RECERCA, REVISTA DE PENSAMENT I ANÀLISI, NUM. 27(1). 2022 ISSN electrónico: 2254-4135 – pp. 1-22
DOI: http://dx.doi.org/10.6035/recerca.5767

Theorizing immune inhibition and TNF inhibitors from the autoimmune

Teorizando la inmunoinihibición y la inhibición del factor de necrosis tumoral (TNF) en la autoinmunidad

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Article received: 15, february, 2021
Revision request: 24, april, 2021
Article accepted: 12, february, 2022

Ben Shimon, Ohad (2022). Theorizing inmune inhibition and TNF inhibitors from the autoimmune. *Recerca. Revista de Pensament i Anàlisi*, 27(1), pp. 1-22.
doi: http://dx.doi.org/10.6035/recerca.5767

Abstract

This article analyses the biochemical object of TNF inhibitors from the perspec-tive of living with an autoimmune disease. The author tries to tease out how the concept of immune inhibition is used in tandem with the biochemical object of TNF inhibitors to dominate in defining and narrating what health and disease, normal and pathological, cure and healing can mean in the context of autoimmune bodies. Specifically, and within the 'pathological' framework of autoimmune diseases, the pharmacological treatment of TNF (tumour necrosis factor) inhibition is designed to suppress the 'overly' active immune system, thus acting as a negative or suppressing biochemical agent aimed at putting the 'malfunctioning' immune system back in balance. As can be seen in the current conjuncture, TNF inhibitors officially —and governmentally— place those tak-ing them in a risk group, as they 'lower' their overall bodily immunity and make them more vulnerable to infectious diseases, while stabilizing their patho-logical, 'over'-immune uninhibited condition. Part personal narrative of being diagnosed with an autoimmune condition, part speculative autoimmune theory inspired by such a diagnosis, the article ultimately calls for a different form of embodiment that is neither negative nor affirmative, and yet is resistant even to itself.

Key Words: immunity, inhibition, governmentality, TNF inhibitors, autoimmune.

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Resumen

En este artículo se analizan los inhibidores del factor de necrosis tumoral (TNF) como objeto bioquímico desde la perspectiva de la vivencia con una enfermedad autoinmune. El artículo trata de desentrañar cómo el concepto de inmunoinhibición se usa junto con los inhibidores de TNF como objeto bioquímico para definir y narrar lo que puede significar la salud y la enfermedad, lo normal y lo patológico, la curación y la sanación en el contexto de cuerpos autoinmunes. En concreto, y dentro del marco *patológico* de las enfermedades autoinmunes, el tratamiento farmacológico de inhibición del TNF (factor de necrosis tumoral) está diseñado para suprimir el sistema inmunitario *demasiado* activo, actuando así como un agente bioquímico negativo o supresor destinado a reequilibrar el *mal funcionamiento* del sistema inmunitario. Como puede verse en la coyuntura actual, los fármacos inhibidores del TNF sitúan oficial —y gubernamentalmente— a quienes los toman en un grupo de riesgo ya que *rebajan* su inmunidad corporal global y les hace más vulnerables a enfermedades infecciosas, mientras que estabilizan su condición patológica de *sobreinmunidad* desinhibida. En parte narración de la experiencia personal de ser diagnosticado con una condición autoinmune, en parte teoría autoinmune especulativa inspirada por tal diagnóstico, el artículo en última instancia explora una forma de encarnación diferente que no sea negativa ni afirmativa y, sin embargo, sea resistente incluso a sí misma.

Palabras clave: inmunidad, inhibición, governmentalidad, inibidores de TNF, autoimune.

