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Mitochondrial Agency: Towards a Host/Guest Theory of Co-Immunity

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Abstract

The ways we conceptualize the immune system and its relationship to the body impacts not only the ways we conceptualize illnesses, both acute and chronic, but the ways we treat said illnesses and the ways we understand the ontology of illness and disease. This essay surveys the anti-imperialist feminist discourse on immunology and medicine in relation to illnesses, immunity, liberal humanism, and posthumanism. I seek to offer a new model of the immune system stemming from Sandra Harding's notion of "strong objectivity" and Jacque Derrida's reflections on hospitality towards what I call a "host/guest theory of immunity." I center the role of mitochondria in both immune responses, immune dysregulation, and autoimmunity and cancers, as well as the material inheritance and lineages of mitochondria to posit chronic illness in the bodies of women as collective phenomena passed through mitochondrial ancestry and stored in the bodily archive of the colonized body. Drawing on the fact that the existing models of immunity fail to capture the realities and ontologies of the generational and chronic illnesses of women of color, which I enter through the subject of Arab women, a new approach is necessary, one that stems from the realities and histories of sick bodies. I explore what can be gleaned from illness if we take seriously our grandmothers, mothers, and our mitochondria as agents of history, who exist long before we are even conceived, and what it could mean for us to be their guests.

Key Words

Arab feminism; autoimmunity; co-immunity; disability; feminist science studies

I have inherited a life in death at the hands of an autoimmune disorder from my maternal grandmother, who died just before my mother immigrated to the United States. Her death served as the catalyst for my mother's self-inflicted exile, a desire to forget, but as many scholars of history and trauma remind us, the past will always make itself known, haunting generations to come (Gordon & Radway, 2008; Hartman, 2007; Kondo, 2018; Overend, 2014; Singh, 2018). Afaf – Fifi, as she was called – lives on in my body in more ways than one. This woman who so intimately touches me every day in profound ways has passed her legacy of premature death down to me, and through this, a secondary legacy of survival by way of our mitochondria. If we are to take seriously Harding's strong objectivity, that research centering those who are traditionally left out of knowledge production only strengthens the standards of research, I cannot frame the inheritance of an unruly immune system and damaged mitochondria as a problem. Fifi's slow death, her rheumatic fever and chronic pain, when situated against the backdrop of the fall of Pan-Arabism, the Six-Day War, the rise of Zionist imperial expansion in the wake of British occupation, and colonization of Egypt are embodied histories stored in the archives of our shared mitochondria and immune systems.

In my case of autoimmunity, the healthy tissues being targeted are my joints and skin, a diagnosis of Psoriatic Arthritis (PsA). In my grandmother, Rheumatic Fever (RF) meant the healthy tissue that

her immune system targeted was her heart valves. While Fifi was one of the less than 0.3% of children who develop chronic RF in the wake of childhood strep, it was her multiple pregnancies that advanced the disease and its lethality (Texas Heart Institute, 2003). The stress of pregnancy on her body meant that while her heart was ripping itself apart from the inside, the fetus of my mother was developing, and inside that fetus were the eggs that would become half of me. As is noted in the growing body of disability and chronic illness narratives, encountering illness – both acute and chronic – changes one's relationship to the body, often eliciting feelings of betrayal, being kept hostage, and feeling confused and distant.[1] There is a split that occurs between body and self, 'my body' against 'me.'[2] I believe this split opens the door for incredibly generative (re)conceptualizations of self, other, the immune system, and our mitochondria. It is this split, the reconciliation of which is so often the desired outcome of treatment and therapies, that allows us to explore what it means to live alongside our grandmother's mitochondria, and potentially accept their invitation to exist relationally with one another. What might be possible if we do not conceptualize the body as housing our mitochondria, but instead as in relation to/with them, and vice versa?

