



# The pluripotent history of immunology

## A review

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### Abstract

The historiography of immunology since 1999 is reviewed, in part as a response to claims by historians such as Thomas Söderqvist the field was still immature at the time (Söderqvist & Stillwell 1999). First addressed are the difficulties, past and present, surrounding the disciplinary definition of immunology, which is followed by a commentary on the recent scholarship devoted to the concept of the immune self. The new literature on broad immunological topics is examined and assessed, and specific charges leveled against the paucity of certain types of histories, e.g. biographical and institutional histories, are evaluated. In conclusion, there are compelling indications that the history of immunology has moved past the initial tentative stages identified in the earlier reviews to become a bustling, pluripotent discipline, much like the subject of its scrutiny, and that it continues to develop in many new and exciting directions.

**Keywords:** Biographical history; Continuity model; Danger Model; Historiography of Immunology; History of Immunology; Institutional history; Self vs. Non-self model.

### Introduction

Two decades ago, in the summer of 1992, the Naples Zoological Station's summer school in the history of the life sciences, a roughly biennial event since the mid-1970s, chose to focus on the history of immunology. Whether the meeting achieved its stated purpose of facilitating dialogue and exchange between immunologists and historians appears to have been a matter of some contention among the attendees (Judson & Mackay 1992; Söderqvist 1993). But for the historians in attendance, the meeting seems to have served as a wake-up call, alerting them to the paucity of serious historical scholarship on the discipline of immunology. Within a few months these scholars organized a second symposium in Boston - this time, pri-

marily for the humanists - where the aim was to “foster the development of a history of immunology that would generate its own questions,” (Cambrosio et al. 1994: 376). The proceedings of this second meeting were published shortly thereafter in a special issue of the *Journal of the History of Biology* (1994, Vol. 27, number 3) which was subtitled “Immunology as a historical object.” A third meeting followed in 1995, the outcome of which appeared yet again in the *Journal of the History of Biology*, this time as a special section in the fall 1997 issue (v30: 317-440). Meanwhile, not to be outdone by their humanist colleagues, many of the scientists who had attended the 1992 meeting published their own version of the history of immunology (Gallagher et al. 1995). However, despite this flurry of activity within a relatively short span of time, the historian Thomas Söderqvist, a prominent presence at these meetings, opined in the title of his 1999 essay that “The historiography of immunology is still in its infancy” (Söderqvist & Stillwell 1999).

By invoking Söderqvist and Stillwell’s claim I might be justifiably charged with creating a straw man to combat, because any field of study by virtue of its very existence is open to historical analysis. Regardless, I believe their review provides a good starting point for a new review of the history and historiography of immunology, not only because of the comprehensiveness of its coverage until that time – the article reviewed a dozen books on different aspects of the history of immunology published between 1991 and 1998 – but also because the criteria by which the authors assessed these books offer useful guidelines for assessing the progress of the field since then. Most of the work on the history of immunology until that time, their review charged, offered perspectives that were rather narrow and “internalist,” or else “quite conventional, approaching their subject matter as intellectual history” (215). While I hesitate to dismiss either internalist analyses or intellectual histories as narrow or conventional – I prefer to characterize them as focused and rigorous – there is no doubt that Söderqvist and Stillwell’s suggestions for broadening the scholarship on the development of immunology to include institutional histories, biographies and studies on sociopolitical contexts would only enrich the history and historiography of the field. An evaluation of whether the historiography of immunology has widened its scope to include such methods and narratives is one of the major aims of this review.

