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750-1000 Summary 4

Gene Regulatory Networks

Words: 780

Imam, S., Noguera, D. R., & Donohue, T. J. (2014). Global analysis of photosynthesis transcriptional regulatory networks. *PLoS genetics*, *10*(12), e1004837.

Israel, J. W., Martik, M. L., Byrne, M., Raff, E. C., Raff, R. A., McClay, D. R., & Wray, G. A. (2016). Comparative developmental transcriptomics reveals rewiring of a highly conserved gene regulatory network during a major life history switch in the sea urchin genus Heliocidaris. *PLoS biology*, *14*(3), e1002391.

Studying gene regulatory networks allows researchers to further explain the relationship from the DNA through transcription of RNA to translation of proteins that perform specific functions. This field aims to elucidate the relationship between genotype and phenotype, and shed light on how the environment can impact that relationship. Clearly defining this relationship in non-model organisms is difficult due to the lack of knowledge about the functions of genes. The rapid development of genomic methods, including whole genome sequencing, has exponentially expanded our ability to address the functions and connections within gene regulatory networks.

Imam and team investigated a photosynthesis gene regulatory network, focusing on explaining the function of gene involved with 4 transcription factors. Chromatin immunoprecipitation and high-throughput sequencing (ChIP-seq) was used to identify a series of operons regulated by each transcription factor. ChIP-seq is commonly used in this field to associate protein function and interactions with DNA by identifying the binding sites of the proteins. To visualize data from the FnrL regulon, the paper shows levels of fold enrichment, a measure of association, for the binding sites identified by ChIP-seq. The higher the fold enrichment, the higher the proportion of your input genes compared to the total number of associated genes. Differential transcription was visualized using a heat map, that shows gene expression of individuals from the wild type and the mutant strain. The mutant strain is shown to downregulate activating genes, compared to the wild type upregulated activating genes. Repressing genes were upregulated in the mutant strain and downregulated in the wild type. The PrrA regulon data was visualized in the same way, but indicated a more stark difference in gene regulation between the wildtype and mutant compared to the FnrL regulon. The CrpK regulon and MppG regulation are discussed using heat maps as well as physiological characteristics. A gene regulatory network map shows both photosynthetic and anaerobic pathways, including transcriptional regulators and the target genes. The authors are able to link the up and down regulation by target genes in the network to specific functions like the production of photopigments.

The four transcription factors were presented with titles of physiological function such as photosynthetic and anaerobic growth, reiterating the connection between genotype and phenotype. The study presented new information regarding two of the transcription factors that had not been characterized before, as well as confirmed previous predictions of the other two transcription factor regulations. Although a model bacterial organism, *Rhodobacter sphaeroides*, was used for this particular study, the authors suggest the regulatory network is likely to be highly conserved and therefore applicable to other non-model organisms.

Israel and research team investigated the developmental change from feeding to nonfeeding mechanisms in sea urchins. There is a gap in knowledge regarding how gene expression changes are associated with this physiological change and how those genes are related to the larger gene regulatory network in play. RNA-seq was used to identify differential gene expression in three urchin species within one genus in an attempt to identify functions for genes involved in the developmental switch. One of the main conclusions of this paper was the development of a framework to compare gene expression profiles, and the phenotypic change was associated with large changes in gene expression as well. Their results from this model indicated substantial gene expression changes that accompanied the dramatic physiological change, and associations with genes that are known to be involved in developing larval skeletal patterns. The data in this paper was visualized using principal component analysis (PCA) to explain variation in gene expression by phylogenetic relationship and larval stages. The gene regulatory network was also separated by physiological characteristic, but this paper section the GRN into skeletogenic, endomesoderm, and ectoderm. The Imam paper was much easier to read since the arrows that represented a type of regulation were not overlapping like the GRN in this paper. This GRN also included jump scores and connections between the three sections of the GRN.

RNA-seq is a molecular analysis technique that looks at the entire transcriptome using next generation sequencing, compared to ChIP-seq that sheds light on the proteome by identifying protein binding sites. Both techniques are used to analyze and construct gene regulatory networks, and provide valuable information about the connections between genotype and phenotype, and how those connections are regulated and controlled. Both papers addressed similar research questions, but used very different systems and methods to answer those questions. ChIP-seq and RNA-seq are applicable to any system, but the conclusions and overarching discussion points may not be comparable between a sea urchin and bacteria. Both papers discussed that the focus gene regulatory networks were thought to be conserved, which has implications on the evolution of those regulatory networks.