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Immunology and Population Health: Collaboration without Convergence

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Abstract

Immunology is a notoriously complex field with distinct concepts and terminology. Yet immunologists regularly and effectively collaborate with other researchers, notably clinicians and experts in population health. How does such "collaboration without convergence" work? This paper offers an answer. Immunology exhibits three features that support collaboration in the absence of major consensus on theories, methods, or concepts. These are a multifaceted target of inquiry, therapeutic aspirations, and a clear interdisciplinary pathway. Building on these features, I sketch a general account of "low-effort interdisciplinarity" and connect this result to recent work on population health.

1. Introduction

The COVID-19 pandemic has brought ideas about immunity and its absence into the mainstream: "Neutralizing antibodies," "breakthrough infection," and "receptor-binding domain" are now familiar terms. Yet the science of immunology remains a closed book for most scientists and the general public alike. In subject matter, terminology, and concepts, immunology is isolated from other life sciences. Immunologists aim to understand the biochemical and physiological mechanisms underlying immune phenomena. But the concepts they use in so doing are distinctive and esoteric. The immune system includes a menagerie of different immune cell types, entangled molecular signaling pathways, elaborately orchestrated immune responses, and host-disease interactions. In one practitioner's words, immunologists speak "a strange language that takes a long time to learn".[1] To some extent, of course, every specialized field has a distinctive vocabulary and subject matter. The difference is one of degree. Immunology has a reputation of being inscrutable, impenetrable to outsiders. Science writer Ed Yong captures this with a joke:

[1] Arabella Young, personal communication, March 1, 2022.

> An immunologist and a cardiologist are kidnapped. The kidnappers threaten to shoot one of them, but promise to spare whoever has made the greater contribution to humanity. The cardiologist says, "Well, I've identified drugs that have saved the lives of millions of people." Impressed, the kidnappers turn to the immunologist. "What have you done?" they ask. The immunologist says, "The thing is, the immune system is very complicated. . . . " And the cardiologist says, "Just shoot me now." (Yong 2020)

The joke is that "[i]mmunology confuses even biology professors who aren't immunologists" (Yong 2020).[2]

Given its conceptual isolation, one would expect immunology to be a science apart. Its subject matter is famously complex, vocabulary unfamiliar to most biologists, and central theoretical notions have few counterparts in other scientific fields. Pandemic-induced vocabulary spread notwithstanding, immunological ideas and theories aren't broadly understood. And yet, immunologists regularly and effectively collaborate with researchers from other fields: other laboratory sciences, areas of clinical medicine (infectious disease, cancer research, etc.), and population health sciences such as epidemiology. During the ongoing COVID-19 pandemic, immunologists responded effectively to epidemiological data and vice versa. These exchanges contributed to speedy development of highly effective and safe COVID-19 vaccines.[3] Although immunology was just one component of these efforts, its role was crucial. Scientific editorials and commentaries from April 2020 onward reflect this:

> The vaccine quest makes it necessary for researchers to answer questions about how the body's immune system responds to the virus. (*Nature* Editorial Board 2020, 473)

> The teams of researchers scrambling to develop a coronavirus disease 19 (COVID-19) vaccine clearly face some big challenges, both scientific and logistical. One of the most pressing: understanding how the immune system interacts not only with the pathogen but with the vaccine itself. (Peeples 2020, 8218)

Immunology continues to partner with other fields in addressing various pandemic-related issues. For example, addressing the problem of waning immunity after vaccination or infection, requires both immunological and epidemiological study. The latter is needed to clarify the phenomenon (extent of waning in human populations, relevant demographic correlates); the former to characterize cell, physiological, and molecular mechanisms responsible for waning immunity. Another focus of joint research is dynamics and risks of reinfection with the same SARS-CoV-2 strain.[4] Among viruses generally, reinfection with the same strain within a few months is unusual. But the phenomenon is seen with some strains of common cold coronavirus. To understand

[2] Yong attributes the joke to Jessica Metcalf, a Princeton evolutionary ecologist.

[3] The SARS-CoV-2 vaccine story is too complex and multifaceted to capture here. Other sectors of society than scientific research were centrally involved, e.g., businesses, governments, and regulatory agencies.

