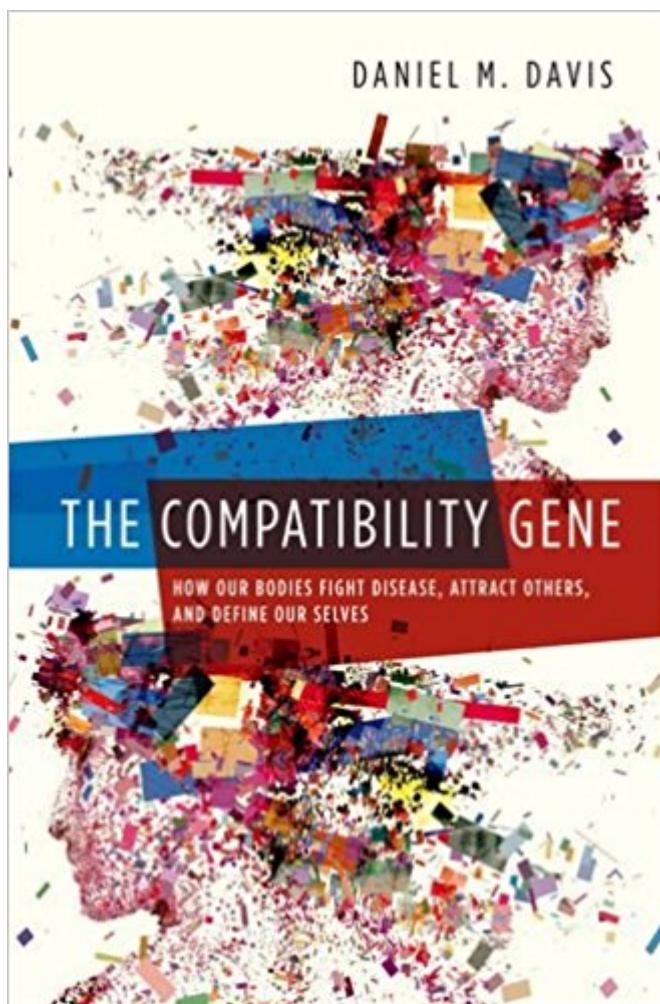


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The Compatibility Gene: How Our Bodies Fight Disease, Attract Others, And Define Our Selves



Synopsis

This is the story of a few human genes and how we discovered what these genes do. We each have around 25,000 genes, but the genes in this story are those that vary the most from person to person. These genes--called compatibility genes--are, in effect, a molecular signature that distinguishes each of us as individuals. Davis tells the remarkable story of the discovery of compatibility genes, and how decades of patient scientific inquiry, punctuated with individual strokes of genius, have unraveled their workings. Davis reveals how our compatibility genes fight disease, and how this fight varies in all of us and is unique. The version of these genes that we have inherited determines the extent to which we are susceptible or resistant to a vast range of different illnesses. What is particularly fascinating is that these same genes influence the wiring of our brains, the lovers we choose, and successful pregnancies. Why this would be so is explored by Davis with provocative new research that uncovers the connections between fighting disease, choosing mates, and having healthy babies. By bringing together evidence from diverse fields of biology, this book argues that our compatibility genes are central to how we live and when we die, and that a shocking amount of what we do and who we are is determined by how we have evolved to survive disease. Science has never been more elusive or tantalizing than in revealing the nature of ourselves--and unlocking the secrets of our compatibility genes will be central to 21st-century medicine.

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"An elegantly written, unexpectedly gripping account of how scientists painstakingly unraveled the

way in which a small group of genes ... crucially influence, and unexpectedly interconnect, various aspects of our lives ... Lab work has rarely been made to seem more heroic." -Bill Bryson, Guardian Books of the Year 2013 "Dr Davis's readable and informative book takes the reader into unexpectedly interesting corners of both the immune system and the lives of immunologists. It is packed with an insider's knowledge -- not just of the field, but of where its bodies are buried." -New York Times "... a fascinating, expertly told story" -New Statesman "Davis provides a well-written and easy-to-read account of the sometimes complicated biology behind the crucial genes that affect our lives so profoundly." -New Scientist "Davis weaves a warm biographical thread through his tale of scientific discovery, revealing the drive and passion of those in the vanguard of research ... unusual results, astonishing implications and ethical dilemmas." -Times of London "Davis makes the twists and turns all count." -Guardian "Wonderful pen-portraits of the many scientists involved in this fast-moving field ... 5 out of 5 stars." -BBC Science Magazine FOCUS "Davis gets a gold star ... for putting over an arcase subject with such infectious enthusiasm." --Nature"...this nonfiction work is a book of the methods, practice, and serendipity of science in which the reader is given a comprehensive yet entertaining glimpse into the lives of scientists whose research still affects us today. ... The stories and insights recounted in the book are an enlightening account of the rewards received as well as the sacrifices needed to be a successful researcher in the sciences..."

