Parallax

Routledge
Taylor & Francis Group

ISSN: 1353-4645 (Print) 1460-700X (Online) Journal homepage: http://www.tandfonline.com/loi/tpar20

Self, Not-Self, Not Not-Self But Not Self, or The Knotty Paradoxes of 'Autoimmunity': A Genealogical Rumination

Ed Cohen

To cite this article: Ed Cohen (2017) Self, Not-Self, Not Not-Self But Not Self, or The Knotty Paradoxes of 'Autoimmunity': A Genealogical Rumination, Parallax, 23:1, 28-45, DOI: 10.1080/13534645.2016.1261660

To link to this article: http://dx.doi.org/10.1080/13534645.2016.1261660

Published online: 29 Jan 2017.

parallax, 2017, Vol. 23, No. 1, 28–45, *Autoimmunities*
http://dx.doi.org/10.1080/13534645.2016.1261660

Routledge
Taylor & Francis Group

Self, Not-Self, Not Not-Self But Not Self, or The Knotty Paradoxes of 'Autoimmunity': A Genealogical Rumination

Ed Cohen

> *What indeed does man know about himself? [...] Does not nature keep secret from him most things, even about his body, e.g. the convolutions of the intestines, the quick flow of the blood currents, the intricate vibrations of the fibers, so as to banish and lock him up in proud knowledge?*[1]
> Friedrich Nietzsche.

Autoimmunity is a rubric currently used to comprehend 60-80 different symptomologies that effect diverse tissues and cells of the human body. By some estimates they may affect up to five percent of the populations of industrialized nations.[2] Autoimmune conditions currently include: Multiple Sclerosis, Myasthenia Gravis, Lupus Erythematosus, Type 1 Diabetes, Rheumatoid Arthritis, Alopecia, Addison's Disease, Grave's Disease, Hashimoto's Disease, Scleroderma, Ankylosing Spondylitis, Ulcerative Colitis and Guillain-Barré Syndrome, among others.[3] For the past fifty years, the prevailing bioscientific paradigm has posited that autoimmune illnesses result from an organism's deleterious immune response to its own vital matter or, as immunologists might put it, from a 'loss' or 'breech' of 'self-tolerance'. According to the paradigm's latest incarnations, autoimmune diseases seem to arise in genetically susceptible individuals when their responses to environmental challenges catalyze 'immune dysregulation'.[4] Alas, despite significant advances in characterizing the biochemical and genetic intricacies that both subtend and animate immune function, the reasons why harmful self-reactivity occurs remain mysterious.[5] Thus, even though biomedicine increasingly invokes autoimmune reactions to explain a myriad of bodily phenomena (not all of them adverse, for example the recycling of effete, dangerous or damaged cells), it does not fully understand why or how any of these phenomena exist, let alone why or how they persist as pathological conditions. Indeed, even as immunology has refined its representations of immunity's biomolecular processes to the point where lay readers might mistake them for occult texts of an esoteric religion, it still offers no consistent explanations for autoimmune pathologies.

Undoubtedly immunology now lies on the cutting edge of biotechnological exploration, in part because, beginning in the mid 1980s, the efforts to understand HIV/AIDS led to vast increases in research funding, and

consequently to explosions of new immunological data. These developments generated important insights both about 'normal' immune function and about the detrimental effects of HIV upon it. They also facilitated the development of retroviral treatments now used (by those who have access to and can afford them) to regulate the precarious dynamics of sero-positivity. Concomitantly, the international underwriting of the Human Genome Project in the last decade of the twentieth century and the first decade of the twenty-first generated server farms full of digitized information that fostered increasingly dense entanglements between immunology and genomics. Nevertheless, even in light of these more and more complex biomolecular mappings, the preponderance of contemporary immunological accounts continues to rely, mutatis mutandis, on a theoretical axiom classically formulated in the late 1950s by Frank Macfarlane Burnet's Clonal Selection Theory. Following Burnet, immunology by and large takes as its shibboleth the precept that the immune system serves to discriminate 'self' from 'not-self', as Burnet robustly framed it in his seminal textbook, *Self and Not Self: Cellular Immunity, Book I*.[6]

As the negative, and 'self-destructive' corollary of this enduring immunological binary, autoimmunity conversely describes a situation that occurs when this essential bifurcation between self and not-self falters or collapses.[7] In autoimmunity, the self and its negative other somehow disregard their putative mutual exclusion, such that self instead appears to itself as both self and not-self. Autoimmune conditions thus violate the law of non-contradiction, the 'law' that since Aristotle has governed the 'rationality' of Western reason, including all its scientific manifestations. Or to put it more affirmatively, if autoimmunity constitutes an immune reaction to tissues of 'the self' itself, then it constitutes a real – and hence a vital – contradiction. In theory autoimmunity shouldn't exist, since self should not 'discriminate' from (or against) itself as non-self while remaining itself–let alone its 'self'. And although, from time to time, some of us might feel that we can no longer tolerate ourselves (or our 'selves') psychically or emotionally, within immunological thinking a self should by definition 'tolerate' itself. Indeed, immunologically speaking what makes a 'self' itself is its self-tolerance. One of immunology's first theorists, Paul Ehrlich, characterized the very possibility that an organism's self-relation could be harmful to itself as a *horror autoxicus*.[8] Yet in fact the immune self can harm itself and it does so with some regularity–and there's the rub. Autoimmunity bespeaks not just a logical but also a *bio*-logical impropriety, and as such it can also produce devastating if not deadly consequences.

Within current immune discourse, autoimmunity's paradoxicality remains irreducible. Notwithstanding the vast sums Big Pharma has spent on developing immunosuppressing drugs to address autoimmune conditions by dampening their symptoms, no treatments yet exist that can mitigate either whatever triggers autoimmune etiologies in the first place, or whatever enables them to persist thereafter. In part, this ongoing failure reveals that *autoimmunity actually names a known unknown* whose (un)knowability continues to befuddle even the best funded attempts to contain it. Indeed, the conundrum of self-mistaking-itself-as-not-self forms an impasse that has resisted

every digitized, high-tech, genetically engineered means that has been thrown at it. Given the persistence of this organismic aporia, it seems there might be more to the paradox that autoimmunity 'is' than conventional bio-scientific thinking about human organisms recognizes. If by virtue of their very existence 'autoimmune' phenomena defy basic immunological dogma (i.e., self/not-self discrimination), then might we begin to wonder whether the theory adequately accounts for all the vital facts?[9] Perhaps immunology's unquestioned appropriation of a *logical* opposition – derived from and embedded in Western thought's governing epistemo-political ontology – as a *bio*-logical axiom unnecessarily limits our capacity to grasp our own complicated nature as living beings.[10] Indeed, the tensions and tendencies that the autoimmune illnesses incorporate suggest that as living beings we might not be so 'logical' after all. In which case, our paradoxical nature might ask us to consider something important, but alas immunologically obscured, about what it means to live as living (human) beings living among other living beings, both human and otherwise. At least, that is my hope.