[4] Examples from Vicente Planelles, personal communication, March 15, 2022.

this aspect of COVID-19, integrated epidemiological and immunological studies are needed. More generally, drug screening projects routinely integrate contributions from immunology, clinical medicine, chemistry, and pathology.[5] Other examples abound.

To sum up the situation, immunologists collaborate often and effectively with other scientists who remain largely ignorant of that field's terminology, main concepts, theories, and methods.[6] Most philosophical discussions of interdisciplinary or interfield collaboration emphasize the need for ongoing communication and exchange of knowledge on both sides (e.g., Boon and Van Baalen 2019; O'Rourke et al. 2016). However, the example of immunology suggests that, in some cases, interdisciplinary research doesn't require extensive communication, knowledge exchange, or mutual understanding. I'll refer to this form of research practice as collaboration without convergence (CWC).[7] My goal here is to articulate conditions that enable or facilitate CWC. Section 2 identifies three features of immunology that do so: a multifaceted target of inquiry, therapeutic aspirations, and a clear interdisciplinary pathway. Section 3 extrapolates these features to a general account of "low-effort interdisciplinarity," centered on norms of openness, outreach, and limited contact.[8] Section 4 relates these ideas to recent work on epistemic humility and population health. Section 5 concludes.

2. Three features

Immunology exhibits least three features that facilitate CWC. I discuss each in turn. The first concerns immunology's overall target of inquiry: the immune system.

2.1 Multifaceted target of inquiry

Immunology as a scientific field is loosely unified around the concept of the *immune system*.[9] That system is notoriously complex. It spans multiple scales of biological organization, from molecules to whole organisms.[10] At each scale, the immune system produces or constitutes a variety of biologically significant phenomena: allergy, autoimmunity, tolerance, chronic inflammation, responses to infection (bacterial, viral, parasitic, etc.), prospects for cancer immunotherapy, and more. The immune system as a focus for research is multifaceted. The overarching goal of immunology as a science is to understand and control that multifaceted system (Löwy 1992; Moulin 1989).[11] Individual immunologists, however, work on one facet of that system, not the whole system at once. In practice, immunology subdivides into a number of different specialties: tumor immunology; studies of neonatal exposure; hematopoiesis (blood

[5] For example, Ippagunta et al. (2018).

[6] This situation is not unique to immunology (see section 3).

[7] "Collaboration without consensus" suits just as well.

[8] Motivation and defense of this general account is beyond the scope of this article; see Fagan (under review). Here I claim only that the immunology case fits the general account, not that a single case adequately supports it.

[9] By "loosely unified," I distinguish this notion from traditional unity of science accounts.

[10] The term "scale" is used here in place of "level," the latter having been cogently criticized as vague and laden with unwelcome metaphysical baggage.

[11] For more on the history of concepts of the immune system, see references in Swiatczak and Tauber (2020).

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cell development (with further subdivisions by developmental pathway); B, T, and myeloid lineages are major foci; inflammation; autoimmunity (with further specialization as to organs; pancreas and brain are major foci; lupus amounts to its own subspecialty); and various host-pathogen interaction individuated by pathogen (HIV, coronaviruses, etc.). Any one immunologist specializes in, at most, a few of these areas. Much immunological research is pathogen specific. This is because the details of an organism's immune response vary according to pathogen, and those details matter greatly for immunological explanations. Research teams (individual laboratories or subgroups within a laboratory) often focus on a single pathogen, human or mouse response to that pathogen, and ways to modulate that response to improve health outcomes.

Immunology's dispersed social organization is a good epistemic strategy. It is a truism that complex phenomena require multiple models to adequately understand, and the immune system is famously complex.[12] Immunology's social organization into subfields reflects this discipline-wide multiple modeling approach. Consequently, individual immunology researchers are members of a wider community (immunology) while working for the most part in smaller communities (subfields) on narrower, more focused topics (aspects of immunity, specific diseases, or both). This dual group membership tends to instill an attitude of epistemic humility among immunologists. No matter how advanced one's understanding and control of some aspect of immunity (say, mechanisms of tolerance and waning immunity), there is always more going on in the immune system than is covered by one's area of expertise. Immunology's social epistemic organization fosters a sense of individual scientists' work as contributing to a broader project, not of fully understanding the topic of inquiry using any single model. That is, immunologists tend to be aware of the limitations, incompleteness, and partiality of the explanatory and predictive models they construct.