### **Defining Immunology**

A good place to begin a historical and historiographic evaluation of any discipline would be with a definition of the discipline; but such a task is not easy in the case of immunology. Indeed, as a survey of the recent literature reveals, a considerable portion of the existing historical scholarship about immunology analyzes and comments on the issue of disciplinary definition. Modern textbooks and dictionaries usually describe the subject as “the study of immune system,” but this definition is dissatisfying not only because it is self-referential, but also because, as the historian Anne-Marie Moulin (1989: 221) has pointed out, the phrase “immune sys-

tem” did not appear in the writings on immunity until the late 1960s, whereas textbooks bearing the word “immunology” in their titles were in evidence decades earlier (e.g. Zinsser & Tyzzer 1927; Dougherty & Lamberti 1946). Simply perusing the table of contents sections of contemporary immunology textbooks or the titles of the various books and articles cited at the outset of this essay will reveal the great diversity of the technical and theoretical topics and problems studied under the disciplinary heading of immunology today: the thymus gland, lymphocytes – the B and T cells, helpers and suppressors – hemolysis, monoclonal antibodies, organ transplantation, antibodies, the articulation of the “self,” yellow fever, plaque assays, immune cognition and inflammation are just some of the topics in these volumes. The picture is complicated further if we look at immunology in earlier periods (e.g. Mazumdar 1972).

The difficulties in establishing a definition and disciplinary identity for immunology are also evident in the historical analyses rendered by humanists scholars attempting to study the field. The philosopher-immunologist Alfred Tauber, for example, noted that “[a]t an important nexus of pathology, clinical medicine, and basic biology, immunology has served several research agendas and thus defies a single, unifying experimental framework,” (2010: para 1). Anderson et al. (1994: 575) assigned a “putative origin” to the discipline, asking how the corpus of work constituting “modern immunology” was shielded by the memory of the discipline. One of the primary foci of their commentary was the definition of immunology as it had come to be articulated in the 1940s and 1950s by such famous immunologists as Frank Macfarlane Burnet and Niels Jerne. These men saw immunology as a science of “self-nonself discrimination,” (Atlan 1998: 125) or the study of the way in which organisms (mainly, but not exclusively, humans) were able to maintain their own integrity and fend off unwanted outside threats such as pathogens and allergens. Such a definition allowed various issues – as apparently disconnected as infectious diseases, allergies and organ transplants – to be studied within a unified system. This definition has persisted, though not without criticism, until modern times, as exemplified in the titles of such books by the practitioners of this field of study as *Immunology: The Science of Non-Self Discrimination* (Klein 1982) and *In Defense of Self: How the Immune System Really Works* (Clarke 2008).

By the mid-1960s, the original authors of this vision of immunology had already predicted the end of their field on the grounds that its principal questions would have been addressed, if not answered, within a matter of a few decades (Burnet 1964, in Anderson et al. 1994; Jerne 1967). According to Anderson et al. (1994: 576), this act of positioning themselves at the end of history served as a “powerful (if unwitting) means of defining the boundaries of one's discipline, and of securing the legitimacy of one's knowledge”. On the other hand, as Anderson et al. argued, it was problematic for historians to accept the scientists' ideas uncritically because the demarcation they suggested carried with it the danger that “the contemporary boundaries of immunology come to appear natural and inevitable,” rather than as constructions in need of reevaluation and reparation (1994: 576). The risk of buy-

ing into the scientists' definition is to, thus, end up with a "perfunctory history of past error and then testimonies to the origin of a science without social connections" (1994: 579). While such renditions may serve the function of providing scientists with a chronology of events in their discipline which would make its boundaries indeed seem natural, they would likely lack the richer insights into the development of the discipline and workings of science that historians seek. Thus, it would seem that by calling for an "unnatural" history of immunology, Anderson et al. are pushing historians of medicine and science toward historicizing its very definition.

This challenge to historicize the definition of immunology, whether intentional or not, is taken up in the writings of Tauber, who in a 2004 essay declared that "[f]or me the history of immunology is precisely the very attempt to define such an entity [self]," the very concept of which, he charges, was "an artifice, a conceit, a model at best" (2004a: 202). The principal author of three of the dozen books reviewed by Söderqvist and Stillwell, Tauber was also, according to these reviewers, "the most philosophically-inclined member of the former immunologists crowd" (1999: 211). He has also been one of the most consistently prolific scholars since that time and is, hence, in a position of some authority to make such a broad claim about the history of the discipline. It is, therefore, towards his oeuvre that we will first turn in the discussion of the immune self, a concept whose historical significance he has acknowledged, even as he criticized its centrality within immunology:

*Underlying each branch of immunology, the concept of an identified and protected "self," a theoretical construction and fecund metaphor, has served as the central theme which integrates this diverse discipline. Indeed, the fate of "the self" in immunology offers a historical understanding of how the science has evolved (Tauber 2010: 1: para 1).*

### **A Critique of the Immune Self**

Tauber's view of the history of immunology shifts its disciplinary scope from the discrimination between self and non-self to what he described, in a self-admittedly heterodox fashion, as the appropriation of "the task of defining the organismal self" (2004a: 201). His criticism was, in fact, the continuation of an argument he developed in the early 1990s and first explicated in *The Immune Self: Theory or Metaphor* (1994b), the second part of the "trilogy" of books reviewed by Söderqvist and Stillwell (1999). According to Tauber, the notion of the organismal selfhood – a metaphor introduced by Burnet in order to explain how the immune system worked, which quickly changed in status to a theory and then to a dominant paradigm – served to the detriment of immunology because the paradigm ignored "a vast body of data and explanation" that makes up the discipline today (Tauber 2010: para 6). "The designation 'self' and the 'other' ignores how neat divisions or

boundaries were adopted, or at best, were drawn with a certainty that remained problematic” (2010: para 5), he contended, recommending that immunologists themselves strive to problematize the objectives of their discipline and widen its scope. Tauber’s position is also evident in his other writings; for example, in an essay review of the Norwegian microbiologist Elling Ulvestad’s book *Defending life: The nature of host-parasite relations* (2007), which is, tellingly, entitled “Expanding immunology” (Tauber 2008). An underlying assumption in Ulvestad’s book was that “the immune system depends ontologically on the ecosystem in which it is embedded” (2007: ix). Tauber honed this idea to suggest that the discipline needed to open itself to ecological considerations and “reorient itself to address more effectively not only the molecular mechanisms of immune reactions, but also their regulation and organization” (2008: 271).

Around the same time that Tauber launched his criticism of the selfhood paradigm, the immunologist Polly Matzinger posed a challenge from within the disciplinary ranks to the notion that the discrimination between self and non-self was the primary driving force in mediating immunity (Matzinger 1994: 991). She provided an alternative explanation with her “Danger Model” which was predicated on the premise that “the immune system is more concerned with damage than with foreignness, and is called into action by alarm signals from injured tissues, rather than by the recognition of nonself” (Matzinger 2002: 301). Now, Matzinger’s model did not deny either the existence of self / non-self discrimination, or its significance for immunology. In her words, “[t]he critical need to discriminate is the evolutionary selection pressure behind the complex set of mechanisms that endow T cell receptors (TCRs) and antibodies with their enormous range and exquisite degrees of specificity” (Matzinger 2002: 4). Where the two models parted company, she went on, was that the Danger Model did not assume that the discrimination was “the critical element in the decision to initiate an immune response” (Matzinger 2002: 4).

In the years since Matzinger first proposed the Danger Model, it has provoked lively debate and discussion – as all good scientific theories should – within the immunological community. That it continues to hold a prominent place in discussions is a clear measure of its dynamic nature. Given his perspective on the immune self, it is not surprising that Tauber has been more sympathetic to Matzinger’s model than to the immunological models of other immunologists such as Melvin Cohn, one of the authors of the “two-signal” hypothesis (Bretscher & Cohn 1970), which modified and expanded upon Burnet’s original theory (Tauber 1998a; 1998b; 2000). In particular, Tauber lauded the Danger Model for replacing self / non-self discrimination with a “contextualist scheme” and for being “fundamentally a process driven, functionally conceived model [that] builds on the antigen-presenting cell as the arbiter of immune reaction, a cell that cannot distinguish self from nonself in traditional terms of lymphocyte recognition” (1998a: 470; 1999: 468). But he took a much more extreme position than Matzinger in his criticism of selfhood, regarding “the evidence as increasingly showing that ‘the immune self’ cannot be defined as

an entity, and not even as a function,” and further arguing that the self was “an impediment to furthering the conceptual horizon of immunology” (Tauber 2000: 242).