* * *

I've been ruminating on the paradoxes of autoimmunity for a long time.[11] I first heard the word more than forty years ago, when I was thirteen. After a four-month festival of flagrant diarrhea, acute abdominal pain, and wasting, I received an autoimmune diagnosis: Crohn's disease. Living with any diagnosis catalyzes a new relation to self, but living with an autoimmune diagnosis does so in spades. Moreover, it precipitates a new relation to biomedicine. Diagnosis has defined medicine's *raison d'etre* ever since the time of Hippocrates, when medicine first anointed itself as 'medicine' to distinguish itself from its competition (magicians, root-cutters, priests, doctor-prophets, purifiers, drug vendors, etc.). Diagnosis, literally 'by way of knowledge', capitalizes medicine's investment in knowing as a therapeutic resource. Abjuring other modes of healing, medicine commits itself to knowing above all else: it takes knowing as its therapeutic trademark. Of course, there's a lot to be said for this approach. Personally, I'd probably be dead without it. But there are also some limits. For example, when my doctors tried to explain what Crohn's disease was, they said: Crohn's is an autoimmune illness. Now I had a pretty extensive vocabulary for an adolescent but autoimmunity didn't happen to be one of my words, so they tried to break it down for me. First, they said: your body is rejecting part of itself. Despite this apparently cogent explanation, I didn't seem to be getting it so they added: it's like your body is allergic to itself. Oddly, this didn't make things perfectly clear, so they threw out one more metaphor: it's like you're eating yourself alive. Ok, that I could grasp. Although to be honest, I don't think it has really been all that helpful in the long run.

In the decades since my diagnosis, I keep trying to get my head around autoimmunity. At first I was motivated mostly by a desire to figure out how to keep my gut in line, although that never really worked out. Then after I

learned that my gut had a brain of its own (a.k.a., the enteric nervous system) and that the brain-in-the-gut contained most of the same neuro-receptors and made many of the same neuro-transmitters as the brain-in-the-head (including 90 per cent of the serotonin whose reuptake we now spend so much money trying to inhibit), I began to suspect something else might be going on. Taking the gut-brain axis to heart, I embraced the insights of psychoneuroimmunology: since the same peptides participate in many organismic functions that subtend our 'selves' (e.g., psychological, emotional, neurological, endocrinological and immunological) might this not suggest that 'selves' are more complicated than we usually suppose? Alas, the situation got even more muddled when, in the wake of the new metagenomic sequencing technologies, the microbiome began to figure into the picture as well, leading to the postulation of a brain-gut-microbiome axis. Needless to say, this new matrix rendered the immunological question of self even more convoluted since it might now have to include our 100,000,000,000 commensal bacteria along with our 'own' 70,000,000 cells (and that doesn't even touch on the viruses whose number is legion).[12] So what 'self' exactly gets mistaken for 'non-self' in the etiologies of autoimmune illness?[13] The paradox of autoimmunity appears to point us to a particularly perplexing problem: what if self and not-self, like subject and object, have never been quite as distinct as their immunological positing supposes? Moreover, what if living beings do not bifurcate in logical ways? And if this could be the case, why has immunology held onto its central binary so tenuously and for so long?

In order to address these questions, it helps to remember that immunity does not constitute a 'natural metaphor', and that it has not always had a biological valence. In fact, from the Roman empire until the end of the nineteenth century, immunity's primary meanings remained legal and political. Only in the 1880s did a Russian zoologist, Elie Metchnikoff, recruit the juridico-political metaphor to describe how living organisms of radically different scales comingle and coexist. Metchnikoff's innovation occurred in the context of the numerous pandemics that plagued Europe during the nineteenth century and in the wake of the subsequent emergence of microbiology (under the auspices of such luminaries as Robert Koch and Louis Pasteur) in response to these infectious events.[14] Prior to the 1860s, immunity rarely appeared in medical discussions of disease because its juridico-political valence clashed with the humoral theories that informed prevailing medical explanations. Indeed, the question of whether diseases could be contagious or not continued to provoke vociferous international disagreement well past the middle of the century. However, in the wake of cholera's repeated and deadly visitations to European cities (1830-32, 1847-49, 1853-54, 1865-66, 1873, 1884, 1892-93) a diplomatic resolution to the contagion question was hammered out at the third International Sanitary Conference, held in Constantinople in 1866, in order to settle the hotly contested issue of quarantine. As it turned out, the biological appropriation of immunity finessed the legal, political and economic problems to which the cholera gave rise, even if it left its morbid consequences entirely unchanged.

Regardless of their many substantial disagreements on the topic, all European nations concurred that cholera had 'invaded' from colonial India where it appeared endemically. (We might now call this 'colonial blow-back'). Nevertheless, given the limited understanding of how these infections propagated themselves and the conflicting stakes raised by their effects, violent international disputes prevailed about how best to circumvent these 'invasions'. Countries that had significant shipping and trade interests (especially Great Britain) insisted that cholera was only contingently contagious, primarily appearing in insalubrious locations or among insalubrious individuals, and therefore did not necessitate quarantines (which would, needless to say, impede the flow of cash and goods). Instead they argued that cholera could be addressed through 'hygienic' or 'prophylactic' means alone. Countries along the southern Mediterranean (especially Greece, Italy, France and Spain) whose ports required much shorter transit times from India and which had much smaller international trade portfolios, however, insisted that quarantines remained the only effective means of forestalling cholera's invasive propensities.

Splitting the difference, the International Sanitary conference invoked 'immunity' for the first time as a simultaneously biological, political, economic, medical and military solution. They decided that while cholera could in fact be transmitted from one person or place to another, not all people and all places were equally susceptible. Hence, places with greater susceptibility (due to hygiene, climate or other environmental factors) might warrant the imposition of quarantines; however, more favorably situated locales need not resort to such (economically) restrictive measures because they possessed natural 'resistance'. They called this resistance 'immunity':

> This immunity, as a general rule, when closely regarded, can be linked to good hygienic conditions existing in these localities, or to notable improvements which have operated there for a while. The relative immunity answers to those who are too inclined to commend the safety of nations against cholera exclusively to quarantine measures.[15]

Thus, when immunity first appeared as a biological – or actually bio-political – concept, it did so not because it explained how individual organisms respond to pathogenic challenge, but rather because its primary juridico-political valence enabled a compromise formation among medical, diplomatic, economic imperatives. If a nation was deemed 'relative[ly] immune' (in a biological sense) from cholera, then it could remain entirely immune (in a legal sense) from quarantine.

