Peertechz

Clinical Group

Rheumatica Acta: Open Access

DOI CC By

Virginia L Naples[1] and Bruce Rothschild[2,3]*

[1]Department of Biological Sciences, Northern Illinois University, DeKalb, IL 60115, USA
[2]Department of Medicine, West Virginia University, Morgantown, WV 26506, USA
[3]Carnegie Museum, Pittsburgh, PA 15273, USA

Dates: Received: 30 December, 2016; **Accepted:** 27 January, 2017; **Published:** 30 January, 2017

***Corresponding author:** Bruce Rothschild, Department of Medicine, West Virginia University, Morgantown, WV 26506, USA, E-mail: spondylair@gmail.com

https://www.peertechz.com

Short Communication

The Complexity of DNA Transcends Epigenetics

Short Communication

Availability of new has afforded rheumatologists the opportunity to investigate molecular pathophysiology of joint disease techniques [1,2]. Attempts to relate DNA polymorphisms to disease activity or addresses one aspect susceptibility [3-5]. Mutations and epigenetics have received consideration [3,6], but there is another pertinent concept that needs a clearer definition when seeking to understand synovial pathophysiology and that is pleiotropy. This concept is not frequently discussed and its significance and implications, rarely recognized. Epigenetics is the alteration of gene function in an organism, but not of the gene itself [7-11], (Reik, 2007). This is in contradistinction to pleiotropic effects, variable somatic changes induced by a single gene often simultaneously, but differentially affecting multiple body systems [12-14].

The genomes of an increasing variety of organisms have been studied in sufficient detail so that trait-coding genes are often specifically localized on chromosomes [15]. Merely because a given gene is present, however, does not mean the information it contains will always be transcribed. Even if transcribed, the process does not necessarily involve the entire gene, but may be limited to only select sequences. Which portions subjected to selection is organ- and sometimes tissue-dependent. Thus, changes in functional morphology do not necessarily require a change in the DNA sequence. Perhaps the effectors of the resultant functions are analogous to allosteric effects on enzyme function [16-18]. These are of great importance because they alter the shape of the DNA molecule, changing the components that are accessible to transfer (t)-RNA transcription.

Traditional thinking suggests that transcription begins with an initiation sequence of several nucleotides, and that the t-RNA continues to move along the full length of the gene until reaching a termination sequence. However, transcription of segments of genes does not always use this mechanism. This difference may be part of maintaining the fidelity of DNA replication, but not necessarily the transcription of separate components of the gene.

Although there may be more than a single DNA sequence that that can be translated into a specific protein, only a limited number of variations will allow for the generation of the correct three-dimensional product [12,14,19]. If the incorrectly copied instructions are accurate enough that a substitute t-RNA is generated, it may not work well or at all. At the least, it is likely to have an altered tertiary shape. The new shape is likely to cause a change or failure of function. In fact, many such molecules that show altered shapes might not be able to fold themselves into units that are functional enough that they are capable of accomplishing the task for which they are intended to code [20].

Another area that has not received as much attention is the number of copies of the gene present in the full organism genome. A most timely example relates to the p53 locus, important in the biochemical pathophysiology of cancer [21-23]. The rarity of cancer in elephants may well be related to their possession of 20 separate chromosome sites (double-stranded DNA providing 40 copies) of the gene responsible for coding this function [24]. What we don't yet know is whether all copies are active or whether their behavior reflects their neighborhood (surrounding gene activators and suppressors – the "deciders" Finally, we are left with the question: How much of functional morphology reflects nature (the genome sequence) and how much is a product of "nuture." (The environment in which the gene finds itself).

References

1. Ansorge WJ (2016) Next Generation DNA Sequencing (II): Techniques, Applications. Next Generation Sequencing & Applications S1: 005. Link: https://goo.gl/rK8BvC

2. Morey M, Fernández-Marmiesse A, Castiñeiras D, Fraga JM, Couce ML, et al. (2013) A glimpse into past, present, and future DNA sequencing. Mol Genet Metab 110: 3-24. Link: https://goo.gl/CxZxa7

Citation: Naples VL, Rothschild B (2017) The Complexity of DNA Transcends Epigenetics. Rheumatica Acta: Open Access 1(1): 004-005.