Even as he praised Matzinger for having “cast the net of immunology well beyond lymphocyte biology alone” (2000: 246), Tauber categorized her intellectual contribution as something that “redefines immunology’s ‘facts’ within an alternative framework to the Burnetian scheme” (2000: 247). In his view then, Matzinger’s Danger Model is “exactly that, a model, not a new theory,” and he accords the exalted status of a theory or “theoretical development in immunology” to only two events in its history. “The first was made by Metchnikoff in establishing that immunity had the dual activity of first establishing organismal identity and then protecting its integrity” (2000: 246). Burnet’s articulation of the self metaphor was, in Tauber’s view, a reintroduction, albeit a fuller articulation, of Metchnikoff’s notion of the primacy of identity. The only other contribution that Tauber conceded was a genuine theoretical advance in immunology was Jerne’s idiotypic network theory, which, he argued, “moved past the identity issue altogether” to propose that “the immune system was fundamentally organized unto itself,” and its protective abilities a side benefit rather than its *raison d’être* (Tauber 2000: 246).

The same prompts and cues that led Tauber (2000) to suggest a move beyond the immune self, however, elicited quite the opposite recommendation from the philosopher Moira Howes, whose earlier work had compared the self concepts in philosophy and immunology (1998). According to her, “there are a number of conceptual reasons to preserve self-concepts in immunology” (2000: 249). Her main argument seems to be a rather pragmatic one for rendering scientific explanations; “[u]nless a biological mechanism can be understood to be about something, it is not understood” (Howes 2000: 251). According to her, stripping immunology of such intention-conveying terms as “self” and “danger” is “an oversimplification that obscures” the biological processes being described (2000: 251).

*...all of the metaphors used in immunology are intentional terms. Possibly, immunologists could find other metaphors to use, ones that are non-intentional. I have a hard time imagining what these metaphors would be...*  
(Howes 2000: 250).

Where Tauber saw a danger of the metaphor of the self achieving the status of a theory, however, Howes contended that “when immunologists use these terms they implicitly empty them of intentionality” (2000: 250), and, therefore, that the metaphor did not imply that the immune system possesses any conscious intentions or goals.

Like Tauber, Howes observed that the Danger Model was important in showing that the “discrete separation of self from nonself in immune function is not the entire basis of the immunological self,” but, rather than criticize Matzinger’s model, she emphasized the fact that it did not “mean that tolerance to self is unimportant” (2000: 256). Her main point of contention with Tauber seems to lie in the im-

plications of the network model – expanded and developed since Jerne’s original formulation by the immunologist Antonio Coutinho (1984; 1989; 2005) – for the concept of self. According to Howes, the theory does not so much obviate the need for the immune self as argued by Tauber, as it does the discrimination between self and non-self:

*[In the network model] the immune system does not regulate itself by first discriminating between self and nonself [...] Rather, immune regulation is achieved by discriminating between unperturbed and perturbed states of immune connectivity. The immune system is busy interacting with itself and with the body all of the time and the appearance of foreign antigens causes a perturbation of this activity. Because nonself is viewed as a perturbation of the system, it is not really viewed as “nonself” by the immune system. There is only “self” and its perturbations; and hence, we have a theory about how the immune system reacts to the self rather than a theory focusing on immunity to nonself (Howes 2008: 278-279).*

Thus, as Howes went on to argue in her commentary, Tauber’s claim that the self was no longer useful in immunology was premature, and that while the issue was “complex and controversial,” it was by no means obsolete. “On the contrary, the question of immunological selfhood appears to be on the cusp of renewed and vigorous inquiry, with revised models of self–nonself relations replacing dated versions” (Howes 2008: 284).