In the decade after the Constantinople conference, attempts to contain the mortal consequences of infectious diseases catalyzed the new science of bacteriology, which finally seemed to settle the contagion question once and for all. As bacteriology propelled itself into both scientific and public awareness – primarily via the labs of Pasteur and Koch – it proffered the 'germ theory of

disease' as its first fruits. While the notion that germs 'cause' disease (as well as bad breath) might now seem self-evident to us, this causal relation in fact needed a bit of tweaking before it could assume the conceptual labor that it now bears. For germ theory itself contained the germ of another problem: if germs can cause disease and if they are everywhere, then why aren't we sick all the time? Or why are we even alive? Moreover, why do some people get sick when exposed to a pathogen while others do not? Since it offered compelling answers to such questions, Metchnikoff's appropriation of immunity was, needless to say, a life-saver for germ theory. Germ theory's initial limitations derived in part from the fact that Koch and Pasteur were both highly attached to – and, quite literally, invested in – the bacteria that they isolated. Consequently, they didn't have much interest in the vital processes of the organisms in which pathogenic microbes proliferated if and when they 'caused' infectious diseases. As a result, the 'fathers of bacteriology' understood infectious disease processes primarily as the direct action of bacterial agents, so that in both Pasteur's and Koch's initial hypotheses infections represented especially harmful forms of parasitism.

Metchnikoff however was a zoologist and so his main interest was not in bacteria, but in the life processes of the organisms they infected. This perspective allowed him to recognize something that the bacteriologists, and especially Koch, could not. Although Koch remains rightly renowned for his famous 'postulates', his explanation of bacterial pathogenesis relied on a questionable analogy. When Koch, a German medical and military officer, looked under his microscope at pathogenic bacteria (especially cholera, anthrax, and TB) he visualized them through the cultural lens of 'invasion' that had crystalized around cholera. Indeed, when he looked at the 'comma bacilli' that he famously defined as cholera's 'cause', he saw them as the actual vectors that enabled cholera to 'invade' Europe; therefore, *by metonymy he characterized infectious pathogenesis itself as a form of bacterial invasion*. Metchnikoff however demurred. Drawing on his previous observations that the intracellular digestion characteristic of unicellular organisms remains evolutionarily conserved in the 'phagocytes' (now called macrophages) of multicellular organisms, Metchnikoff argued that if bacteria 'invade' larger organisms this cannot be a one-sided battle, or else we'd all just be collateral damage. Instead, he conceptualized infectious disease as an inter-species struggle in which an infected organism mounts its own 'defensive' response and then, mobilizing the juridico-political term that the International Sanitary Conference settled on, he named this defensive capacity immunity. The rest is history.

However, Metchnikoff's analogy of immunity with host defence contained its own germ of a contradiction: in its original legal sense, if immunity obtains then there is no need of defence – it is literally a moot issue – and if one must mount a defence immunity does not obtain. Nevertheless, despite this conceptual contradiction, Metchnikoff's hybrid legal-political-military metaphor stuck, implicitly characterizing life as war by other means. In short order, Pasteur scooped Metchnikoff up and ensconced him in a lab at the

Institut Pasteur, the world's first for-profit bio-tech enterprise, where he worked for the rest of his life. Because his concept rectified the (il)logical germ contained in germ theory (i.e., it explained why we're not all already dead meat), the theory's proponents quickly inoculated themselves with 'immunity' as an effective conceptual vaccine. In addition to its manifest theoretical benefits, this conceptual vaccination helped to explain why the actual vaccines that they now began to market profitably worked; hence immunity justified why these new biotechnologies should be medically *and* commercially promoted. Given such tangible assets, it is of no surprise that by the mid 1890s, immunity appeared to belong to germ theory quite 'naturally'. Although Metchnikoff's emphasis on immunity as a cellular activity soon ceded pride of place to Paul Ehrlich's chemically-oriented 'side-chain' theory (the precursor for antibody-antigen models and the basis for the immunochemistry that dominated the field for the next half a century), Metchnikoff's conceptual invention 'immunity-as-defense' remained – and indeed remains – central to how bioscience has thought about immunity ever since.[16]

Fast forward fifty years. When Burnet introduced his 'clonal selection theory' in the late 1950s, incorporating 'self/not-self discrimination' as its theoretical crux, he explicitly returned to Metchnikoff's cellular position which had remained largely undeveloped.[17] Until Burnet's revival, immunology (or 'serology') was dominated by Ehrlich's emphasis on the chemical formation of antibodies and antitoxins which it envisioned as the armaments of host defence.[18] Given its non-cellular orientation, the immunochemical approach took the organism's identity as unproblematic in order to foreground its defensive capacities as immunology's proper bailiwick. Hence, its central question concerned how organisms generate such a diverse humoral arsenal that they can respond to almost any antigen they ever encounter (including synthetic molecules that never before existed, and thus whose recognition could not have been conserved through evolution). By the middle of the twentieth century, a number of competing theories about antibody formation emerged, foremost among them the antigen-template theory (antibodies formed by molding themselves to the molecular shapes of antigens), the 'modified-enzyme' theory (antibodies are 'enzymatic units' produced when antigens become engulfed in macrophages containing enzymes, which break down effete cells and other debris, that are then modified to destroy these same antigens outside the cell), and the 'natural selection' theory (an antigen acts as a 'selective carrier' that transports naturally occurring antibodies, keyed to the antigen's molecular structure, to special cells where they precipitate the mass production of 'specific antibodies' with the same antigenic keys).

The last theory, developed by Niels Jerne (who would subsequently win the Nobel prize for characterizing immune response as a function of the 'immune system') represented a point of inflection between humoral and cellular immunity. According to Jerne's theory, during embryogenesis the organism generates a vast repertoire of diverse antibodies of 'random

specificities', that serve as prototypes for the post-natal production of 'specific antibodies' if and when sparked by the presence of antigens for which they have affinity.[19] However, Jerne immediately recognized a fundamental problem with his theory: if the embryo randomly generates a multitude of natural antibodies, some of them would have to correspond to molecules native to the organism itself. In order to correct this theoretical deficiency, Jerne hypothesized that antibodies to 'auto-antigens' must bind with these antigens during gestation such that these 'auto-antibodies' would 'no longer be available for reproduction'. Jerne's notion that self-reactive elements generated by the embryonic immune system are 'deleted' in thymus during embryogenesis remains central to contemporary immunological dogma (albeit now considered in terms of cells rather than antibodies).[20]

In his essay 'A Modification of Jerne's Theory of Antibody Production using the Concept of Clonal Selection', Burnet first formulated his clonal selection theory as a direct response to Jerne's hypothesis.[21] Their key point of difference concerned the manner of antibody replication. Burnet argued for a cellular origin for the mechanism (via what we now call B- and T-cells) rather than locating it in extracellular proteins as Jerne did. For Burnet, his biological (rather than chemical) hypothesis retained the advantages of Jerne's theory but overcame the objection that 'a molecule of a partially denatured antibody could stimulate a cell, into which it has been taken, to produce a series of replicas of the molecule'. Yet in framing this critique, Burnet assimilated Jerne's perspective to his own 'self' centered thesis. He cannily claimed that both he and Jerne shared the same two premises for immune function:

