How Gene Expression affects the anti-aging process.
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Some individuals' skin appears more youthful than their chronologic age. In 2017 the Journal of the American Academy of Dermatology found that women with a much more youthful skin appearance than would be expected based on their chronological age, also presented a specific gene expression profile mimicking the biology of much younger skin, as if their skin looked younger because it behaved younger. Comparing sun-exposed and sun-protected skin samples revealed that certain genetic changes are likely due to photoaging. However, overall, the gene expression patterns from the women in the study who were younger appearing were similar to those in women who were actually younger in age. These women had increased activity in genes associated with basic biologic processes, including DNA repair, cell replication, response to oxidative stress, and protein metabolism. Women with exceptionally youthful-appearing facial skin in older age groups also had higher expression of genes associated with mitochondrial structure and metabolism, overall epidermal structure, and barrier function in their facial epidermal samples, as well as dermal matrix production.

The rate of expression of a particular gene is controlled by its location within nucleosomes and by the activity of the cell's transcriptional machinery. Transcription of a gene requires the unwinding of a nucleosome, which makes the gene accessible to a basal transcription complex. This complex is comprised of RNA polymerase (which transcribes the new RNA strand) and numerous regulatory proteins.

Gene expression is regulated by genetic effects and environmental factors (Brem et al. 2002; Cheung et al. 2003; Morley et al. 2004; Grundberg et al. 2012). A large number of studies have investigated the expression quantitative trait loci studies, (eQTLs) and discovered that most genes are affected by at least one eQTL in at least one tissue (Albert and Kruglyak 2015; The GTEx Consortium 2015). Julien Byois et al (2017) demonstrated that gene expression levels change with age. They analysed gene expression changes with age in abdominal skin, subcutaneous adipose tissue and lymphoblastoid cell lines in 856 female twins in the age range of 39-85 years. Skin showed the most age-related gene expression changes of all the tissues investigated, with many of the genes being previously implicated in fatty acid metabolism, mitochondrial activity, cancer and splicing. A significant proportion of age-related changes in gene expression appear to be tissue-specific with only a few genes sharing an age effect in expression across

tissues. The 43 shared genes in skin and adipose tissue showed a single common identifiable pathway related to the stress response.

Signalling pathways are the key biological mechanisms that transduce extracellular signals to affect transcription factor mediated gene regulation within cells. A key role cell signalling plays within biological systems is to relay extracellular signals in order to regulate intracellular gene expression. The signal transduction process is typically initiated by the binding of a ligand to a membrane-bound receptor, which triggers a cascade of intercellular signalling activities through multiple kinases - ultimately impacting on how transcription factors regulate downstream gene expression. The coordinated activity of different signalling pathways within and between multiple cell types is the basis of many important biological processes, such as development, tissue repair and immunity. Cells detect input signalling molecules using receptors, proteins usually located on the cell surface which transmit the signal to the interior of the cell through a series of downstream processes that typically lead to changes in gene expression, resulting in an appropriate output response to the input.

The response of biological systems to changing environmental conditions and aging factors is a dynamic process. Activation of different signalling pathways can lead to numerous physiological or cellular responses, such as cell proliferation, death, differentiation, and metabolism. Any interruption that occurs within these extra—/intra-cellular communication chains can cause diseases including developmental disorders and cancers. Conversely, a clear understanding of the activity of, and interaction between, signalling pathways can help to design rational disease treatment and tissue regeneration strategies. It is therefore important to understand the signalling pathways that are activated in a cell, in order to provide a framework for understanding critical pathways affected by disease.

In principle, it should be possible to identify the important signalling pathways of a cell by using gene expression and protein-protein interaction (PPI) data sets. Extensive, publicly available PPI data provide an opportunity to establish a general signalling pathway blueprint, to which cell type-specific gene expression data can be mapped so as to refine the general signalling pathway blueprint into a cell-type specific blueprint. In this way it should be possible to construct a set of cell-type specific active signalling pathways for any cell that summarizes the information flow from a receptor (R) to kinases (Ks), then to transcription factors (TFs).

A number of computational methods utilize PPI data along with gene expression data to uncover known signalling pathways. In these methods the

gene expression data sets are usually used to calculate the edge weight by gene expression correlation for the network. One approach utilizes PPI and gene expression data sets and applies integer linear programming to get an optimal subnetwork from the PPI network starting from membrane proteins and ending at transcription factors. A recently published method called HISP uses the same approach, but in addition applies genetic algorithms with operations including selection, crossover, and mutation to select the candidate topologies of resultant signalling pathways and uses gene knockout data to get directionality of the signalling pathways.

In conclusion, Signalling technology offers the most direct and comprehensive method in both understanding gene expression and in utilizing interactions between specific signalling pathways and gene expression as a successful interventions in several diseases as well as in Anti-aging Medicine.