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scientists whose research still affects us today. ... The stories and insights recounted in the book are an enlightening account of the rewards received as well as the sacrifices needed to be a successful researcher in the sciences..." --PsychCritiques "The book is written in a chatty informal style that is easier to follow than many others." --The Quarterly Review of Biology "The book is skillfully written and easy to read. Dr. Davis has used his immunology expertise to produce a fine informative book that does not shortchange the elegant and complicated science, but illustrates it with clarity and insight." --Oncology Times Mentioned in Bill Bryson's *The Road to Little Dribbling: More Notes from a Small Island*

Daniel M. Davis, PhD, is a distinguished immunologist whose work has established new concepts on how immune cells communicate with each other, how immune cells recognize disease, and how viruses spread between cells. He is currently Professor of Immunology at the University of Manchester, UK, where he is the Director of Research at the Manchester Collaborative Center for Inflammation Research. Davis pioneered the use of microscopy to help visualize key molecular components of immune responses. His work helped establish a new concept of how immune cells communicate with each other and how they recognize disease. He has published over 100 academic papers, including papers in *Nature* and *Science*, collectively cited over 6,000 times. He was the recipient of a Lister Prize in 2005, a Wolfson Royal Society Merit Award in 2008, and became a Fellow of the Academy of Medical Sciences in 2011.

Daniel Davis gives a masterful account about the discovery of compatibility genes and their fundamental role to human biology: in the generation of specific immune responses to combat viruses and bacteria, mediation of auto-immune diseases, and successful organ transplantation. Davis further unveils fascinating and cutting edge work today showing that the importance of these genes reaches farther than the immune system: in the wiring of the brain, generation of successful pregnancies, and even mate selection. Thus, Major Histocompatibility Complex (MHC) genes, the most variable of all human genes, may be key to what makes us humans so successful in biological processes requiring compatibility both internally in the human body and at the interface with the outside world. Davis is an appropriate ambassador for the field, currently conducting important immunological research in his own laboratory. In "The Compatibility Gene", he begins with Peter Medawar's pioneering work on transplantation research and Frank Burnet's theory of self-tolerance, leading to the discovery of MHC and eventually revealing crystal structure of MHC proteins bound to their peptides. It is very exciting to read in such a clear style the interesting history of

immunological research, accounts of personal experiences, struggles and eventual scientific breakthrough and discovery. As one with primary training in immunology, it is very refreshing to see such a well-written account of significant immune discoveries and the people who conducted them. This book is a pure joy to read and brings cutting edge science to the everyday reader.

Disguised as an informal history of immunology, Daniel Davis' multi-tasking book brings us up to speed on immune system research. This includes a new understanding of immune function in the brain as well as in pregnancy. Formerly, the immune system was thought to remain outside the blood-brain barrier, to avoid damaging neurons. Now it's increasingly clear that the immune system not only plays a role in learning and mental illness, its cells function very much like neurons. Like neurons, they form synapses. These are juncture points where proteins are emitted and received by other cells. Molecular immunologist Davis' own contribution to the research has been to show that these synapses occur in more than one kind of immune cell, and that the synapse is where the immune cell gets switched on and off either to destroy a cell or withdraw. Not only do immune cells act like neurons, Davis points out that stroke and many other neurological problems can be triggered or exacerbated by immune responses. Narcolepsy may even be an auto-immune disease. The newer research also shows that immune function determines the success of pregnancy, by affecting how well the placenta embeds in the uterine wall. Too much immune response from the mother and the placenta will be rejected or weakened. In a rare presentation for a lay audience, Davis lays out the fundamental way the system works. Certain "compatibility" genes, which let our body recognize the difference between self and other, exist in nearly all our cells. Their role is to make proteins that hold up to the cell's surface components of various proteins inside the cell. This way, an immune system cell can tell whether it has encountered a healthy "self" cell or one possessed by a virus. We each have six of these compatibility genes in our cells, three from the mother and three from the father. Sounds straightforward, but because of the subtypes (A, B, and C) of each, and a thousand or so different versions of each subtypes, the actual range of combinations is astronomical. Depending on which combination you have, you might be protected from certain diseases but not others. Davis reasons that, for the human race as a whole, these genes could cover the spectrum of disease, thus ensuring that some subgroup or tribe can defend against almost any pathogen. But there is no one optimal combination. And there are trade-offs. The same gene that gives some protection against HIV also causes ankylosing spondylitis, an arthritic