INTRODUCTION

TNF inhibitors are pharmaceutical drugs meant to suppress the excited and 'out of control' process of inflammation —also called a "cytokine storm" (Tisoncik et al., 2012)— that TNF causes in autoimmune diseases. TNF (tumour necrosis factor) is a type of a cell signalling protein (cytokine) that is expressed by a wide variety of immune cells in the process of inflammation. In this article I try to tease out how the concept of inhibition is used in tandem with the biochemical object of TNF inhibitors to dominate in defining what health and disease, normal and pathological, cure and healing can mean in the context of autoimmune bodies. In this context, I follow Beth Ferri's (2018) definition of the "autoimmune body" as a body in which "the immune system declares war on a part (or parts) of the body it no longer recognizes and attacks itself as if confronting a foreign, antagonistic, threatening other (or enemy)" (8). Problematically, as I will later develop in my analysis, it is hard to disentangle the disease that is 'harboured' within the autoimmune body from the diseased autoimmune body 'itself' as this involves complex —and at times paradoxical and self-harmful, rather than self-protective or self-sustaining— notions of agency that go against fundamental conceptions of modern personhood. This

ontological, epistemological, and methodological complexity is what drives my usage and understanding of the concept of the *autoimmune body* and *autoimmune condition* in this article.

Importantly, my theorization and analysis will depart from being methodologically situated in such an autoimmune body, inhabiting it, embodying it, and speaking from it *as*, rather than *with*, an autoimmune *condition*, after being diagnosed with or *conditioned by* an autoimmune disease in 2013. In other words, I theorize from an autoimmune methodological perspective "as an interpretive horizon, not an essential state" (11). In debt to Donna Haraway's paramount *Situated Knowledges* (1988), the scientific 'objectivity' I am grasping for is grounded in a feminist epistemology and objectivity that is limited by location and the situatedness of knowledge. To attend to the potential personal bias in theorizing from the vantage point of personal experience, I align myself again with Haraway: "it is precisely in the politics and epistemology of partial perspectives that the possibility of sustained, rational, objective inquiry rests" (584). It is surprising to testify to how potent and resonating Haraway's words are, even more than 20 years since its publication. I will therefore add one final beacon of light from *Situated Knowledges*:

> I am arguing for politics and epistemologies of location, positioning, and situating, where partiality and not universality is the condition of being heard to make rational knowledge claims. These are claims on people's lives. I am arguing for the view from a body, always a complex, contradictory, structuring, and structured body, versus the view from above, from nowhere, from simplicity (Haraway, 1988: 589).

Lastly, this article speculatively, yet insistently, is driven by an urge to epistemically refuse and refute a disembodied Cartesian rationality, in favour of "other and Other ways of knowing" (Rajan, 2021) and acting in the world. Here, my analysis is focused on problematizing how, once an ontological point of origin is identified or essentialized, this unnuanced ontology leads to a naturalized teleology of domination. In that sense, in the article I seek to challenge how, once a human body is defined as healthy or stricken by disease, normal or pathological, temporarily cured or chronically ill, the normative and prescriptive implications of what to ought to be done with this body rush in. Specifically, and within the framework of autoimmune diseases, the pharmacological treatment of TNF inhibition is designed to suppress the 'overly' active immune system, thus acting as a negative or suppressing biochemical agent aimed at putting the 'malfunctioning' immune system back in balance.

In that sense, I look at how a concept such as immune inhibition can lend itself to explore what it means to have a negative/positive, bad/good, pathological/normal immune response in autoimmune bodies.

Specifically, my exploration in this article departs from the concept of (biological, physiological, pharmaceutical) inhibition and how such a physiological disciplinary bodily form of inhibition can come to perform two completely opposing forms of immunity. As can be seen in the current conjuncture, TNF inhibitor drugs officially —and governmentally— place those taking them in a risk group as they 'lower' their overall bodily immunity and make them more vulnerable to infectious diseases, while stabilizing their pathological, 'over'-immune uninhibited condition. At the same time, the same official protocols leave those autoimmune bodies that do not take part in this pharmacological therapy outside the contours of officially labelled vulnerable risk groups. In that sense, the bodies that are not administered the pharmacological drug or medicine are inversely labelled 'naturally vulnerable' by the medication of TNF inhibitors they do not take. Simply put, the TNF inhibitor drug acts as an embodied and embodying process in the sense that it signifies and situates different bodies either as pharmacologically curable or naturally vulnerable. Additionally, what for a very general non-specific human body would mean a disciplinary, almost punishment-like practice or form of bodily intoxication, for other more specific autoimmune bodies, this form of inhibition can ambivalently produce two contrasting understandings of bodies and how these bodies have or do not have an ability to preserve and sustain.