Fundamental to the immune system, to which our mitochondria are integral, is the question of what it means to be a human. Is there really a self in opposition to an other? Are we active agents in our own environments or are we merely subjected to them? Is our fundamental molecular understanding of self-recognition pre-inscribed, or is it learned? Nowhere else in the body can these questions be explored. The immune system lies at the heart of philosophical modern and postmodern inquiries concerning social inequalities along the lines of class, race and gender, militarism and imperial expansion, and positive science, its failures, its limitations, and its political priorities. The immune system is a site for theorization the lines of class, race and gender, militarism and imperial expansion, and positive science, its failures, its limitations, and its political priorities. The immune system is a site for theorization embodied anti-colonial archive preserving a subaltern history which houses me, and I it, then I suggest that a *Host/Guest* model of immunity might better capture its complex entanglements.

Mitochondrial Roles in Immunity and *Anarkhê*

We may have all learned in primary school that the mitochondria are the powerhouse of the cell. These organelles lie inside every cell working to convert the oxidation of food into energy for our cells and bodily systems to function. However, they are so much more. Mitochondria are key agents in our immune responses, they are also responsible for the communication between and across systems.

Mitochondria also carry with them a distinct genetic ancestry and lineage which they store within our cells. They are, themselves, descendants of bacteria incorporated into our cellular and bodily processes (Lionaki et al., 2015). It is precisely this distinct genetic ontology that makes them hyper-susceptible to mutations, which I concur with previous research are often caused by environmental factors and social conditions (Clayton, 2021). Their distinct genome, *mitochondrial DNA*, is maternally inherited through lineage spanning centuries, some theorists even putting forth the idea of a singular "mitochondrial Eve" (Lionaki et al., 2015; Ayala, 1995). We inherit identical mitochondria from our grandmother, who inherited them from her grandmother, who inherited it from her grandmother, and so on–identical copies duplicated, passed down through generations. Epigenetically, however, as environmental justice, trauma studies, post-humanist and feminist science studies have demonstrated, nothing biological is divorced from the social.[3] Every part of that which comprises us as an ecosystem is subject to environmental changes, mitochondria included. The political conditions that we are subjected to become encoded in our DNA(s), and in some cases, embodied through mitochondrial dysregulation, and inefficient mitophagy (the disposal of dead or damaged mitochondria) or autophagy (the disposal of dead or damaged cells.

Medicine, immunology, and biology are attempting to concretize the connections between the mitochondria and idiopathic and inherited illnesses of the immune system, locating mitochondrial dysfunction as one of the consistent throughlines across illnesses like cancers and autoimmunity. Mitochondrial dysregulation is an integral agent in the body's inflammatory responses, both generative

and degenerative (Green 2011). It is not a stretch to suggest that, on a cellular level, survival mechanisms as well as autophagy of the body are passed down alongside, and possibly through, the mitochondria (Auxémery, 2012). Mitochondria remember how to survive conditions of slow death, and hold the memories of the traumas and violence experienced in our great-grandmothers, grandmothers, and mothers. According to Derrida, through repetition of indexing, categorization, storing, and circulation, the colonial archive becomes a place of *consignation*, the place where things are not only gathered, but entrusted to be kept. The relationship of the colonized body to the colonial archive is one of haunting, compelled by the death drive, in this case the urge to destroy the corpus of the archive. Our mitochondria embody this process through their own death drive, destroying the bodies that host them. This *Thanatos*, fueled by anger destined to compulsively repeat and relive that which undoes the self, exists in opposition to the *Eros*, the generative drive invested in preservation and life (Derrida, 1998). The violence that the host body of the mitochondria are subjected to are compulsively repeated and re-lived through generations by way of autoimmunity, the literal self-destruction of the body.

This process of self-destruction is the necessary *anarkhê* that shadows *arkhê*, the anarkhê that destroys in silence, "never leav[ing] any archives of its own. It destroys in advance its own archive, as if that were in truth the very motivation of its most proper movement" (Derrida, 1998). This is the trace. The colonized body in the archive engages in its own This is the trace. The colonized body in the archive engages in its own destructive death-drive against its confinement, an anti-colonial reckoning. The mitochondria of the colonized body are, through repetition, indexing, categorization, storing, and recirculating of illness, leaving their own historical trace of *life-in-death* under subjugation. Understanding the necropolitical ecosystems of which our bodies, cells, and organelles are members means taking seriously time, empire, trauma, and embodied memories as parts of those ecosystem-entanglements. For if we are confined within a necropolitical system that, as Mbembe outlines, marks our bodies for premature death, overexposed to the harshest conditions as colonized bodies, then these are the conditions that have occupied the project of mitochondrial consignation (Mbembe, 2011). Mitochondrial Thanatos, dysregulation, is the trace of these histories repeating themselves, recirculating the death through generations.