3. Castañeda S, López-Mejías R, González-Gay MA (2016) Gene polymorphisms and therapy in rheumatoid arthritis. Expert Opinion on Drug Metabolism & Toxicology 12: 225-229. Link: https://goo.gl/wm804t

4. Lo SF, Wan L, Huang CM, Lin HC, Chen SY, et al. (2012) Genetic polymorphisms of the DNA repair gene UNG are associated with the susceptibility of rheumatoid arthritis. Rheumatol Int 32: 3723-3727. Link: https://goo.gl/tvN0ND

5. Rego-Pérez I, Fernández-Moreno M, Blanco FJ (2008) Gene Polymorphisms and Pharmacogenetics in Rheumatoid Arthritis. Curr Genomics 9: 381-393. Link: https://goo.gl/pIYmVw

6. Tough DF, Tak PP, Tarakhovsky A, Prinjha RK (2016) Epigenetic drug discovery: breaking through the immune barrier. Nat Rev Drug Discov 15: 835-853. Link: https://goo.gl/CaZ93u

7. Bird A (2007) Perceptions of epigenetics. Nature 447: 396-398. Link: https://goo.gl/OgdD6K

8. Burdge GC, Hoile SP, Uller T, Thomas NA, Gluckman PD, et al. (2011) Progressive, transgenerational changes in offspring phenotype and epigenotype following nutritional transition. PLoS ONE 6: e28282. Link: https://goo.gl/pNojwr

9. Fraga MF, Ballestar E, Paz MF, Ropero S, Setien F, et al. (2005) Epigenetic differences arise during the lifetime of monozygotic twins. Proceedings of the National. Proc Natl Acad Sci U S A 102: 10604-10609. Link: https://goo.gl/0FsL65

10. Holliday R (1990) DNA Methylation and Epigenetic Inheritance. Philosophical Transactions of the Royal Society of London Series B, Biological Sciences 326: 329-338. Link: https://goo.gl/fLXOZQ

11. Jablonka E, Raz G (2009) Transgenerational epigenetic inheritance: prevalence, mechanisms, and implications for the study of heredity and evolution. Q Rev Biol 84: 131-176. Link: https://goo.gl/dTqfFx

12. Lobo I (2008) Pleiotropy: One Gene Can Affect Multiple Traits. Nature Education 1: 10. Link: https://goo.gl/mVeCcn

13. Razeto-Barry P, Díaz J, Cotoras D, Vásquez RA (2011) Molecular Evolution, Mutation Size and Gene Pleiotropy: a Geometric Reexamination. Genetics 187: 877-885. Link: https://goo.gl/a7mO3k

14. Williams GC (1957) Pleiotropy, natural selection, and the evolution of senescence. Evolution 11: 398-411. Link: https://goo.gl/Bz1M7U

15. Rogers J, Gibbs RA (2014) Comparative primate genomics: emerging patterns of genome content and dynamics. Nat Rev Genet 15: 347-359. Link: https://goo.gl/Hc3mrQ

16. Huang Z, Zhu L, Cao Y, Wu G, Liu X, et al. (2011) ASD: a comprehensive database of allosteric proteins and modulators. Nucleic Acids Res 39: D663-669. Link: https://goo.gl/JgnJ8e

17. Monod J, Wyman J, Changeux JP (1965) On the nature of allosteric transitions: A plausible model. J Mol Biol 12: 88-118. Link: https://goo.gl/J4xsGz

18. Sethi A, Eargle J, Black Alexis AA, Luthey-Schulten Z (2009) Dynamical networks in tRNA:protein complexes. Proc Natl Acad Sci U S A 106: 6620-6625. Link: https://goo.gl/4sQLiM

19. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, et al. (2002) Molecular Biology of the Cell. 4th edition. New York: Garland Science Link: https://goo.gl/cvbiwH

20. Alexander PA, He Y, Chen Y, Orban J, Bryan PN (2007). The design and characterization of two proteins with 88% sequence identity but different structure and function. Proc Natl Acad Sci U S A 104: 11963-11968. Link: https://goo.gl/nKlWt1

21. Kikuno N, Shiina H, Urakami S, Kawamoto K, Hirata H, et al. (2008) Genistein mediated histone acetylation and demethylation activates tumor suppressor genes in prostate cancer cells. Int J Cancer 123: 552-560. Link: https://goo.gl/1cHjbS

22. Rodier F, Campisi J, Bhaumik D (2007) Two faces of p53: aging and tumor suppression. Nucleic Acids Res 35: 7475–7484. Link: https://goo.gl/uNTcZd

23. Tabish AM, Poels K, Hoet P, Godderis L (2012) Epigenetic factors in cancer risk: Effect of chemical carcinogens on global DNA methylation pattern in human TK6 cells. PLoS ONE 7: e34674. Link: https://goo.gl/qCc9Dl

24. Abegglen LM, Caulin AF, Chan A, Lee K, Robinson R, et al. (2015) Potential mechanisms for cancer resistance in elephants and comparative cellular response to DNA damage in humans. JAMA 314: 1850-1860. Link: https://goo.gl/b37arv

Citation: Naples VL, Rothschild B (2017) The Complexity of DNA Transcends Epigenetics. Rheumatica Acta: Open Access 1(1): 004-005.