> The first is the absence of immunological response to 'self' constituents and the related phenomena of immunological tolerance; the second is the evidence that antibody production can continue in the absence of antigen. Some means for the recognition and differentiation of potentially antigenic components of the body from foreign organic material must be provided in any acceptable account.[22]

While Jerne himself did not employ the language of self and not-self, Burnet nevertheless lauds him for providing a 'method of recognizing self from not self'. Moreover, he extrapolates from Jerne's notion that 'auto-antibodies' are 'removed' during embryological development, to the notion that this constitutes the mechanism by which self produces immunological 'tolerance': 'Clones with unwanted reactivity can be eliminated in the late embryonic period with the concomitant development of immune tolerance'.[23] Yet Burnet's idiom is somewhat peculiar. If 'immune tolerance' refers to 'the absence of immunological response to "self" antigens' (and all 'self' is potentially antigenic), then self is defined negatively as that which does not react to itself. The choice of 'tolerance' to describe this situation underscores Burnet's curious and somewhat nebulous understanding of self as the absence of self-relation.

The word tolerance derives from the Latin translation of a Greek root (τλαω) that meant to endure or to suffer. The Latin *tolero* meant to bear, support, sustain; to continue, remain; and by transference: to support a person or a thing; to nourish, maintain; preserve by food or wealth; to sustain.[24] These etymological traces suggest that self-tolerance bespeaks a temporal process that sustains the iterations of self through time as a relation of self to itself. The immunological self remains 'the same as' itself insofar as it does not respond to itself during the course of its life.[25] It maintains itself as a self by immunologically tolerating itself. Conversely, autoimmunity corresponds to the event in which this self finds aspects of itself intolerable.[26] Consequently, Burnet found the proof of his immune pudding in the autoimmune *failure* of self-tolerance: 'It is only when things go wrong that it becomes possible to perceive that there is something in normal function which requires understanding'.[27] In other words, for Burnet, the regular existence of autoimmune pathologies demonstrated that Metchnikoff's defensive rendering of immunity essentially prefigured and corresponded to his own opposition of self and not-self.

The key issue, Burnet contended, concerns the fact that while

> […] we were all taught to regard antibody production and other immune responses as manifestations of a process of defense against invading micro-organisms or any other type of foreign material entering the tissues […] [t]he meaning of foreigness was something that seemed to worry nobody. Only with the recognition that there are disease conditions in which antibody is actually directed against body components–acquired haemolytic anemia, for instance–did a real sense of the importance of the body's ability to differentiate between self and not-self come into being.[28]

As the exception which proves the rule, autoimmunity emerges in Burnet's theory as evidence that immune response normally relies on a *logical and biological* bifurcation of the world into self and not self. According to Burnet – and to most immunologists after him – from an organism's point of view, a fundamental hostility must exist between what it recognizes as itself and everything else. This ontological and ontogenic perspective translates into biological terms a Hegelian proposition about consciousness, neatly summarized by Simone de Beauvoir: 'Following Hegel, we find in consciousness itself a fundamental hostility towards every other consciousness, the subject can be posed only in being opposed'.[29]

In Burnet's estimation this opposition simultaneously describes and explains the fundamental 'reason' (in the double sense of logic and motive) that underlies Metchnikoff's defensive interpretation of immunity:

> When foreign and hence potentially dangerous material enters the body–classically as an invading micro-organism–it requires it be recognized as foreign […] Equally obviously, any body

> component must not provoke the appearance of antibody or cells which can react specifically to contact with it. Any defense force must know how to distinguish friend from enemy. The characteristic feature of what might be called the new immunology is its interest in the nature of the process by which this recognition of the difference between what is self and what is not self is mediated.[30]

Aligning the oppositions friend/enemy with self/not-self, Burnet's theory supposes that a body 'obviously' ought not to 'react specifically' to self-contact (because we're always such good friends to ourselves?). This means that self is predicated on the recognition of not-self as enemy insofar as its self-recognition (à la Hegel) must always be mediated through an other. Burnet's paradigm hence affirms 'natural' hostility as the essential condition of life (or at least of human life, which is what he's ultimately concerned with). The problem that Burnet defines as fundamental to 'the new immunology' – and which immunology has taken as its *raison d'etre* ever since – is how the organism can properly direct its hostile negativity towards the other. On this interpretation, autoimmunity constitutes a failure of defence 'intelligence' and hence manifests an instance of 'friendly fire'. If it escalates it can turn into 'a chronic immunological civil war'.[31]

The trouble with Burnet's metaphors and their ongoing legacies arises from the ways that they import certain political and philosophical assumptions to explain biological phenomena as if these assumptions are themselves 'natural'. Neither friend/enemy nor self/not-self derive from reflections on living processes; instead they issue from the way Western political philosophy has depicted how (some) humans behave towards other humans. Unfortunately, this may not adequately characterize how all organisms behave towards other organisms, especially ones of such different scales as microbes and multicellular animals. (It may also not characterize how all humans necessarily relate to other humans). Indeed, in addition to the recognition that immune function includes the clearing of an organism's effete, dangerous or damaged cells and molecules, the recent insights of microbiology concerning both the symbiotic origins of eukaryotic cells from fusions of bacterial lineages and our dependence on the commensal bacteria with which we have coevolved belie the entangled oppositions (self/not-self, friend/enemy) that have underwritten immunological thinking for more than fifty years.[32] Moreover, the persistent unknowability of why autoimmune conditions exist and persist suggests that these oppositional logics might not fully appreciate the complications entailed in being a living 'self', let alone a living being. While a few theoretically inclined immunologists have attempted to rethink aspects of this dilemma, none yet seems inclined to dispute the irreducibility of logical opposition per se as the condition of possibility for our biological existence.[33] Yet it may be the case that by inscribing oppositional logic within the vital dynamics of living organisms, immunological frameworks skew in unreasonably bifurcating ways.

Since I am not an immunologist, I'm neither capable of, nor interested in, proposing an alternative to the dominant immunological framework. However, as someone who has lived with an autoimmune diagnosis for more than forty years, I can attest that the prevailing immunological paradigm does not adequately explicate my own experience of what living with an autoimmune condition has entailed. From my vantage point, immunology's self-conception (as well as its 'self' conception) as the science of self/not-self discrimination leans on an unacknowledged and unnecessary political ontology, derived in part from its own historical emergence in the late-nineteenth century as a hybrid diplomatic solution to the economic problems of quarantine that was subsequently recruited by bioscience to supplement germ theory's contradictions. It supposes that multicellular life, and especially that of humans, incarnates hostile opposition as its condition of possibility – which means *our* condition of possibility – as living beings. Finally, by using the Greek reflexive pronoun '*autos*' (αὐτός) (which refers the action of a verb back to its subject) to modify a Latin legal concept (*immunitas*) (which it takes to mean the opposite of what its legal valence entails), immunology suggests that *auto*immunity represents the inversion of this 'natural' defensive hostility back towards the organism itself.