Giving credence to her claim of the endurance of the self, even as they vigorously and radically challenge the concept are the contributions of another philosopher of biology, was Thomas Pradeu, a relative newcomer to the selfhood debate in immunology. Pradeu collaborated with Edgardo Carosella, an immunologist, to criticize the “self” concept on both philosophical and scientific grounds, and to suggest an alternative framework for understanding immunity based on a notion of “continuity” (Pradeu & Carosella 2004; 2006a; 2006b). Pradeu’s engagement with immunology stems from an interest in the issue of defining biological identity, the study of which, as he claimed, echoing Tauber (2004a: 201), modern immunology has appropriated almost exclusively as part of its domain (Pradeu, 2012: 1). His description of a living organism’s identity encompasses a much broader terrain:

*A being is defined by two aspects: first, the individual characteristics that make it distinct and different from everything else [...]; second, the fact that, in spite of the changes that occur to it, it can be said to remain the ‘same’ being (Pradeu 2006a: 245).*

He describes biological identity as being a more ‘open’ concept, one that deals “with both endogenous and exogenous elements in order to determine eventually the combined, and always precarious, nature of a given organism” (Pradeu 2004: 484).

Pradeu's characterization of the nature of an organism as 'precarious' confers a temporality in addition to the corporeal aspect on the notion of biological identity. This temporality, in turn, renders the concept of selfhood inadequate, if not meaningless, because, with the organism's ability to change at any instant, there is no defined limit or boundary between the self and the so-called non-self at the molecular level (Pradeu & Carosella 2004: 483). Thus, an immune reaction is viewed as "a sudden appearance of antigenic patterns in [an] organism that differ strongly from those with which the immune system is continuously interacting" (Pradeu 2012: 132). In other words, immunity is a reaction to any sort of disturbance in "the spatio-temporal continuity" between the receptors present on the surface of the immune cells of an organism and the specific antigens – irrespective of their source – to which these receptors react (Pradeu & Carosella 2004: 483). According to Pradeu and Carosella, their theory for immunity is able to consistently explain a much wider set of immunological reactions than the selfhood model, which resorts to exceptions. For example, the selfhood model is unable to explain why immune cells called phagocytes are able to engulf and degrade cells after they have died, even though these cells were protected as "self" while still alive (Pradeu & Carosella 2006: 243). The continuity hypothesis, on the other hand, simply explains the death of the cells as a break or disturbance in molecular continuity, to which the immune cells then react.

The continuity theory is still quite new, with Pradeu's monograph in English literally hot-off-the-press, making an assessment of its impact on either the science or historiography of immunology premature and inadequate at this time. Already, however, some researchers have begun to invoke its explanatory power – for example, to understand interactions between cancer and the immune system (Blankenstein et al. 2012). Certainly, continuity is an exciting and provocative idea – a break in the continuity of the discipline, to borrow the model itself as a metaphor – and its effect on future debates about immunology and issues of identity promises to be significant.

One issue that is perhaps underplayed in some of the philosophical critiques of the self is the way in which the concept itself has evolved and changed in the years since Burnet first formulated his idea. A contemporary textbook on immunology, while giving due credit to Burnet for the origins of idea, will contain a recognizably different description of the immune self. Many of these changes are due to the dramatic changes in our understanding of genetics and molecular biology, the latter of which Burnet notoriously admitted feeling "positively schizophrenic" toward (1968: 175). Irun Cohen's introductory description of the immune self in his book *Tending Adam's Garden: Evolving the Cognitive Self* (2004) in contrast, defines the immune system as the "biological system that defines the individual," (2004: 5) in language that is entrenched in the language of molecular biology, although the fundamental notion of immune function has remained stable. His description continues as follows:

*The immune system has nothing to say about the spiritual, logical, legal or poetic self, but the immune system has much to say about the molecular self. By its acts, the immune system defines the material components that make up the self. The immune system is the guardian of our chemical individuality; [...] By deciding which macromolecules and cells are allowed residence within us, the immune system establishes the molecular borders of each person* (2004: 5).

In order to maintain the robustness of their critiques of the self, then, philosophers must take into deeper consideration the historical changes in the conceptions of said self.

