

Book Review

The Causes of Chronic Disease

A New Theory Implicates Viruses

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MICROCOMPETITION WITH FOREIGN DNA AND THE ORIGIN OF CHRONIC DISEASE

Hanan Polansky, PhD

The Center for the Biology of Chronic Disease, Rochester, NY (www.cbcd.net)
2003; 543 pp.

ISBN: 0-9740463-0-2; USD: \$79.99

Dr. Hanan Polansky's book presents a theory by which viruses are held as causative agents of a number of chronic conditions including, obesity, cancer, cardiovascular disease, apnea and autoimmune diseases, which appear otherwise unrelated.

In his book, Dr. Polansky describes the current paradigm in medical research as "foreign protein"-dependent. According to this paradigm, if foreign DNA, such as a fragment of viral DNA or an "empty" vector, does not express a protein, the DNA is harmless. In accordance with this paradigm, the medical community concludes that a latent viral infection, which expresses no protein or almost no protein, does not cause disease. However, according to Dr. Polansky, foreign DNA can directly modify cellular gene transcription, independent of protein expression. The direct effect of foreign DNA on cellular gene transcription is called microcompetition. The following example illustrates the effect. GABP is a transcription factor that binds the promoter/enhancer of many cellular genes, such as CD18, Fas, BRCA1, Rb, and others. GABP also binds many viral promoters/enhancers, such as the promoter/enhancer of Polyomavirus, Rous Sarcoma Virus (RSV), Cytomegalovirus (CMV), Epstein-Barr virus (EBV), Herpes Simplex Virus 1 (HSV-1), Moloney Murine Leukemia Virus (Mo-MuLV), Human Immunodeficiency Virus (HIV), and Human T-cell lymphotropic virus (HTLV). GABP forms a complex with the p300/cbp co-activator. The p300/cbp coactivator is limiting. Hence, the transcription complex GABP•p300/cbp is also limiting. Foreign DNA that binds this transcription complex competes with the cellular genes and decreases the availability of the complex to the cellular genes. The decreased availability of the complex decreases or increases the transcription of the cellular genes to abnormal levels, resulting in abnormal cell functioning, and disease.

After presenting microcompetition, the book systematically compares the predicted effect of a latent viral infection on many GABP regulated genes with the observed expression of these genes in disease. The correlation is intriguing. For instance, the BRCA1 gene shows low expression in breast cancer tumors without being mutated or hypermethylated. Since GABP transactivates BRCA1 transcription, an infection with a latent virus would decrease BRCA1 expression to abnormal levels as observed in tumors. Next, the book presents the function of the proteins expressed by these genes and compares the predicted effect of protein malfunction on cell behavior in disease. Again, the correlation is surprising. For instance, BRCA1 is a cell cycle suppressor. Since an infection with a latent virus decreases BRCA1 expression, the infection should result in excessive cell replication. Finally, the book compares the predicted effect of cell malfunction on tissue physiology, and again the correlation is exciting.

STRONG POINTS

First, I would like to congratulate the author for putting together such an insightful theory and impressive collection of supporting evidence, and most importantly, for being able to delineate functional links between seemingly distinct sets of observations. This is a well-organized, highly rigorous presented theory. The concept of microcompetition will change our approach in the study of chronic diseases and will furthermore give scientists a higher level of understanding in biology. Presentation of this concept undoubtedly provides a new set of opportunities for attacking chronic diseases. The idea that viruses are the cause of chronic diseases is not new, but the underlying mechanism, the evidence put

forward, the molecular observations, the analyses, and conclusions certainly are. They lead the way to new approaches in chronic disease treatment.

In my opinion, this book could be of great use to fundamental researchers. Investigators of specific areas will find well-presented concepts that transform our way of thinking about chronic diseases, and about the implication of viruses in biology and health in general. This work will eventually also have an impact on medical research and drug discovery, although realistically not in the near future; these areas not being typical bearers of new ideas.

This is a very good theory, one that makes a lot of sense, and one that helps a lot in terms of trying to identify possible causes for chronic diseases. Time will tell, but regardless of being proved right or wrong, this theory has the merit of changing our current way of thinking, and this is probably the greatest contribution a new theory can bring.

PERSONAL SUGGESTIONS

The main idea put forward in this book is superb. In my opinion, this work might have served a higher number of people, for example students, if the concept of microcompetition had been presented in a more “casual” way. At times, I had the feeling of reading an extensive PhD thesis, with explanations and multiple references for almost every concept presented. While there is no doubt, whatsoever, that explanations are rigorous and well-documented, most of them were written in such a way that only the people who are already familiar with these concepts would understand. Usefulness of a book can sometimes be found in presenting a concept which initiated people understand and explaining that concept to the uninitiated. This book is more “from initiated to initiated.” This is not to say that the structure of the book is not good, far from it; it is a superb piece of work, just less open to masses than it could have been.

CALL FOR ACTION

The current paradigm concludes that a latent viral infection does not cause disease. However, considering microcompetition, this conclusion might be misdirected. Moreover, since viruses, such as CMV or EBV, latently infect 50%–90% of the population, we ought to seriously research this effect.

In finishing, thank you for the opportunity of reading this book. It was a great (and sometimes challenging) experience, which helped in crystallizing some of the ideas I had about viruses and their possible role in biology.