Mitochondrial mitophagy, the self-destruction of old and damaged mitochondria, is activated under stress, and mitochondria under conditions of chronic stress are subjected to quicker and premature mitophagy as they accumulate the free radicals responsible for the activating transcription factor (ATSF-1) which contain a specific genomic sequence that targets mitochondrial DNA, forever altering the gene expressions that we inevitable inherit (Nargund et al., 2012). Put simply, when we are exposed to conditions of stress, the genes of our mitochondria are subjected to mutations that lead to the death of the organelle, and have the potential to damage the body that they are passed down to (Salim, 2012). Furthermore, the altering of mitochondrial DNA expression can cause degenerative diseases as well as impact our immune system's ability to properly dispose of dead or damaged cells, as is the case in cancers. In the case of autoimmunity, altered or damaged mitochondria become catalysts to an overactive immunological inflammatory response, as the cellular autophagy targets healthy tissue (Rai, 2021). In my case, I need a model of the immune system that understands this process as part of a larger embodied history, not an anomaly or a danger, but the reckoning and survival of a history that no longer allows itself to be contained.

Feminist Approaches to Immunity

Feminist Science scholar Sandra Harding puts forth a call for *strong objectivity* when engaging in scientific knowledge production. For Harding this means starting research from the lives of women and is an expansion on her foundational contribution of standpoint theory to feminist studies (Harding, 1995). Questions of assumed objectivity in medical and biological research are well covered, including the inherent racism, sexism, ableism, transphobia, and imperial foundations and undercurrents of medical research are also explored thoroughly by scholars across the humanities and the STS fields. Feminist approaches to the immune system take up the same call: build a model of the immune system

that stems from the lives and realities of people assigned female at birth (AFAB), LGBT people, and poor communities, and their encounters with HIV/AIDS and other immunocompromised people, instead of relegating them to the margins of textbooks. Scholar Lisa Weasel troubles the existing *self/non-self* model of the immune system and offers an alternative approach, the *danger model*, which I seek to further trouble in this essay (Weasel, 2001). I offer a third model, a *Host/Guest* model, which expands on the concept of "co-immunity" to continue this genealogy (Bazin et al 2018).

In her essay, *Dismantling the Self/Other Dichotomy in Science: Towards a Feminist Model of the Immune System*, Lisa Weasel maps out different theories of immunity. The self/non-self theory asserts that the body learns which parts fall into the category of self and which do not through a series of infections and vaccines, an acquired immunity (Weasel, 2001). The recognition of the self becomes the parts of the body that are tolerated, while encounters with foreign or *non-self* parts trigger an inflammatory immune response. This theory presumes that there is an inherent self to be recognized, and that the self can only be known in opposition to an other. Elsewhere, Palestinian-born scholar Edward Said gives us the term orientalism to highlight the ways in which what we have come to know as 'the West,' civilized, modern, liberal, objective, built the essence of itself against the racialized Arab and Muslim other (Said, 1979). This self/non-self conceptualization of the immune system mirrors the kinds of racialized and gendered logics that inform modernity. However, Weasel notes this theory is troubled when looking at two specific biological processes. One of these processes is the lack of a triggered immune response in pregnant people towards their fetus, fetuses that are, by definition 'not self' on genetic levels. The second is autoimmune diseases. The self/non-self theory offers no explanations for why these two phenomena (both of which occur predominantly in cisgender women) unfold.