2.2. Therapeutic aspirations

A second feature of immunology facilitating CWC is its medical orientation. In the United States, immunology departments and training programs are often located in medical schools, while a large proportion of research funding is through the National Institutes of Health. These contextual factors encourage the idea that immunology research should in principle have clinical applications. Of course, not all immunologists work on clinical projects or contribute to translational medicine. But the idea that clinical medicine is relevant to immunology, and that therapeutic benefits are a long-term goal for most immunology research, is a widely shared background assumption of the field. This therapeutic aspiration counteracts more insular tendencies encouraged by laboratory benchwork. As noted, individual immunologists perforce work on narrowly specialized topics: aspects of immunity and/or particular host-pathogen interactions. Much of this work uses mouse models (although engineered human cell lines are increasingly prominent alternatives). A standard research strategy is to construct a model of a human disease and immune response in a suitable strain of laboratory mouse. Such projects are both time and

[12] E.g., Mitchell (2009).

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labor intensive. The tinkering process of making a mouse disease model more detailed and realistic has no natural endpoint. Immunologists, like other bench scientists, often become absorbed in the intricate details of their particular model, tweaking its abilities to reproduce different more aspects of human disease and/or immunity. (One practitioner describes this as "go[ing] to ground on what's happening within this individual mouse.") Because immunology's main concepts and theories have no counterparts in other fields, this mode of laboratory practice tends to be "isolationist." The model becomes the main object of research, fostering an insular attitude and a tendency to ignore any information that doesn't directly bear on one's laboratory model.

Therapeutic aspirations counteract these insular, inward-looking tendencies. Many immunologists who work on mouse models endorse the norm that immunology research should extend beyond the laboratory to have clinical relevance. The normative aspect is explicit. As one practitioner puts it, "good immunology" applies not just to mice but also to human populations "in real life," and it's incumbent on "good immunologists" to connect their work to human well-being in some way or other.[13] The normative commitment bridges gaps with population studies of humans "in the field": population health sciences, epidemiology, and more. In this way, therapeutic aspirations give immunology an "outreaching" character, motivating connection with fields that directly impact human health.

2.3. Clear interdisciplinary pathway

This outreaching character is realized using a clear path from immunology research to studies of human populations.[14] Motivated by therapeutic aspirations, immunologists working on mouse models or in vitro human cells often seek to extend their findings to human patients. That extension involves a conceptual shift from individual organisms to populations, which brings immunologists into closer alignment with clinicians and population health scientists. Typically, immunologists work on mice or in vitro human cells to discover molecular and cellular mechanisms underlying immune phenomena within a single animal. As models of these mechanisms are painstakingly worked out in years of laboratory experimentation, immunologists are alert to the possibility that one or a few components might have clinical impacts for humans. This is a standard preclinical strategy: Identify one molecule within a mouse or in vitro immune mechanism that may function analogously in human patients. To find evidence supporting such an analogy, immunologists need to identify a relevant and sufficiently large human patient population with a mutation or otherwise altered expression of that molecule. This move prompts immunologists to conceptualize their experimental results in terms of populations, not only physiological mechanisms within a single animal. This in turn facilitates collaboration with clinical researchers to identify and collect data from relevant patient populations. Once a patient cohort is identified, clinical and other population studies are possible. This amounts to a simple, established path linking

[13] Vicente Planelles, personal communication, March 15, 2022.

[14] For reasons of space, I discuss only one such pathway here. There are in fact multiple pathways linking immunology with a range of human health fields. The one described here is prominent but not unique.

immunology to clinical research, epidemiology, and other population health fields. (With the rise of cancer immunotherapies, this pathway is increasingly well-traveled.)