autoimmune disease of the spine. Davis even speculates, based on the notorious (and inconclusive) sweaty t-shirt experiments, that compatibility genes might determine sexual preference in humans as they do in mice. It's not hard to see how compatibility for successful pregnancy and warding off of disease would be a winning combination in natural selection. The book is by no means all science and no play. Davis uses brief sketches of the major players—lives to show us how science really works—through collaboration and a very human exchange of ideas. He starts with Peter Medawar, who showed, back in the 50s, that transplant rejection is the result of an immune cell reaction. He goes on to introduce us to the discoverers of the thymus-mediated T-cells that discriminate between self and other, the antibody- secreting B-cells and the tumor-hunting Natural Killer cells. Immunology has since moved on to a whole new era, one in which proteins and genes can be manipulated within the cell itself. Several women have played key roles in this more recent research. Pamela Bjorkman gave us the actual structure of the compatibility gene through X-ray crystallography. Form follows function in that the top of this protein is a clamp for seizing and presenting protein bits on the surface of the cell. The illustration of this on p. 77 (location 1473) is alone worth the price of the book. Whither immune cell research? Davis notes that “. . . our variation in these genes has been linked to many neurological disorders such as schizophrenia or bipolar disorder.²² This is consistent with an intimate connection between compatibility genes and our nervous system. But researchers studying schizophrenia, and other neurological diseases, differ in their view of how important these genes are. Although many tens of studies link compatibility genes to schizophrenia, dispute remains because each comes to a different conclusion about which versions of these genes are risk factors for illness.²³ Indeed, because it's very rare for any single gene (as in Huntington's disease) to cause a disease, immunologist Eric Schachter's approach has been a multivariate one, to find out which sets of genes function together to influence a specific disease. This requires some higher-order number-crunching. As for me, an allergy sufferer, who had an adolescent tendency towards depression, I'm happy to find confirmation of my long-held intuition that the immune system plays a role in mental illness. But I wonder whether victims of autism, bipolar disorder and schizophrenia have ever been systematically screened for the presence of Immunoglobulin E, the immune factor responsible for allergy and autoimmune disease. Wouldn't this be a simpler way of establishing whether this system underlies much mental illness? If all such sufferers do belong to the 20% of the world's population that has this immune activity (originally a system for fighting parasites), wouldn't it

this be useful to know in developing therapies? Wouldn't then the treatments, at least from some of these diseases, tend to be similar to that of allergy or certain autoimmune conditions? The science in Davis' book requires concentration and attention, but it isn't beyond anyone who has had a good high-school biology course. I used the Kindle Notes function to highlight and review. Kudos to Davis for enlightening us non-scientists with an engaging, illuminating and very well-written work. Patricia Lawson, author of *HARD ASPECTS*, a satire on offshore academia.

The *Compatibility Gene* by Daniel Davis is a very interesting and skillfully written book. One can feel the author's passion for immunology, as well as science in general. I thoroughly enjoyed it. I am an immunologist myself, so it was quite a thrilling read. One person had criticized the book for its biographical feel, but I think that is what makes the book really stand out. It is fascinating to see the process, the motivation, and the personalities of people responsible for many essential discoveries in medical sciences. You may read about HLA molecules in text books, Wikipedia, or multiple websites, but those are dry facts. Dr. Davis gave all those discoveries and stories a human side. Biological research is not like any other work. The excessively high rate of failure, constant trials and errors, technical and intellectual challenges make it one of the most taxing and demanding jobs. I think the author perfectly captured and described the human struggle in search for answers and understanding how the immune system functions. It is a fascinating book about scientific discoveries that, in a very reader-friendly fashion, explains very complex and critical issues in immunology. It is a great read. I am looking forward to the next book by Daniel Davis.

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