To set this article's theoretical framework of analysis for the close reading of the object-concept of TNF inhibitor, I will depart from Georges Canguilhem's (1991) seminal work *The Normal and The Pathological* as a theoretical reference point. Following the theoretical background framework of this article, I will introduce the concept of inhibition through an autoimmune methodology and set it amongst the concepts of the katéchon, governmentality and mutation in order to distil from this a more specifically developed concept of immune inhibition. I will then use this concept of immune inhibition, as I develop it through an autoimmune methodology, in my object analysis of TNF inhibitors. Lastly, I will perform an object analysis of TNF inhibitors (and TNF) from which I try to tease out their critical potential in theorizing immunity and immune inhibition from an embodied and situated autoimmune perspective.

1. THE NORMAL AND THE PATHOLOGICAL

To theoretically frame my close reading of the object of TNF inhibitors I first examine some of the central concerns raised in the theoretical work of Georges Canguilhem (1991) on the concepts of the normal and the pathological. I will try to distil Canguilhem's account by comparing these concepts with other similar generative concepts such as disease, health, and cure/poison. Together, these concepts form the theoretical background upon which my analysis of the TNF inhibitor medication for autoimmune diseases rests. In synthesizing these concepts, I aim to extract a working definition of what a healthy state of the individual means, and then explore it further in tandem with the concept of inhibition as the main conceptual prism of this article.

Firstly, Canguilhem's understanding of what pathological and normal mean does not imply they are mutually exclusive in the sense that they are not opposites of each other. Thus, the sick individual is not a less healthy individual, nor is the healthy individual or state a standard of measurement of a sick individual with less illness. In other words, the normal and the pathological do not oppose each other in an equally symmetrical way. In that sense "disease is not a variation on the dimension of health; it is a new dimension of life" (Canguilhem, 1991: 186). Furthermore, for Canguilhem disease is a "positive, innovative experience in the living being [rather than] a fact of decrease or increase" (Canguilhem, 1991: 186) in an otherwise perfectly balanced healthy state. Importantly, the event of disease in the living body does not mark a categorically negative occurrence that the normal, healthy body must flee from. If anything, for Canguilhem the state of disease sets a criterion upon which the healthy body measures its healthy state. In that sense, disease is the standard or criterion from which "the healthy man" (200) can deduct "his capacity to overcome organic crises in order to establish a new order". Ultimately, "man feels in good health — which is health itself— only when he feels more than normal —that is, adapted to the environment and its demands— but normative, capable of following new norms of life" (Canguilhem, 1991: 200). This last formulation of "health itself" as being "more than normal" resonates well with Gilbert Simondon's formulation of the process of individuation that is at the root of the ontologically "overabundant" (Cohen, 2017: 39) individual; an individual who is driven by an innovative ongoing process of change and becoming, together with the demands for adaptation to/of its environment.

I now shift to what this "innovative experience in the living being" or creative "new dimension of life" (Canguilhem, 1991: 186) would mean not for the formulation of health, but of disease. In that sense, disease itself is also independently self-constituted as a creative, innovative, ever-changing and adaptive life force or, similar to Spinoza's formulation of the principle of the conatus as that which "strives to persevere in its being" (Spinoza, 1994: 159), with an agency of its own. Disease has its own process of evolving, mutating, and adapting to the current circumstances and environment in which it is present or said to be 'alive'. Thus, in Canguilhem's view —and as I will try to further problematize later in my reading of the object of the TNF inhibitor— when disease is misunderstood as lacking its own constructive and innovative conatus or 'life of its own', and is regarded as "[something] evil, therapy is given for a revalorization; when disease is considered as deficiency or excess, therapy consists in compensation" (Canguilhem, 1991: 275).

