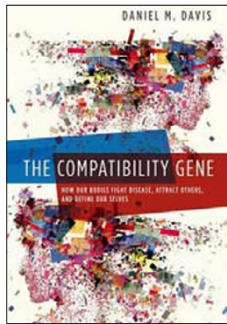


Our antigens, our selves



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

Daniel M. Davis

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Reviewed by Alison Farrell

For any scientist who is not an immunologist, trying to make sense of the complexity of the major histocompatibility complex (MHC) genes and their role in immunity is a daunting task. To try to do so for a lay audience is far harder. But Daniel M. Davis has attempted just that in his detailed account of the studies surrounding the discovery of the MHC and the scientific insights that have since been derived from it that extend far beyond the immune system.

The book is divided into three sections that loosely follow the timeline of discoveries on MHC. The first section of the book provides a historical account and perspective of the early studies that revealed the ability of the body to distinguish self from nonself and that eventually led to an understanding of its molecular underpinnings. We are introduced to Peter Medawar, whose work on skin grafts beginning in the 1940s helped form the foundation of our future understanding of how the immune system recognizes self and nonself and the role of MHC genes in this process. Frank Macfarlane Burnet and Medawar worked independently to discover acquired immunological tolerance—a state in which the immune system is unresponsive to an antigen that would normally stimulate it—which won them both the Nobel Prize in Physiology or Medicine in 1960. Burnet would later go on to formulate the idea of clonal selection that gives rise to antibody specificity. The early revelations of these and many other now prominent scientists, some of whom are also Nobel Prize winners, as well as the initial resistance to some of their ideas, are chronicled so that the reader can envisage how they shaped both the scientific community's views and research in immunology.

From a scientist reader's viewpoint, the book presents a window into a prolific period of novel insights, early hypotheses that have since been rejected and groundbreaking discoveries that have culminated in our understanding of T, B and natural killer (NK) cells and their roles in mediating immune recognition. The first part of the book ends with the literal and figurative crystallization of MHC, detailing the work that finalized the structure of one of the human leukocyte antigens (HLAs, which correspond to the MHC proteins in humans) that are responsible for much of human self versus nonself recognition.

The second section of the book extends our understanding of the importance of HLAs beyond the setting of transplantation to other diseases, including autoimmunity and HIV infection, and delves into the concept of variability in HLA genes and its role in disease susceptibility. At the end of this section, the author presents the discovery of NK cells and their function in distinguishing self from nonself, where NK cells can detect the absence of self HLA on foreign cells rather than the presence of nonself antigens.

Towards the end of the book, Davis goes on to cover more preliminary findings that associate MHC genes with neural development, sexual compatibility and pregnancy. Here the book covers more uncertain territory—areas that are as yet unresolved and mechanistically unclear. Although the research in these areas is provocative, the findings are either not described in depth or the depth of our understanding is not yet great.

The author does a good job at humanizing the scientists he describes. He introduces the reader to Medawar and to his family life, describing his interactions with World War II burn victims as the impetus to his studies on skin grafts, which resulted in our understanding of graft rejection and the ability to induce graft tolerance in animals. The reader is led to appreciate the time, effort, devotion and personal cost expended by the researchers driven to ask and try to answer these key scientific questions, as well as the collaborations required to achieve great results; notably, the contributions of these collaborators were not always equitably recognized. Davis reflects on the camaraderie and the competition among scientists of strong opinions and competing views, as well as the not infrequent opposition of the scientific community to new concepts or hypotheses.

The writing is not always linear—rather, Davis attempts to give a reasonably full picture of some of the central players involved in the major discoveries before moving on to detail the next prominent scientist or advance. This works in some instances, but a broader view of the contributions (less focused on a handful of selected individuals) and their reception at the time (to the extent that there is a record) would be of interest to the reader, in my view. Moreover, some contributions are mentioned only briefly—such as those of Peter Gorer, a contemporary of Medawar and Burnet who recognized the genetic component of transplant rejection—and the focus of the book is primarily on European and Australian researchers. Nevertheless, the reader does come away with a rich appreciation of some of the landmark findings in immunology.

Where the writing may reflect an attempt to interest a lay audience is, I think, where it is the weakest—such as referring in a single sentence to a scientist's purported interest in sadism and masochism or in detailing the untimely death of Harvard structural biologist Don Wiley, anecdotes that inform the reader very little with respect to understanding the role of HLAs in immunity. Yet there is much to enjoy in this book even for the lay reader who is interested in an accessible account of some of the major scientific players in immunology, their discoveries and the broad relevance of HLAs and immune recognition of self and nonself to human disease.

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