Weasel shifts, or re-orients us, towards a feminist alternative to this existing theory: the danger model. The danger model suggests an approach rooted less in liberal humanist frameworks that center autonomy and individuality of a biological citizen of a 'western' nation-state and instead argues that immunity is not achieved "on the premise of the body's need to identify and defend itself against foreign invaders but guided instead by an understanding of the body's need to recognize and respond to signals of danger, regardless of their origin" (Weasel, 2001, p. 32). She notes that this model comes out of a growing mound of evidence that the self/non-self model does not account for the realities of people's lives. Thinking back to pregnancy and autoimmune diseases we can see that whether it is a lack of immune response or an overactive one respectively, it is the perceived danger that guides the body's reaction, even if the source of danger originates in the same body. This model of immunity also highlights that acquiring immunity is a process that involves an entire network of bodily tissues, proteins, and fluid exchanges.

A similar concept exists elsewhere in theories of co-immunity. Co-immunity suggests that microbiota, specifically those in the gut, play active roles in the process of acquiring either immunity or tolerance to colonizing bacteria independent of the body's mechanisms of immunity. This post-humanist immunological theory accounts for the symbiotic relationships between the host body and its guest gut ecosystems, but a Host/Guest model of immunity extends this ecosystem to encapsulate mitochondrial organelles and the social histories encoded into mitochondrial DNA. This orientation away from one model towards another based off on the realities of peoples' (usually women's) lives, the recentering of the fluidity of science, and refusing narratives of mastery, allow for new perspectives to come to fruition and gain popularity and validity, or at least be entertained (which the danger model is widely not). This relational work benefits both feminist studies as well as the biological sciences.

We are given the energy required to sustain us in the present and mitochondria are agents of their own futurity while they store the history they subject us to. For women and colonized people, these histories are those of violence and survival ultimately contributing to the mitochondrial dysregulation that is responsible for generations of death and decay at the hands of our immune systems. Autoimmunity, if we use Weasel's danger model, occurs when our immune systems misread our own bodies as dangerous, and in cancers, fails to detect the danger

of the rapidly multiplying cells and tumors, but this is not the whole picture.

Mitochondria plays a significant role in setting the foundation of our immune system, and while the danger model attempts to account for the realities of those who are excluded from the self/non-self model, for the traumatized and colonized body, we need to step back and examine the conditions under which the dysregulated immune system is developed. In the case of autoimmunity – of which two of every three diagnoses are assigned to women or people AFAB and anecdotally impact every Arab woman I know – the strong objectivity must stem from these organelles. Mitochondria are now being recognized as critical agents in the biophysiological mechanisms of autoimmunity and chronic inflammation (Barrera, 2021). The gendered components to autoimmunity might hint to the centrality of mitochondria, and their maternal lineages (Di Florio, 2020).

A Host/Guest Model of Immunity: Alternatives to Danger and Self-Non-Self Models

I find myself wanting to shift away from existing models of immunity, even the feminist danger model, because I do not believe that the stress, trauma, and illnesses that the women in my family went through and passed down to me are dangers to myself. Simultaneously, I want to take co-immunity into the realm of post-humanist world-making. The disabilities and histories I have inherited are invitations to new ways of living and dying. Resilience, *sumood*, "*a constant revolutionary becoming*" (Meari, 2011. P. 1), strategic survival, and untimely deaths shaped the conditions of my arrival and ensure, in their own ways, a futurity in which the legacies of European colonialism and Orientalism that erase colonized histories are preserved. My family – our bodies – extend what Derrida calls "unconditional hospitality" towards the mitochondria that have made home in our cells (Derrida, 2000, p. 3. This invitation gestures to a family lineage and makes space for me and our mitochondria within the collective histories experienced by the generations of Arab women who came before me. Central to Derrida's reflections on hospitality is the conundrum of the fact that we do not truly know what hospitality is, we do not know what it means to welcome, and we do not know what it means to be welcome (Derrida, 2000, p. 6). He says:

> "Hospitality, if there is such a thing, is not only an experience in the most enigmatic sense of the word, which appeals to an act and an intention beyond the thing, object, or present being, but is also an intentional experience which proceeds beyond knowledge toward the other as absolute stranger, as unknown, where I know that I know nothing of him." (Derrida, 2000, p. 8)

