Clinical Summary

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Cole SW. Social Regulation of Human Gene Expression: Mechanisms and Implications for Public Health. Am J Public Health 2013;103:S84-S92.

Social Dynamics Guide Gene Expression and Immune Balance

Humans are remarkably attentive to environmental inputs—objectively as well as subjectively—and there is increasing interest in the long-term health impacts of changing social conditions. This review describes how our genetic programming allows us to adapt to social experiences and explores why negative social inputs have especially persistent effects on human physiology.

Complex social interactions have been a cornerstone of human evolution, altering how we respond to stress and immune challenges, the environment, and one other. Our history as hunter/gatherers has much to do with patterns in behavior and metabolism that are not always adaptive in modern contexts, and adverse social circumstances have been linked with heart disease, cancer, chronic inflammation, neurodegenerative conditions, susceptibility to viral infection, metabolic illness, and other health issues.

Certain genes are emerging as especially sensitive to social inputs, which can alter cell signaling, gene expression and its regulation, and epigenetic modulation of DNA. Polymorphisms in 'socially-sensitive' genes add a further dimension to the highly variable ways we individually react to social dynamics.

Social interactions represent a major infusion of information that is critical for the survival and evolution of a species as well as for each individual. Early-life exposures are especially impactful, and social inputs that strongly influence gene regulation can range from social instability, traumas, and bereavement to low socioeconomic status, difficult relationships, social failures, and events that affect large populations.

Environmental and social information is gathered and processed through neural, psychological, hormonal, and immune pathways, leading to adaptations in genetic regulation of cell function

that are aimed at addressing new living circumstances. This data can influence gene expression by altering gene transcription (the 'reading' of genes and production of associated proteins) or through epigenetic modification of DNA and chromosomes to silence or amplify their genetic messaging.

Studies conducted in humans and other mammals have discovered a consistent pattern of adjustment in gene expression that alters immune balance after experiences that are perceived as stressful for extended periods of time. This pattern is characterized as proinflammatory and yet suppressive of the body's normal reaction to viruses, and it is hypothesized that it may have proven more adaptive for survival earlier in the course of human evolution.

According to Dr. Cole:
"Social factors can play a significant role in regulating the activity of the human genome."
"The effects of subjective and objective conditions are often transduced into gene expression via different molecular signaling pathways."

Review Summary

The author of this review notes that individuals' subjective perception of situations, based on the whole of their life experiences, may impact socially-mediated gene regulation as much or more than objective health facts. As examples, immune-related genetic transcription profiles in subjects with breast cancer or pediatric asthma relate more strongly to their personal interpretation of how illness threatens their life than objective measures of disease severity or household security.

Research findings highlighted in this review include the following:

- In one study of healthy older adults, feeling lonely or distant from others was associated with heightened expression of genes involved in the early, proinflammatory phase of the immune response, while those related to antibody production and protection against viruses were downregulated.
- Neurotransmitters released during an acute stress reaction can modulate the expression of genes coding for interleukins and interferons, altering overall immune balance.
- Cognitive-behavioral and mindfulness interventions have been seen to downregulate proinflammatory gene expression and upregulate that of genes involved in the production of interferons—a direct reversal of some of the effects of socially-mediated stress.
- People who have had significant social adversity show greater activation of genes involved in a "fight-or-flight" stress response, reducing synthesis of beta-adrenergic receptors that govern blood pressure and kidney and adrenal function.

- Disadvantageous social experiences (post-traumatic stress disorder, bereavement, etc.) can downregulate glucocorticoid receptor activity, resulting in decreased responsiveness to circulating cortisol and de-inhibition of factors associated with the proinflammatory NFκB signaling network.
- In animal models, lower social status and poor maternal care relate to significant, widespread differences in epigenetic patterning in critical brain and organ structures compared to better social conditions, and analogous correlations are increasingly found in DNA methylation profiling of humans with low socioeconomic status or a history of childhood trauma.

CONCLUSION

Through social dynamics, humans regulate the genomes of other humans, and our ever-changing social ecology contributes to human evolution. This species-wide genomic network of influence is termed our shared "metagenome," and it reflects how social interactions cultivate adaptation in human cognitive and metabolic function.