2. ANALYSING THE AUTOINMUNE BODY: A THEORETICAL PROPOSAL

2.1 Inhibition

My departure point for developing the concept of inhibition emerges from my personal experience of being diagnosed with an autoimmune disease in 2013. In the first few medical appointments I had when my disease broke out, I was offered a cocktail of various first line immunosuppressant corticosteroid drugs meant to suppress my entire overactive immune system. In the following months I struggled with my diseased bodily autoimmune symptoms, which included severe skeletal pain in my shoulders, upper back, and waist and pus-filled infectious formations on the skin of the palms of my hands and soles of my feet. When my condition did not seem to stabilize and after a few rounds of first line immunosuppressant corticosteroid treatments, the doctors offered me an experimental biological immunosuppressant. This treatment would involve a life-long treatment of weekly injections of the TNF inhibitor drug adalimumab (HUMIRA®) —currently the world's largest-selling pharmaceutical product—(Urquhart). At the moment, five such biological TNF inhibitors (Etanercept, Infliximab, Adalimumab, Golimumab, and Certolizumab Pegol) "and in total 25 drugs that inhibit or modulate the effects of TNF, are approved for clinical use by the Food and Drug Administration (FDA) and

European Medicines Agency (EMA) [...] another 151 TNF inhibitors are in the clinical pipeline" (Steeland, Libert and Vandenbroucke, 2018: 15). The difference between the first line corticosteroid immunosuppressant treatments and the experimental biological TNF inhibitor immunosuppressant treatment was that the latter selectively targeted —by inhibition— specific inflammation-inducing proteins (cytokines) in the immune system shown to be associated with the inflammation related to my disease, and the former were more generally suppressing my entire immune system. When I inquired about the nature of the pharmaceutical drug and its potential side effects, I was told that due to its inhibitory nature, those 'overly-active' proteins in my immune system would be inhibited in such a way that would put my body at higher risk of infection from a wide variety of infectious diseases, and could also potentially result in the development of certain types of cancers and possibly lead to death. In other words, the drug would act as a negatively suppressing biochemical agent by inhibiting the activity of certain cell signalling proteins (TNF) of my immune system, thus both putting my immune system 'back in balance', and at the same time, placing it at higher risk of becoming diseased once again.

To more specifically develop the concept of inhibition through an autoimmune methodology, I now look more closely at other 'related' concepts that might help accentuate the elements that interest me in the concept of inhibition itself. Here, I look briefly at the concepts of the katéchon, governmentality and mutation and how these, as they are developed by different thinkers, can come to inform my analysis of the concept of inhibition, which I will then put to work in my analysis of the object of TNF inhibitors.

2.2 Katéchon

The Katéchon is a Greek term meaning "the one who withholds" or the "force that holds back" (Virno, 2018: 20). As such a force or subject, the katéchon continuously and endlessly postpones or restrains the arrival of an 'evil' entity or a 'negative' state of affairs. In the case of theological-political discourse this has been the suspension or withholding of the moment in which the Antichrist would triumph over Christ. In the case of the social political order, the katéchon is that which would prevent, by postponement upon postponement, the eruption of the inherent chaos and disorder in modern society. Problematically, the notion of the katéchon has been used by various political philosophers to mean different and at times opposing things. For

some political philosophers and theorists (Hobbes, 1651; Schmitt, 2006), the katéchon comes to be embodied in the sovereign state as that which legitimately protects society by withholding and restraining from flaring-up the 'natural' violence that is inherent to society and thus needs to be tamed and controlled. The justification for this external form of suspension and inhibition of violence by the state is that society is incapable of withholding or restraining this violence on its own. In turn, for other political philosophers, such as Giorgio Agamben (2005), the removal of the katéchon as a restraining force would allow political thought to imagine social life beyond any political notions formulated along the 'logical' coordinates of sovereignty that protect society by violently controlling and restraining it.