The conceptual shift is from individual organisms to populations. Importantly, the link to clinical populations does not involve any distinctively immune phenomena, and discussions with clinicians and other population health experts can bypass the conceptual and terminological complexity for which immunology is notorious. The link to human population studies is through one or a few molecules, potential targets for therapeutic intervention.[15] In vaccine and drug development (at least in the United States), this pathway is instituted by regulatory requirements. For example, a prerequisite for US clinical trials is laboratory data supporting a mechanistic model of how a new pharmaceutical agent is thought to work: immunological studies on model organisms, nonhuman primates, and small-scale preclinical human studies. That is, immunology input is required for clinical efforts aimed at drug or vaccine development. The regulatory-industrial process thus imposes CWC, to some extent.[16] My point here is that individual immunologists in academic research settings travel a similar pathway *without* industry or regulatory mandates. Moreover, immunologists' participation in business-driven and regulated projects of vaccine or drug development is facilitated by the presence of the pathway described here. Many scientists, when offered the prospect of interdisciplinary research, reject it as a waste of their time. Immunologists however, for the reasons stated here, don't generally consider human population studies involving immune phenomena to be a waste of time. Instead, those studies can follow a simple pathway toward realizing the discipline's therapeutic aspirations.

3. Low-effort interdisciplinarity

Together, these three features—multifaceted subject matter, therapeutic aspirations, a simple interdisciplinary pathway—enable a notoriously abstruse and impenetrable discipline to effectively collaborate with other scientific and medical fields. The latter, importantly, needn't learn anything about immunology for these projects to go forward. CWC does not require ongoing interaction, agreement on key concepts, or even much knowledge beyond one's own area of expertise. The three features stem from immunology's own goals, subject matter, and work practices. So, there's no "external" or top-down institutional pressure involved either. All these characteristics contrast with mainstream views of interdisciplinary work. This section builds on the previous, proposing conditions for CWC as "low-effort interdisciplinarity."

Interdisciplinarity is broadly defined as "whatever relevant relationship between two or more disciplines or their parts" (Mäki 2016, 331). Bibliometric and sociological studies show several decades of increased interdisciplinary activity across the sciences (e.g., van Noorden 2015). Such projects are encouraged by top-down funding initiatives, notably aimed at complex "Grand Challenges" of climate and health. It is

[15] The penetration of business interests (especially pharmaceutical companies) into medical research raises a host of epistemic and ethical concerns. These issues are beyond the scope of this short paper. It is worth noting, however, that 'single-molecule' connections to clinical and population research have an epistemic role orthogonal to profit motive and other economic inducements encouraged by the current bench-to-pharmaceutical pipeline.

[16] Thanks to Robert Fujinami for this insight.

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widely thought (by policy makers and many scientists) that contributions from multiple disciplines are required to address complex problems, spur conceptual and theoretical innovation, and make scientific progress. Despite the popularity of its slogans among administrators and funding bodies, the road to successful interdisciplinary research is littered with obstacles. Interdisciplinary research is challenging and often fails (Jacobs and Frickel 2009; MacLeod 2018). Philosophical responses to this situation emphasize the need for communication and knowledge-exchange across disciplinary boundaries (e.g., Boon and Van Baalen 2019; O'Rourke et al. 2016). Low-effort interdisciplinarity, as characterized here, complements those accounts. Some interdisciplinary projects, I propose, require comparatively little discussion and knowledge-exchange among participants. This is not to say that no interaction is required ("low-effort" is not "no-effort"), nor that high-effort interdisciplinary projects are scientifically unimportant. Clearly they are. But CWC is also a feature of scientific practice, and so it's worthwhile to clarify conditions for its success. The immunology example suggests three conditions for low-effort interdisciplinarity: openness, directed outreach, and limited contact. Researchers acknowledge epistemic activities outside their own area of expertise, identify specific fields as relevant to their goals, and make limited, narrow connections with those fields. I'll unpack each of these ideas in turn.

Immunology's multifaceted target of inquiry (the immune system), alongside the discipline's social epistemic organization into related but distinct subfields of expertise, fosters an attitude of *openness* to contributions from other fields. Immunologists recognize that understanding the immune system demands contributions from outside their own specialized area, alongside their own. This attitude lowers barriers to interdisciplinary work. Recognizing that a task needs contributions beyond one's own area of expertise implies pluralism and tolerance of diversity—at least within the sphere of that interdisciplinary project. Contributors should each see their work as contributing to, but not wholly accomplishing, a project's overall aims. Recognizing this incompleteness requires some humility. Immunologists are accustomed to this, recognizing other subareas of immunology as legitimate and valuable though outside their own individual expertise. It's a further step to clinical research (and other fields) being so.