The mitochondria inside me pre-date my own conception, their ancestry connecting hundreds of generations of women in my family, and it is this lineage that I am relationally entangled with/in. This lineage showed up at my doorstep, these mitochondria do not ask anything about me, they simply infected someone a long time ago, as bacteria, and made themselves essential. They aided in my development in utero and continue to contribute to my encounters with illness and infection, in exchange for a place to stay. And I do let them stay, host them. Unconditionally, and without a full understanding of what that even means, we exist in this dialectic experience that goes beyond knowledge of the other or the self. The rumblings of their rebellion only flare up and debilitate me when I am beyond the limit of my bodily or emotional capacity, reminding me to live slowly and intentionally and relationally, reminding me that this body is not mine to ignore, and deprive, because it is host to more than just me. I have an ethical responsibility of relationality to move differently because of the assemblage of disability, immunity, and the ecosystems inside this body. This is the potential of an alternative understanding of immunity. A Host/Guest model might allow for an anti-colonial, post-humanist relational exchange between the assemblages that comprise immunity.

The task of hospitality requires the relinquishing of mastery over the dwelling – be it a home, a nation-state, or a body. Derrida continues, "the master in his own home, the host*, can only accomplish his task as host, that is, hospitality, in becoming invited by the other into his home, in being welcomed by him, whom he welcomes, in receiving the hospitality he

gives" (Derrida, 2000, p. 9). The host must relinquish control akin to the drive for domination and mastery that modernity demands of its subjects by extending hospitality to the guest, similar to how mitochondrial DNA relinquishes control, mutates in the face of stress, becomes ill, and embodies the violences of the conditions under which it lives. They preserve the memories of those conditions and pass them down through the lineages of their most precarious bodies. An ontology of illness – in my case autoimmunity – did not begin with me. It may have been triggered by the stress and trauma this life subjected me to, but it existed outside of any self, and the inheritance is the invitation. If I am the Host, then these illnesses and mitochondria are Guests, and the task of hospitality lies in relinquishing mastery over this body and illnesses. The relationship necessitated by this invitation is a crip one, one that recognizes illness and debility and re-structures life to accommodate them. Rather than chasing cure, erasing, or suppressing illnesses and their symptoms, the task of hospitality is a world-making that resists compulsory able-bodiedness.[4] What might the treatment of autoimmunity look like if we understood it outside of the language of a scientific anomaly, requiring the suppression of an immune system leaving the body hyper-vulnerable to infections and organ failure.

Conclusion

At the heart of this preliminary exploration is the idea that mitochondria are agents of their own histories, and that we exist in a relationship of exchange and tension alongside one another. I welcome them, and in turn am welcomed, and enter the complex matrix of history, pain, illness, and premature death that are stored in the embodied archive and retrieved through illness. This exchange is not necessarily an easy one. It comes laced with loss, pain, isolation, frustration, helplessness, and at times the desire for death. Nonetheless, we must welcome the invitation for exchange. Through receiving the hospitality that we are offered, or extending it, we engage in a process of anti-colonial and post-humanist worldmaking. This lies at the heart of a Host/Guest model of immunity. The histories inherited by way of illness are not dangerous, they are not non-self. They are the most intimate embodiment of our histories and the conditions of violence that permanently altered our bodily ecosystems. It is an acceptance of the fact that to live in a body that is destroying itself is not an anomaly but instead a perfectly rational consequence of colonial and imperial conditions.

Notes

1. See the work of Eli Clare, Christina Crosby, Audre Lorde, Susan Sontag, Leah Lakshmi Piepzna-Samarasinha, Edward Said, and Virginia Wolfe.

2. I draw heavily from Elaine Scarry's A Body in Pain to tease and complicate this distinction of self/body.

3. See the work of Need Ahuja, Ruha Benjamin, Rita Chiron, Eli Clare, Ed Cohen, Donna Haraway, Sandra Harding, Paul Kelton, Emily Martin, Natalia Molina, Nayan Shah, Priscilla Wald, Harriet Washington, among others.

4. A term coined by Robert McGruer, compulsory able-bodiedness is entangled with compulsory heterosexuality and other systemic institutions that create the rationales for valuing certain bodies at the expense of others. Living otherwise, living and dying queerly, opens space for modes of relation that rest outside of capitalism, colonialism, and ableism. I would expand this to include anthropocentrism as well.

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