For me these knots of paradox that autoimmunity knits together make it less and less useful, not just to think with – to invoke Claude Levi-Strauss's idiom – but more importantly to live with. Indeed, in positing that my own cells and molecules evince a bio-molecular hostility towards my 'self' (and myself), immunological explanations of autoimmune conditions disregard the most vital thing that I have learned from living under the shadow of autoimmunity: i.e., *it's complicated*. Complicate literally and etymologically means 'to fold with'. Living beings are complicated in the sense that they are folded into the world and the world is folded into them.[34] This pleating both defines and sustains our lives. Much as immunology might want (us) to believe that self and not-self oppose one another, whether as friend and enemy or as thesis and antithesis, this framework cannot *and does not* account for the necessary intimacy that all life maintains with the world from which it arises, of which it consists, with which it coexists, and to which it inevitably returns. Francisco Varela (one of the twentieth century's great polymath thinkers of both immunology and neurology, and co-inventor with Humberto Maturana of the biological concept 'autopoesis') underscores the strictly non-logical nature of this necessity, referring to it as

> […] the intriguing paradoxicality proper to an autonomous identity: the living system must distinguish itself from its environment, while at the same time maintaining its coupling; this linkage cannot be detached since it is against this very environment from which the organism arises [that it] comes forth.[35]

If paradoxicality obtains as the condition 'proper to an autonomous identity', then perhaps autoimmunity's perceived paradox only extends a more fundamental paradox that living itself entails. Thus, encompassing what we

currently call autoimmunity – which bioscience cannot yet do – might require us to reject logical opposition as the proper basis for thinking living being and to embrace a more complicated understanding of life processes as ways of living together. In other words, perhaps what we now call biological immunity is at best an exceptional mode of biological community or conviviality.[36]

Alas this is not how immunology orients our thinking. Although my doctors were no doubt trying to help me understand what was happening to me when they told me I was eating myself alive, I now believe that 'self' was not my main problem. Instead, living with Crohn's disease has encouraged me to consider that the dynamic processes of self-formation, or what we might call individuation, remain ongoing and that they only occur in conjunction with the constitution of associated milieus or 'life worlds'. Conversely, the ongoing and creative nature of these processes opens up the possibility that we might innovate new ways to individuate and that some of these might be healing (a possibility that thinking in terms of autoimmunity unfortunately excludes). This reframing of my autoimmune diagnosis derives from the confluence between my own experiences of healing with Crohn's disease and my deep appreciation for the work of the philosopher Gilbert Simondon. By an ironic coincidence, at exactly the same moment that Burnet was promoting self/not-self as immunology's defining opposition, Simondon elaborated a non-dualistic prospect for thinking living being otherwise.[37] And, whereas Burnet's self/not-self model posits self as its point of departure and then defensively focuses on its persistence or failure to persist in terms of the negation of a negation (i.e., a proper immune response negates the negation that not-self (re)presents to the self), Simondon suggests that this positing puts the cart before the horse. Rather than begin with the individual as an already achieved – albeit vulnerable – accomplishment, Simondon suggests that we consider the relentless activity of individuation itself as the vital phenomenon.

In Simondon's view individuation unfolds from a prior condition of 'preindividuation', in which a system exists as a metastable equilibrium that contains more potential than it realizes. Given their ontological overabundance, metastable systems always tend towards change. The preindividual expresses 'a system under tension [*système tendu*], supersaturated, beyond the level of unity, not consisting only in itself, and which cannot be adequately thought by means of the principle of the excluded middle'.[38] The tensions that manifest within the preindividual pose 'problems' rather than expose contradictions, and the system then temporally resolves these problems by 'dephasing' into individual/milieu. Yet insofar as individuation always contains unrealized pre-individual potentials, all such resolutions remain only temporary and provisional, continually subject to new problematizations and new (temporary) resolutions. The dyad individual/milieu, then, does not represent a static opposition or negation, but rather establishes a 'complementarity' in which traces of the preindividual continue to resonate.

Instead of posing and opposing self and not-self as the ontological ground for living being, as immunology has since Burnet, Simondon encourages us to think

'life itself' as the 'permanent activity of individuation'. Moreover, he conceives this activity as an ongoing resolution of tensions that spur the living system to forge new connections across multiple scales of being (e.g., subatomic, molecular, cellular, anatomical, psychic, collective, spiritual, and transindividual).

> The living being resolves problems, not only by adapting itself, that is to say by modifying its relation to the milieu (as a machine would do), but by modifying itself, by inventing new internal structures, by introducing itself completely into the axiomatic of vital problems.[39]

To my mind, Simondon's notion of self-modification as a form of problem solving resonates much more deeply with what living with an autoimmune diagnosis has taught me. When I relied on autoimmunity to inform how I lived with the vicissitudes of Crohn's disease, I remained locked in a battle with myself and depended on mass quantities of (quite toxic) immunosuppressing drugs to dampen the fallout. However, once I began to allow the possibility that what I experienced *and what I am* is more than self, or not-self, or not not-self but not self, something else started to happen. Let me call this something else 'healing'.

Immunology does not encompass healing as one of its precepts, because it conflates healing with immunity. When Elie Metchnikoff forged the paradoxical concept immunity-as-defence by identifying it with the activity of phagocytes, he assimilated the notion of healing into it: 'The phagocyte therefore represents the healing power of nature'.[40] For the previous two and a half millennia, the *vis medicatrix naturae* (the healing power of nature) had nothing to do with struggle or defence. Instead it named a natural potential which medicine sought at best to enhance or support. Immunity radically changed that understanding. For those of us given autoimmune diagnoses, healing remains especially unthought. In biomedical terms, autoimmune conditions may recede, they may shift from acute to chronic (or vice versa), they may go into remission, but the propensity for self-negation remains irreducible because immunity primarily exists in order to negate not-self. However, by foregrounding the unrealized potential of the preindividual that endures through all individuations, Simondon's way of thinking living being suggests that unknown possibilities always remain. Whatever known unknowns 'autoimmunity' represents, its formulation as self-intolerance, as self-mistaking-itself-as-not-self, cannot exhaust the vital capacities that we as living beings fold into, and are folded into, as our 'selves'. Perhaps by heeding Nietzsche's admonition (cited in my epigraph), rather than remaining tangled up in our 'proud knowledge', the knotty paradoxes of autoimmunity might challenge us to consider that we are not just self or not not-self, but that in fact we are more than we know.

Disclosure statement

No potential conflict of interest was reported by the author.

Notes

[1] Nietzsche, "On Truth and Falsity."

[2] See Johnson, et al. "Epidemiology and Estimated Population Burden of Selected Autoimmune Diseases in the United States."