That brings us to the second condition. Immunology research is directed toward clinical outcomes; that orientation amounts to a disciplinary norm. Not only are immunologists open to "outside" contributions but also there's a particular direction where contributions are to be found. *Directed outreach* is a feature of immunology research. More generally, if a field's explicit goals involve another sphere (human behavior, ecological environments, virus populations, etc.), this motivates research that connects with those field(s). It's very common for scientific researchers to become absorbed in their own difficult technical specialties, treating other research areas as irrelevant and less epistemically valuable. Directed outreach counteracts this tendency: Research in another area contributes to a field's own goals, motivating efforts to engage it. Relatedly, directed outreach is an equalizer, in a sense. This is not to say that immunologists should award clinicians and other health experts a superior epistemic position, think of them as having the same expertise as immunologists, or as needing to gain expertise in immunology. Rather, directed outreach gives immunologists a standing reason to collaborate with clinicians and other health experts on projects aimed at benefiting human health.

The key attitude is that immunologists recognize those other fields as directly bearing on the goal of benefiting human health. That is, immunologists and members of those other fields have a common goal, and immunologists alone can't accomplish it. Recognizing this requires some humility—a key goal of the field cannot be accomplished without others' help. An implication of directed outreach is that clinicians and other population health experts (for example) have significant epistemic standing in relation to that goal.[17] One must recognize another field as contributing to a goal of one's own. So, methods and results in one or more other fields of research (inside or outside academia, scientific or otherwise) are relevant to one's own field's aims. The interdisciplinary (or interfield) connection is internally motivated. Sciences differ (over time and from one another) in the extent of outreach incorporated into their major aims. More insular fields are, plausibly, hampered in bringing about real-world changes, epistemic and practical, and fit the stereotype of ivory tower knowledge.

The third condition is the main contrast with traditional forms of interdisciplinarity: *limited contact*. Directed outreach motivates a connection with one or more other fields. Crucially, in CWC that connection is slight or narrow. That is, a pathway connecting research in one field (e.g., immunology) to another (e.g., clinical medicine, epidemiology) involves one or a few concepts or ideas, minimizing the need for transmitting knowledge across disciplinary boundaries. Little knowledge exchange is needed, apart from what's involved in the connecting path. This makes interdisciplinary work following such a pathway less arduous than more extensively integrative projects ("convergence research," in the parlance of the US National Science Foundation). Within a scientific field, there is a fair amount of common knowledge; background assumptions that ease and enable collaboration. But very little specialized knowledge is shared across fields unless to begin with those fields are closely related. Knowledge common within each is uncommon to the other: ways of acquiring and interpreting data, constructing models, crafting explanations.[18] In such cases, collaborative work is more likely to succeed if these differences are sidestepped. Interdisciplinary connections are narrowly focused, and therefore meet fewer obstacles due to interfield differences. All that matters is that the connection between fields fits smoothly into practices on both sides. Knowledge exchange is minimal, restricted to the connecting link.

To sum up, low-effort interdisciplinarity is characterized by three conditions: openness, directed outreach, and limited contact. These can be articulated as norms for this kind of collaborative work:

- *Openness*: acknowledge an epistemic role for other fields outside one's own specialty.
- *Directed outreach*: identify other fields contributing to goals of one's own field.
- *Limited contact*: interdisciplinary efforts should be narrowly focused.

[17] Explanatory imperialism is a defeater for directed outreach (see Mäki 2016).

[18] Of course, a new field of inquiry that develops from the juncture of earlier ones will, as part of that process, add to a store of common knowledge of the nascent field. But the problem at issue here is how such "interfield" perspectives can become established in the first place—or how explanatory models can be constructed without presupposing an interfield perspective (cf. Darden and Maull 1977).

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4. Epistemic humility and population health

Epistemic humility is implicated in two of three conditions for low-effort interdisciplinarity: openness and directed outreach. The concept is a focus of recent work on biomedical practice by Anita Ho and Sean Valles, among others. The main ideas are as follows. Full understanding of population health exceeds the capacities of any individual person or perspective: "No one has a firm grasp on the full scope of knowledge about a given population health case" (Valles 2018, 185). Consequently, health professionals (and other experts) should be committed to mutual collaboration and trust with patients (Ho 2011). Epistemic humility is the attitude associated with that commitment. Valles (2018) argues, further, that epistemic humility should be a guiding norm in studying the causes of population health and disease: "the thread that ties together the disparate strands of population health research and practice" (18).[19] Epistemic humility so understood rejects any hierarchy among disciplines (e.g., epidemiology as "the foundation of public health") as well as "dominance" by any single sector of society (e.g., government agencies). No single sector or discipline should be elevated over others in projects aimed at understanding and improving population health. Instead, each sector/discipline, and individuals working within them, should be epistemically humble in their efforts toward those ends. Efforts to engage patient perspectives in nonhierarchical ways are an important theme.