### **Other than the self: alternate approaches and other immunologies**

If the immune self has dominated the scene thus far in this essay, it is because it has been one of the busiest areas for scholarship on immunology by those not engaged hands-on in laboratory or clinical immunology. For instance, aside from the Pradeu translation and an expanded second edition (2009) of Silverstein's seminal *A History of Immunology* (first edition 1989), there seem to be few single-authored books about the history of immunology published in the last decade. Thus, Söderqvist and Stillwell's charge (1999: 215) that the historiography of immunology lacked any "sustained attempts to place the development of immunological thought and practice" in broader scientific, social and political contexts, still appears to be mostly true, though not entirely so. The 2003 abridged translation of Söderqvist's own biography of Niels Jerne, *Science as Autobiography*, originally published in Danish in 1998<sup>4</sup> is an exception, but an anomalous one, in part because the author published the original before he wrote his commentaries about the history of immunology, and, in fact, drew his ideas about the discipline from his biographical project rather than the other way around. "I actually had been on the lookout for an interesting person to write a biography about when Jerne showed up by accident," he wrote later (Söderqvist 2006: 100).

The most notable example of a book attempting to offer a systematic argument about the field of immunology is *Crafting immunity: Working histories of clinical immunology* (Kroker et al. 2008), the outcome of a 2004 conference at the University of Toronto. The organizers of the conference had initially issued a call for papers "that sought to understand the diverse ways in which immunological knowledge had been articulated in clinical medicine," an attempt as it were, to examine the historical links between the "bench and bedside"<sup>5</sup> (Kroker et al. 2008: 1). According to the organizers, however, the results of the conference (attended almost exclu-

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<sup>4</sup> The title of the Danish version of this book is *Hvilken kamp for at undslippe*, which translates as "what struggle to escape," a line from "Ode on a Grecian Urn" by the nineteenth century English poet John Keats.

<sup>5</sup> This phrase, which comes from the title of Illana Löwy's 1997 book (and which was part of the cohort reviewed by Stillwell and Söderqvist in 1999), was deliberately used by the conference organizers, with due credit to the author (Kroker et al. 2004: 1).

sively by historians and philosophers of science) were somewhat unexpected: “[i]t was not so much the pretense of immunology as a branch of biological knowledge with clinical applications that came under scrutiny as it was the very fact of immunity itself” (Kroker et al. 2008: 1). Presented as a series of thirteen case studies by the conference participants, organized in thematic clusters ordered more or less chronologically, the book does an admirable job of developing a “systematic argument,” (Gradmann 2010) that immunity was “crafted” over the course of two centuries. What makes Kroker et al.’s argument particularly effective, I believe, is the broad time span and the variety of contexts in which the different contributors have demonstrated how “immunity served its interlocutors as both idea and experience, as telos and as technique” (Kroker et al. 2008: 1). But as a series of case-histories, the book is limited in that lacks a broader synthetic argument about the history of immunology against the backdrop of biology.

The second edition of *A History of Immunology* (2009) deserves at least a passing glance here if for no other reason than that the original version in 1989 was the first book-length treatment of the discipline of immunology from a historical perspective. As he was an immunologist who became interested in the history of his field, Silverstein’s purpose in expanding his earlier effort was not only to “clarify further the conceptual developments of the field,” but also to incorporate his growing historical consciousness of the “important contributions of more sociological factors to the development of a science” (2009: xvii-xviii). Readers familiar with the first edition will find it reproduced in its entirety, albeit somewhat reorganized, within the pages of the second edition, along with ten new chapters. Where the first edition was organized chronologically, the new version is, roughly speaking, divided into two halves. The first part covers the intellectual history, while the second half is largely devoted to the sociological influences on the development of the field. The extent of Silverstein’s transformation from a scientist to a historian is a matter I prefer to leave to the readers’ judgment, but the broadening both of his perspective and of the treatment of the discipline is difficult to dispute, not only when we compare the two editions, but also when the later edition is juxtaposed with his 2002 monograph about the immunologist Paul Ehrlich, *Paul Ehrlich’s Receptor Immunology: The Magnificent Obsession*.