[3] For a basic explanation of autoimmune etiologies that includes a link to a table of diseases, syndromes and conditions considered to derive from them see http://autoimmune.pathology.jhmi.edu/whatisautoimmunity.html (accessed November 20, 2015). Recently a new parsing of the field has introduced a bifurcation of 'autoimmune' and 'autoinflammatory' diseases, the former referring to those mediated through acquired immune activity and the latter referring to those mediated through innate immune response. However, this distinction is not yet well established and it is not yet clear which diseases (if any) currently classified as autoimmune will be rechristened autoinflammatory. See for example: Kanazawa et al. "Autoimmunity versus Autoinflammation – Friend or Foe?;" Touitou. "Inheritance of autoinflammatory diseases: shifting paradigms and nomenclature;" Kastner et al. "Autoinflammatory Disease Reloaded: A Clinical Perspective;" Grateau et al. "Autoinflammatory conditions: when to suspect? How to treat?;" Masters et al. "Horror Autoinflammaticus: The Molecular Pathophysiology of Autoinflammatory Disease;" Yao and Furst. "Autoinflammatory diseases: an update of clinical and genetic aspects."

[4] While this represents the prevailing interpretation of autoimmune diseases, recently a few immunologists have begun to suggest that autoimmunity derives primarily from immune deficiencies in which the regulatory aspects of the immune system fail to limit autoreactivity, rather than primarily for excessive autoreactivity. This theory derives primarily from the evidence that deleterious autoimmune manifestations occur in those diagnosed with Primary Immune Deficiency Disorders. For examples, see: Lehman, "Autoimmunity and Immune Dysregulation in Primary Immune Deficiency Disorders;" Maggadottir and Sullivan, "The intersection of immune deficiency and autoimmunity;" Atkinson, "Immune deficiency and autoimmunity;" Bussone and Mouthon. "Autoimmune manifestations in primary immune deficiencies;" Carneiro-Sampaio and Coutinho, "Tolerance and autoimmunity: lessons at the bedside of primary immunodeficiencies;" Marks et al. "Crohn's Disease: an Immune Deficiency State;" Folwacznya et al. "Crohn's disease: an immunodeficiency?"

[5] See Tsumiyama, Miyazaki and Shiozawa, "Self-Organized Criticality Theory of Autoimmunity." 'Since 'clonal selection theory of immunity' of Burnet and subsequent molecular biological discoveries on V(D)J recombination and the diversity and individuality of immune response, how autoimmunity arises remains unclear'. For a summary of current hypotheses about autoimmune causalities see Root-Burnstein and Fairweather, "Complexities in the Relationship between Infection and Autoimmunity," 407.

[6] See Burnet, *The Clonal Selection Theory of Acquired Immunity* and *Self and not-self; cellular immunology, book one*. For a survey of the field since then see Mackay, "Autoimmunity since the 1957 clonal selection theory: a little acorn to a large oak," 67-71.

[7] Burnet, "Auto-immune Disease: 1. Modern Immunological Concepts," 645-650 and "Auto-immune Disease: 2. Pathology of Immune Response," 720-725.

[8] Ehrlich, *Studies in Immunity*:[O]ne might be justified in speaking of a "horror autotoxicus" of the organism. These contrivances are naturally of the highest importance for the existence of the individual. During the individual's life, even under physiological though especially under pathological conditions, the absorption of all material of its own body can and must occur very frequently. The formation of tissue autotoxins would therefore constitute a danger threatening the organism more frequently and much more severely than all exogenous injuries. (82-83)For a consideration of how Ehrlich's dogma gave way to the study of autoimmune disease, see Silverstein. "Horror Autotoxicus versus Autoimmunity: The Struggle for Recognition," 279-281.

[9] Indeed, classical immune theory, whether defined in terms of self/non-self, or its analogue friend/foe, gives rise to a number of regular aporia: e.g., autoimmunity, cancer, pregnancy, host versus graft disease, along with questions about why we don't develop

autoimmune responses to cells that only appear later in the life cycle (including sperm, breast milk) while we don't mount immunological responses to commensal bacteria and viruses. Matzinger offers the most robust alternative to self/non-self with her 'danger theory' which attempts to break with the immunological dogma that immunity is a form of 'self-defence', and instead suggests that immune response might better be understood in terms of an organism's attempts to negotiate dangerous situations and events. Matzinger's interventions have catalyzed a number of revisions to and defences of MacFarlane's theory. For an overview of the debates, see both the special issues in *Seminars in Immunology* 12:3 (2000) and the *Scandinavian Journal of Immunology* 54 (2001) and the special section of *Nature Immunology* 8:1 (2007); 1-13. For several other recent theoretical attempts to explain autoimmunity, see Tsumiyama et al. "Self-Organized Criticality Theory of Autoimmunity;" Irie and Ridgway, "A Modular Theory of Autoimmunity."

[10] The opposition self/other, or any other logical opposition, is neither universal nor transhistorical. Rather it emerges from the coetaneous development of political and philosophical technologies for generating "truth" in Ancient Greece as both Michel Foucualt and Jean Pierre Vernant demonstrate (see Foucault. *Leçons sur la volonté de savoir*; and Vernant, *Myth and Thought among the Greeks*). To the contrary, as Jullien illustrates, in ancient Chinese thought, logical opposition appeared as 'partial' and regarded the complementarity of contraries as a more encompassing "logic" (see Jullien, "Did Philosophers Have to Become Fixated on the Truth?").

[11] Cohen. "My Self as an Other: On Autoimmunity and 'Other' Paradoxes."

[12] The fact that commensal bacteria and viruses do not usually catalyze immune responses seems to imply that they exist in the interstices of self/not-self. In other words, that this binary is not as oppositional as its negative formulation might first suggest. Some recent hypotheses about several autoimmune illnesses suggest that the microbiome could play a significant part. See for example: Moran, Sheehan and Shanahan, "The small bowel microbiota;" Raedler and Schaub, "Immune mechanisms and development of childhood asthma;" Peng et al. "Long term effect of gut microbiota transfer on diabetes development;" Meelu et al. "Impaired innate immune function associated with fecal supernatant from Crohn's disease patients: insights into potential pathogenic role of the microbiome;" Huang, "The respiratory microbiome and innate immunity in asthma;" Van Praet, "Commensal microbiota influence systemic autoimmune responses;" among many, many others.

[13] For the best overview how immunology construes 'self', see Tauber, *Immune Self: Theory or Metaphor*.

[14] The following account summarizes my longer argument in my *A Body Worth Defending: Immunity, Biopolitics and the Apotheosis of the Modern Body*.

[15] Fauvel, *Le Choléra*, 281.

[16] Metchnikoff's focus on cellular immunity comes back into vogue in the second half of the twentieth century when visualizing technologies revealed the existence of T- and B-lymphocytes, whose role in HIV/AIDS proved so central. Today even Metchnikoff's focus on phagocytes (macrophages) appears to have been prescient, as new studies foreground the way "innate immunity" centrally participates in inflammatory processes. The best survey of immunology remains: Silverstein, *A History of Immunology*.