Immunology is not counted among the population health sciences, in these recent works. That's for good reason. Immunology is a laboratory bench science, not in the first instance concerned with human populations. However, as argued in the preceding text, immunology does have ties to population health research, realized in low-effort interdisciplinary projects characterized by CWC. This kind of interdisciplinary work has several commonalities with population health science as outlined in Valles (2018). For one, population health science is an inclusive, pluralistic research community spanning multiple fields and social sectors. Interdisciplinary collaboration is an important means of progress for such a community. Second, the target of inquiry—human population health and its causes—is a complex, multifaceted phenomenon. Epistemic limitations for understanding this target motivate humility as a guiding norm. The same holds for the immune system, as shown in previous sections. Third, epistemic humility is incompatible with epistemic hierarchies and other antipluralist approaches to science. This all fits well with the themes of CWC and low-effort interdisciplinarity. However, Valles, Ho, and others advocating epistemic humility for biomedical practitioners do not drill down into ways of implementing that norm. The account proposed here offers such an analysis: a finer-grained study of factors that encourage and can help institute epistemic humility in the way Valles and others envisage. Openness to outside contributions, directed outreach stemming from a field's aims and

[19] Valles defends a broad conception of health "as a life course trajectory of complete well-being in social context" (13). This developmental (entire life course) approach doesn't exclude individual physiological health but expands beyond it to include social determinants and factors. The breadth and scope of causes of population health and disease implies that no single discipline can cover them all: "[W]e each need to recognize our limitations as knowers, and moving forward in population health science requires humble and non-hierarchical collaborative relationships" (2).

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aspirations, and limited contact across disciplinary borders together lead to low-effort interdisciplinarity and CWC. Projects of this kind instill and benefit from epistemic humility, without making large epistemic demands of participating researchers or requiring external motivation.

There is one further way the account presented here bears on recent studies advocating epistemic humility in population health science. Although immunology is (rightly) not included in the latter, its aptitude for CWC makes it a promising partner for Valles's socially engaged philosophical efforts. Immunologists do not have the exact same grounds for epistemic humility as population health scientists. But their field occupies a similar pro-collaborative space. Immunologists are potentially very good partners in the broader scheme of population health science. Although they aren't (as such) population health researchers, immunologists do engage in collaborative activities with attitudes of epistemic humility—and without others having to learn much (or any) specialized immunological concepts, terminology, or methods. They are already motivated and interested in forging connections with clinical research. Extending these ties to include more causes of human population health could be very productive.

5. Conclusion

Immunology is a largely closed book to outsiders. Few outside the specialty are familiar with its subject matter and main concepts. But this impenetrability doesn't stop immunologists from collaborating widely and effectively with other bench scientists, clinicians, and public health experts. This situation motivates an account of CWC. I've identified three features of immunological practice that facilitate CWC and used these to sketch more general conditions for low-effort interdisciplinarity. The latter is, plausibly, widespread in life and medical sciences, although I've not argued for that here. Low-effort interdisciplinarity requires openness, directed outreach to another field, and a limited but substantive connection between that field and one's own. Failure to meet these conditions indicates either a lack of epistemic humility or of internally motivated, clear connections to other fields. The former can in principle be inculcated as an aspect of scientific practice, for example, by making explicit the limits of models in any given scientific field. It is a truism that any model is partial and incomplete. Such limitations afford opportunities for connecting with other fields using CWC. This kind of interdisciplinary work requires less effort than more deeply integrative projects, the latter being labor intensive and beset by many challenges. Low-effort interdisciplinary projects don't require learning another field's key terms and concepts—only enough to traverse a clear interdisciplinary pathway. This is how immunology can be both notoriously obscure and a collaborative partner with many fields.

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