Based on a detailed analysis of the antibody side-chain or receptor theory which Silverstein holds to be the conceptual foundation stone of Ehrlich’s immunology, *The Magnificent Obsession* qualifies as the type of “internalist” intellectual history described at the outset of the essay. Historians reviewing this book have concurred that while it furnishes a wealth of scientific and medical detail about Ehrlich’s intellectual development drawn from a detailed reading of Ehrlich’s papers, Silverstein failed to provide a broader social or cultural contextualization for Ehrlich’s ideas and work (Prüll 2003; Söderqvist 2003). “Silverstein writes mainly from the perspective of an immunologist,” observed Prüll (2003: 267), while Söderqvist stopped short – but only just – of characterizing the book as hagiographic.

As far as it is no biography, it is no hagiography either, of course - but the author's obsession with Ehrlich's magnificent obsession is at times eulogistic to an extent that rings somewhat strange to an ear trained in the historiography of science and medicine of the last decades (Söderqvist 2003: 450-451).

Given Söderqvist's love-hate relationship with his own subject, Jerne, which is evident in both his book and subsequent writings, it is not surprising that Silverstein's uncritical attitude toward Ehrlich irritated Söderqvist. Consistently with his overall discontent with the ways in which historians have or have not treated immunology, he described *The Magnificent Obsession* as "no biography," a characterization that may tell us more about Söderqvist's notions of what biography should be than about his evaluation of Silverstein's book. In contrast to Silverstein, who was an immunologist first and came to Ehrlich through his interest in the latter's research, Söderqvist entered the history of immunology through his interest in Jerne as a biographical subject (2002; 2006; 2011).<sup>6</sup> Consequently, Söderqvist's view of the history and historiography of immunology was heavily colored by his perspective as a biographer. In his view, for the history of science the value of writing biographies of recent scientists - i.e., "[s]cientists active within the life-span of the biographer" (2006: 99) - is manifold, with other uses than simply functioning as histories of science "by other means," (Söderqvist 2011: 634). He identified no less than six purposes for scientific biographies besides that of serving as contextual histories or "ancillae historiae" (2011: 635-637). Of these, two others, which are probably most relevant to the discussion at hand, include serving, first, as ways to understand how scientific knowledge is constructed (2011: 637-639), and, second, as conduits for the public understanding of science (2011: 639-640). Although Söderqvist approached his project as an existential rather than scientific biography (2003: xi), focusing on Jerne's life, of which his science was just one albeit an inseparable part, *Science as Autobiography* succeeded quite admirably in providing a contextual history of mid-twentieth century immunology, a window into the way immunological knowledge was constructed by Jerne and his contemporaries. It also made aspects of the discipline more accessible to a wider public, even if unintentionally: "I had no particular wish to inform the general reader [...] But as it turned out, some reviewers nonetheless noticed its value for the public understanding of immunology" (Söderqvist 2011: 640).

Considering Söderqvist's success, it is rather surprising that other historians of immunology have not followed suit and produced biographies of other immunologists. One particularly apt subject for the type of detailed contextualizing biography that Söderqvist has advocated would seem to be Burnet. So inextricably is his name linked with the shaping of the discipline that even as Anderson et al. criticized the demarcation of immunology by its practitioners and the reductionist nature of the histories to emerge, they conveyed a tacit acknowledgement of the place of these practitioners in both the history and definition of the field: "Putting it

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<sup>6</sup> The 2011 paper is a "revised and shortened" version of the 2006 chapter and will be used in this discussion because it presents the ideas and arguments more concisely.

bluntly,” they remarked, “to do ‘immunology’ seems inevitably to do what Burnet and his followers were doing” (Anderson et al. 1994: 579). Yet there is nothing more recent about Burnet than a rather traditional biographical monograph (Sexton 1992) updated on the occasion of his centennial (Sexton 1999) by someone who was neither a historian nor a scientist. Peter Medawar, who shared the Nobel Prize with Burnet, is another fitting biographical subject, but his life, too, has been largely neglected by the historians of science.