[17] Pololsky and Tauber, *The Generation of Diversity: Colonal Selection Theory and the Rise of Molecular Immunology*, 19-57.

[18] On the history of humoral immunology and its focus on immunochemistry, see Mazumdar, *Species and Specificity: An Interpretation of the History of Immunology*.

[19] Jerne, "The Natural-Selection Theory of Antibody Formation."

[20] The theory is currently supplemented by the notion that in neo-natal life specific T-regulatory cells are generated that inhibit autoimmune illnesses and sustain self tolerance by modulating those self-reactive T-cells that escape pre-natal deletion in the thymus.

[21] Burnet. "A Modification of Jerne's Theory of Antibody Production using the Concept of Clonal Selection."

[22] Burnet, "A Modification of Jerne's Theory," 119.

[23] Burnet, "A Modification of Jerne's Theory," 121.

[24] Lewis and Short**,** *A Latin Dictionary*.

[25] This aspect of the theory developed in order to account for what is now

considered acquired immune response rather than innate immune response. Today it is clear that certain aspects of the immune system (macrophages in particular) do respond to self insofar as the clear effete or damaged cells and molecules. Matzinger's danger theory evolved in part to account for this fact.

[26] In this sense, Burnet's adoption of tolerance to describe self as that which does not elicit immunological response recapitulates a classic precept of liberal political philosophy, first articulated by John Locke in the second edition of *An Essay Concerning Human Understanding* (1690). In the chapter "Of Identity and Diversity," Locke argued that the personal identity (from the Latin *identidem*: repeatedly, several times, often, now and then, at intervals, ever and anon; continually, constantly, habitually) persists through and despite diversity (which he refers to as 'constantly fleeting particles of matter'). The famous crux of Locke's thesis rests on the continuity of memory: so long as we remember ourselves as our 'selves' we remain the same person. Locke's argument primarily concerned legal and moral responsibility (he states 'person is a forensic term'), nevertheless his argument has underwritten numerous theories of the self –including Sigmund Freud's–over the past three hundred years. Not surprisingly then following the triumph of Burnet's Clonal Selection Theory, immunology foregrounded the question of 'immunological memory' as one of its key concerns.

[27] Burnet, "Auto-immune Disease: I. Modern Immunological Concepts," 645.

[28] Burnet, "Auto-immune Disease: I. Modern Immunological Concepts," 645.

[29] De Beauvoir, *The Second Sex*, xxiii.

[30] Burnet, "Auto-immune Disease: I. Modern Immunological Concepts," 645.

[31] Root-Bernstein, "Antigenic Complementarity in the Induction of Autoimmunity: A General Theory and Review," 274.

[32] Gilbert, Sapp and Tauber, "We Have Never Been Individuals."

[33] Given the increasing number of aporia that characterize the reigning immunological dogma, the paucity of immunological alternatives to the interlocking oppositions of self: not-self and friend: enemy seems surprising, not to mention the extreme hostility that these few alternatives generate among the immunologically indoctrinated. Matzinger's 'danger theory' remains the most robust of the alternative.

[34] On the philosophical significance of folding, see Deleuze. *The Fold: Leibniz and the Baroque*.

[35] Varela, "Organism: a meshwork of selfless selves," 85.

[36] "Immunity does not merely guard the body against other hostile organisms in the environment; it also mediates the body's participation in a community of 'others' that contribute to its welfare" see Gilbert, Sapp and Tauber, "We Have Never Been Individuals," 333.

[37] Simondon, *L'Individuation à la Lumière des Notions de Forme et d'Information*. This text (re)presents Simondon's 1958 dissertation, which was subsequently published in two parts. The citations used here appear in the second published volume: *L'Individuation Psychique et Collective*.

[38] Simondon, *L'Individuation à la Lumière des Notions de Forme et d'Information*, 13.

[39] Simondon, *L'Individuation à la Lumière des Notions de Forme et d'Information*, 17.

[40] Metchnikoff, "A Yeast Disease of Daphnia: A Contribution to the Theory of the Struggle of Phagocytes against Pathogens," 193.

Bibliography

Burnet, Frank MacFarlane. "A Modification of Jerne's Theory of Antibody Production using the Concept of Clonal Selection." *Australian Journal of Science*, 20:3 (1957): 67-69 (reprinted in *CA—A Cancer Journal for Clinicians,* 26:2 (1976): 119–121).

Burnet, Frank MacFarlane. "Auto-immune Disease: 1. Modern Immunological Concepts." *British Medical Journal*, 2:5153 (1959): 645–650.

Burnet, Frank MacFarlane. "Auto-immune Disease: 2. Pathology of Immune Response." *British Medical Journal*, 2: 5145 (1959): 720–725.

