase pathways impact ER actions in the nucleus in breast cancer and metabolic syndrome associated with menopause.

Effect of neural influence in synchronization of cardiac oscillators

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Biological rhythms generate from large populations of mutually interacting cellular oscillators. The ability of such a population to generate a stable, regulated rhythm depends critically on the nature of interactions among the oscillators, particularly so since a network of nonlinear oscillators is intrinsically unstable. The phenomenon resembles to the naturally occurring cardiac rhythm generated by interaction among autonomic “pacemaking” cells of the nodes, the conduction system and apparently nonrhythmic myocytes. Although the entire cardiac system beats in perfect synchronization in vivo, the intrinsic frequencies of auto rhythmic cells experience a significant dispersion. The normal cardiac rhythm is the result of collective, synchronized action of a large number of cardiac oscillators. Two nonlinear oscillators operating at different frequencies can synchronize only under special conditions, which augur to be more stringent for a large network of oscillators (like the heart) with a wide range of intrinsic frequencies. The normal pacemaking in the heart depends on the coordinated discharge frequency of thousands of pacemaker cells comprising the sinoatrial (SA) region. The entrainment of cardiac pacemakers at a rate different from their intrinsic frequency leads to changes in the intrinsic beating frequency. The most contributing factor towards cardiac communication is the Gap junctions that permit large areas of cardiac tissue to contract as a single unit, a functional syncytium, by synchronizing oscillations of large number of cells. The electrical activation of the heart requires cell-cell transfer of current via Gap junctions, which are arrays of densely packed protein channels that permit intercellular passage of ions and small molecules. Because current transfer occurs only at Gap junctions, the spatial distribution and biophysical properties of Gap junction channels are important determinants of the conduction properties of the cardiac muscle. Owing to the fact that the heart is under the continuous influence of sympathetic impulses, the sympathetic nervous system plays a major role in the regulation of cardiovascular function. Therefore it becomes interesting to analyze the intrinsic frequencies of few coupled nonlinear oscillators and extend it to a simulated SA node cell for creating the variations in gap junction channels. The role of gap junctions plays a major role in synchronizing the pacemaker cells of the cardiac system.