Institutional histories, as pointed out by Söderqvist and Stillwell (1998: 212), present another underexplored area in the historiography of immunology. The Walter and Eliza Hall Institute (WEHI) in Melbourne, Australia and the Basel Institute of Immunology in Switzerland, associated with Burnet and Jerne respectively<sup>7</sup> are obvious candidates for such treatment, but thus far any serious historical scholarship about these or other institutes are lacking. As with individual immunologists, there is no dearth of candidates for such institutional histories, but, unfortunately, a reviewer cannot do much more here than remark on the lacunae in scholarship.

### **Conclusion: Is the historiography of immunology past its infancy now?**

The issue of gaps in the historiography brings us back to Söderqvist and Stillwell’s 1999 essay, which, on the basis of the lacunae in the field, concluded that the historiography of the discipline was still too young at the time. While it is true that some of the gaps they identified still exist, their claim regarding a general lack of historical scholarship about immunology cannot be said to hold true any longer, if indeed it ever did. For one, there was a certain prescriptiveness to their critique and just because the type of histories they suggested have not been written, it does not mean that scholarship has not grown in other, perhaps unexpected, directions. Such immunological sub-fields as allergy and autoimmunity, for example, which this essay has bypassed almost entirely – both due to space constraints and more importantly, the specialized nature of these topics – have been subjects of rich and varied scholarship (e.g. Löwy 2003; Parnes 2003; Jackson 2003; 2007; 2009; Smith 2009; Jamieson 2010). Meanwhile, although famous figures may not be the subjects of stand-alone biographies, the work of Burnet, Medawar, Jerne and Jules Bordet, to name but a few, continues to receive historical scrutiny not only in immunology, but also in other disciplines and contexts, which integrate the history of immunology into the broader fabric of the history of medicine (Park 2004; 2010a; 2010b; Pasqualini 2009; Schmalstieg, Jr. & Goldman 2009; Sankaran 2010). The history of immunology is embedded in the histories of the disciplines such as chemistry and biology, and while the extant literature appears to be missing work that explicitly

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<sup>7</sup> Burnet was director at WEHI from 1944 until 1965 and it was under his directorship that “[a]lmost overnight, immunology became the major preoccupation of the institute and over the next 10 years or so it contributed almost 50 per cent of the world immunology literature,” ([http://www.wehi.edu.au/about\\_us/history/the\\_burnet\\_era/](http://www.wehi.edu.au/about_us/history/the_burnet_era/)). Jerne was the founding director of the Basel Institute of Immunology.

looks at the development of the field in these broader contexts, one might well find hidden histories of immunology in the historical literature of those broader fields – a historiography that is well beyond the scope of this review. Also not to be overlooked is the fact that immunology is a field whose practitioners remain active in writing their own historical analyses in many of their scientific journals. These accounts, in turn, constitute an area for potential scholarship among historians and philosophers.

In light of these different histories, then, one cannot help feeling that it is perhaps time to drop the age metaphor in considerations of the historiography of immunology. Instead digging into the discipline's own history and ranks, we might borrow a property of immune cells used in classifying the cells in the bone marrow and lymphatic glands to describe the state of the history of immunology. Unlike most other cells in an adult body which divide to form replicas of themselves – skin cells, for example, will give rise to skin cells, and muscle fibers to more muscle fibers, the early generations of these stem cells are “pluripotent” and have the potential to become one of several different types of mature immune cells as they undergo cycles of cell duplication and division. It is only after a few cycles of cell division that these stem cells lose their pluripotentiality and become committed to becoming one specific type of immune cell, e.g. a B or T lymphocyte, a granulocyte or a monocyte. The history of immunology seems akin to these pluripotent stem cells; while not yet committed to any single path of development, it is prolific nonetheless, brimming with the potential to grow in diverse directions.

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