Burnet, Frank MacFarlane. *Self and not-self; cellular immunology, book one*. London: Cambridge University Press, 1969.
Burnet, Frank MacFarlane. *The Clonal Selection Theory of Acquired Immunity*. London: Cambridge University Press, 1959.
Bussone, Guillaume, and Luc Mouthon. "Autoimmune manifestations in primary immune deficiencies." *Autoimmunity Reviews*, 8:4 (2009): 332–6.
Carneiro-Sampaio, M., and A. Coutinho. "Tolerance and autoimmunity: lessons at the bedside of primary immunodeficiencies." *Advances in Immunology*, 95 (2007): 51–82.
Cohen, Ed. "My Self as an Other: On Autoimmunity and 'Other' Paradoxes." *Medical Humanities*, 30:1 (2004): 7–11.
Cohen, Ed. *A Body Worth Defending: Immunity, Biopolitics and the Apotheosis of the Modern Body*. Durham, NC: Duke University Press, 2009.
Beauvoir, De. S. *Simone The Second Sex*. Trans. H.M. Parshley. New York: Vintage, 1980.
Deleuze, Gilles. *The Fold: Leibniz and the Baroque*. Trans. Tom Conley. Minneapolis: University of Minnesota Press, 1992.
Ehrlich, Paul. *Studies in Immunity*. Trans. Charles Bolduan. New York: John Wiley, 1910.
Fauvel, Antoine. *Le Choléra: Étiologie et Prophylaxie, Origine, Endémicity, Transmissibilité, Propogation, Mesures d'Hygiène, Mesures de Quarantaine et measures Spéciales a Prendre en Orient Pour Prévenir de Nouvelle Invasions de Choléra en Europe*. Paris: J.-B. Ballière, 1868.
Folwacznya, Christian, et al. "Crohn's disease: an immunodeficiency?" *European Journal of Gastroenterology & Hepatology*, 15:6 (2003): 621-626.
Foucault, Michel. *Leçons sur la volonté de savoir. Cours au Collège de France, 1970–1971*. Paris: Gallimard, 2012.
Gilbert, Scott, Jan Sapp, and Alfred Tauber. "We Have Never Been Individuals." *Quarterly Review of Biology*, 87:4 (2012): 325–341.
Grateau, Gilles, et al. "Autoinflammatory conditions: when to suspect? How to treat?" *Best Practice & Research Clinical Rheumatology*, 24 (2010): 401-411.
Huang, Yvonne. "The respiratory microbiome and innate immunity in asthma." *Current Opinion in Pulmonary Medicine*, 21:1 (2015): 27–32.
Irie, Junichiro and William Ridgway. "A Modular Theory of Autoimmunity." *Keio Journal of Medicine*, 54:3 (2005): 121–6.
Jerne, Niels. "The Natural-Selection Theory of Antibody Formation." *Proceedings of the National Academy of Sciences*, 41:11 (1955): 849–857.
Johnson, Denise et al. "Epidemiology and Estimated Population Burden of Selected Autoimmune Diseases in the United States." *Clinical Immunology and Immunopathology*, 84: 3 (1997): 223–243.
Jullien, François. "Did Philosophers Have to Become Fixated on the Truth?" *Critical Inquiry*, 28:4 (2002): 803–24.
Kanazawa, Nobuo, et al. "Autoimmunity versus Autoinflammation – Friend or Foe?" *Wiener Medizinische Wochenschrift*, 164 (2014): 274–277.
Kastner, Daniel L., et al. "Autoinflammatory Disease Reloaded: A Clinical Perspective." *Cell*, 140 (March 19, 2010): 784–790.
Lehman, Heather K. "Autoimmunity and Immune Dysregulation in Primary Immune Deficiency Disorders." *Current Allergy & Asthma Reports*, 15:9 (2015): 53.
Lewis, Charlton T. and Charles Short**,** *A Latin Dictionary*. Available online http://www.philolog.us (accessed December 5, 2015).
Locke, John. *An Essay Concerning Human Understanding*. 2nd edition. 1690. http://www.gutenberg.org/cache/epub/10615/pg10615-images.html (accessed December 5, 2015).
Mackay, Ian. "Autoimmunity since the 1957, clonal selection theory: a little acorn to a large oak." *Immunology and Cell Biology*, 86:(2008): 67–71.
Maggadottir, Solrun M. and Kathleen E. Sullivan. "The intersection of immune deficiency and autoimmunity." *Current Opinion in Rheumatology*, 26:5 (2014): 570–578.
Marks, Daniel J. B., et al. "Crohn's Disease: an Immune Deficiency State." *Clinical Reviews of Allergy and Immunology*, 38 (2010): 20-31.
Masters, Seth L., et al. "Horror Autoinflammaticus: The Molecular Pathophysiology of Autoinflammatory Disease." *Annual Reviews in Immunology*, 27 (2009): 621–68.

Mazumdar, Pauline. *Species and Specificity: An Interpretation of the History of Immunology*. New York: Cambridge University Press, 1995.
Meelu, Parool, et al. "Impaired innate immune function associated with fecal supernatant from Crohn's disease patients: insights into potential pathogenic role of the microbiome." *Inflammatory Bowel Diseases,* 20:7 (2014): 1139-46.
Metchnikoff, Elie. "A Yeast Disease of Daphnia: A Contribution to the Theory of the Struggle of Phagocytes against Pathogens." In *Three Centuries of Microbiology*, eds. Hubert A. Lechevalier and Morris Solotorovsky, 193. New York: Dover, 1974. [The original appeared in *Archiv fuür pathologische Anatomie und Physiologie* 96 (1884): 178–93.
Moran, Carthage, Donald Sheehan, and Fergus Shanahan. "The small bowel microbiota." *Current Opinion in Gastroenterology*, 31:2 (2015): 130–6.
Peng, Jian, et al. "Long term effect of gut microbiota transfer on diabetes development." *Journal of Autoimmunity,* 53 (2014): 85-94.
Pololsky, Scott, and Alfred Tauber. *The Generation of Diversity: Colonal Selection Theory and the Rise of Molecular Immunology*. Cambridge, MA: Harvard University Press, 1997.
Prescott Atkinson, Thomas. "Immune deficiency and autoimmunity." *Current Opinion in Rheumatology*, 24:5 (2012): 515–21.
Raedler, Diana, and Bianca Schaub. "Immune mechanisms and development of childhood asthma." *The Lancet Respiratory Medicine*, 2:8 (2014): 647–56.
Root-Bernstein, Robert. "Antigenic Complementarity in the Induction of Autoimmunity: A General Theory and Review." *Autoimmunity Reviews*, 76:5 (2007): 272–277.
Root-Burnstein, Robert, and De Kisa Fairweather. "Complexities in the Relationship between Infection and Autoimmunity." *Current Allergy and Asthma Report*, 14 (2014): 407.
Silverstein, Arthur. "Horror Autotoxicus versus Autoimmunity: The Struggle for Recognition." *Nature Immunology*, 2:4 (2001): 279–281.
Silverstein, Arthur. *A History of Immunology*. San Diego, Calif.: Academic Press, 1989.
Simondon, Gilbert. *L'Individuation à la Lumière des Notions de Forme et d'Information*. Grenoble: Èditions Jérome Millon, 2005.
Simondon, Gilbert. *L'Individuation Psychique et Collective*. Paris: Aubrier, 1989.
Tauber, Alfred. *Immune Self: Theory or Metaphor*. New York and Cambridge: Cambridge University Press, 1994.
Touitou, Isabelle. "Inheritance of autoinflammatory diseases: shifting paradigms and nomenclature." *Journal of Medical Genetics*, 50 (2013): 349–359.
Tsumiyama, K., Y. Miyazaki, and S. Shiozawa (2009) "Self-Organized Criticality Theory of Autoimmunity." *PLoS ONE*, 4:12 (2009): e8382.
Van Praet, Jens. "Commensal microbiota influence systemic autoimmune responses." *EMBO Journal*, 34:4 (2015): 466–74.
Varela, Francisco. "Organism: a meshwork of selfless selves." In *Organism and the origins of self*, edited by A Tauber, 79–107. Boston: Kluwer Academic Publishers, 1991.
Vernant, Jean-Pierre. *Myth and Thought among the Greeks*. Trans. Janet Lloyd and Je Fort. New York: Zone, 2006.
Yao, Q. and D. E. Furst. "Autoinflammatory diseases: an update of clinical and genetic aspects." *Rheumatology*, 47 (2008): 946–951.

Ed Cohen teaches Modern Thought in the Department of Women's and Gender Studies at Rutgers University. His most recent book is *A Body Worth Defending: Immunity, Biopolitics and the Apotheosis of the Modern Body* (Duke University Press, 2009). He is currently finishing a new book *Shit Happens: Ruminations on Illness and Healing*. For more information check his websites: www.healingcounsel.com and http://womens-studies.rutgers.edu/faculty/core-faculty/122-ed-cohen. Email: edcohen@rci.rutgers.edu.