In my reading of the concept of the katéchon I focus on its ability to function in two completely opposing or contradictory ways, while opening up to a possibility of not following either on this point of aporia. Instead of following the line developed by either biopolitical theorists such as Agamben or the political theories developed by Hobbes (1651) and Schmitt (2006), I will focus my analysis on the Italian philosopher Paolo Virno's (2008, 2018) reading of the katéchon. Later, when I put to work the concept of inhibition in analysing the object of TNF inhibitors, I will focus on the concept's ability to embody or encompass a sense of a double negation or an inhibition of inhibition that Virno's reading of the katéchon similarly embodies or encompasses.

In Paolo Virno's account, the 'evil' or 'violent' forces that humanity harbours within itself might well exist, but importantly —differently from Schmitt's account— they do not imply creating an external state sovereign power that is able to counter these negative forces (Virno, 2018: 21). Instead, Virno suggests understanding the human condition in its radical openness and incompleteness; an openness, which in the absence of any other ordering or controlling body or entity, also includes the possibility that it can be violent, 'evil' or destructive, even to itself. Here the katéchon comes to function as that 'magical' power within this open condition that can avoid or negate the negative state of affairs, but it does so not by affirming or preferring another state of affairs instead. The katéchon in that sense, as read by Virno, does not represent or justify an embodiment of the force that would counter any evil tendencies within society by delegating the need to restrain this force to an external power or authority; instead, it is able to restrain or withhold the 'evil' forces by keeping them at bay, close to home, without evoking the need to defeat or eliminate them. In building upon Derrida's (1981) concept of the pharmakon as both a remedy and a hazardous toxin, the katéchon, for Virno,

"safeguards the 'radical evil' that it has engendered: the antidote here is no different from the poison" (Virno, 2008: 189). In other words, instead of reducing the potential of the concept of the katéchon to the political power of the sovereign state that must withhold the negative forces in society for society's 'own sake', Virno understands the katéchon as itself embodying the capacity to 'magically' turn away from absolute self-destruction. The katéchon continues to preserve itself and avoids its absolute self-destruction precisely by not trying to restrain or inhibit the aggressive or violent tendency within itself. The natural "bioanthropological" (57) tendency of the katéchon to inhibit self-destruction is itself inhibited by itself, for itself, by allowing a certain amount of 'negative' self-destructiveness to flourish so that it can ambivalently create new conditions that it will thrive in.

2.3 Governmentality

I would now like to briefly address Michel Foucault's concept of governmentality which, together with the concept of the katéchon, could help me explore more specifically the concept of inhibition. For Foucault, governmentality represents the "technologies of power" (2007: 118) employed by apparatuses of law and order, or institutions such as the state, the main target of which is to administer processes of subjectification of the general population. Importantly, governmentality is also the way in which actions and behaviours of individuals or groups within society are given a direction. My focus here is to tease out of Foucault's concept of governmentality, a notion of inhibition that can be imposed on a body as a directing or governing act from outside, and following Lemke (2011) *from within*, the contours of the body. Thomas Lemke (2011) attends to how Foucault's concept of biopolitics could not have considered how:

> Various [recent] technological innovations, such as [...] the redefinition by molecular biology of life as a text, biomedical progress involving new techniques extending from brain scans to DNA analysis, and transplantation medicine and technologies of reproduction, have broken with the idea of an integral body. The body is increasingly viewed not as an organic substrate but as a kind of molecular software that can, as suggested, be both read and rewritten (Lemke, 2011: 170).

Thus, this molecular form of biopolitics is operative "both inside and outside the human body's boundaries" (Lemke, 2011: 170) and a "transformation of inner nature stands at the center of this political epistemology of life" (Lemke,

2011: 170). This molecular politics, which the object analysis of TNF inhibitors later in this article will further exemplify, "opens a new level of intervention within [the] body" (Lemke, 2011: 170) and complements as a third dimension Foucault's formulation of the "two dimensions of 'life'-orientated power: on the one hand, the disciplining of the individual body; on the other hand, regulation of the populace" (Lemke, 2011: 166). More specifically it resituates "the biopolitical problematic within an analytics of government" (Lemke, 2011: 173), or in Foucault's own words, an "art of government" (Foucault, 2008: 1) "that takes account of the relational network of power processes, practices of knowledge, and forms of subjectification" (Lemke, 2011: 173). To inhibit in this sense would be a technology of power that governs or moves the body of the individual or group in a direction which is almost opposite or of a lesser degree to the direction the individual or social body would move towards without such a governing act. This act of governing, or inhibition, is imposed upon the population and paradoxically puts the individual or society "on a [certain] path" (Foucault, 2007: 121), a path which is not their chosen or uninhibited path, but one that they are governed to follow. Finally, the act of governing would also refer to the "movement in space, material subsistence, diet, the care given to an individual and the health one can assure him" (Foucault, 2007: 122). In that sense, Foucault's employment of the notion of governmentality seems to also include an idea of care given to individuals or groups, which has an abstract idea of a preferable direction that the people being governed should follow. Foucault also evokes the "shepherd-flock relationship" (124) to typify such a governing relationship in which a higher form of authority exercises power over a group's movement or direction in a certain territory.

Problematically, the idea of governing in such a shepherd-like fashion, or taking a certain path towards subjectification, also implies that there is an idea of a teleological end goal or direction towards which such a body should move. It is easy to see how a suggested and normative notion of a 'right' path to follow is laid out for the people being governed where even the "self-constitution of individual and collective subjects" (Lemke, 2011: 174-175) is governed by an external power. According to Foucault, modern biopolitics, with such a shepherd-flock governing principle at its core, is a trace or "historical form of articulation of a much more general problem: the linkage between pastoral and political power extending back into Christian antiquity" (Lemke, 2011: 175). As such, and with the advent of liberal forms of government, "specific political knowledge" was developed which "made use of disciplines like

statistics, demography, epidemiology, and biology [...], in order to 'govern' individuals through correcting, excluding, normalizing, disciplining, and optimizing measures" (Lemke, 2011: 176). It is also easy to see how this connects to the notion of the katéchon as developed by Hobbes (1651) or Schmitt (2006) in the sense that it is supposedly in the people's best interest that an external form of power such as the sovereign state inhibit the 'bad' tendencies or maladjustments within society to save it from its own destructive powers. Inhibiting here, taking Foucault's concept of governmentality and Hobbes or Schmitt's understanding of the katéchon as it is embodied in the sovereign state, would mean exercising a technology of power which knows in advance, and prior to the population being governed, what the 'right' direction or path is and what the means of getting there are; means that are within its own scope of power and authority. Inhibition is thus the act, which at one and the same time prefers, allows or encourages one process to happen (governing in a certain direction), whilst preventing or postponing another process from taking place.

At the same time, Virno's notion of the katéchon not only means that it should not be embodied in such an external agential governing entity, which acts by inhibiting the individual or the population's own violent tendencies and leads them away from chaos and disorder. It also means, contra even to the notion of self-governmentality Foucault (2010) developed later in his life, that there is no such agent or body, self or non-self, within or without the individual or the population, that is capable of knowing the direction which the individual body or population should direct its conatus or life force towards. This is because when read from an autoimmune embodied perspective, even the 'self-governing' agent or body is self-undermining and incapable of governing itself, as I encountered in my own experience of living with an autoimmune disease. Even Foucault's later work on the "technologies of the self" (1986, 1990), which could allow individuals to affirmatively take more control of their own bodies by their own means and possibly escape some of the entrapment of subjectification by an external power, is questionable, as the 'anarchic' autoimmune body is even from within its own contours, and by its own means, less in control of itself. The technologies of the self of the 'self-attacking' autoimmune body are not at all "intentional and voluntary actions by which men not only set themselves rules of conduct, but also seek to transform themselves" (Foucault, 1990: 10). In fact, the technologies of the autoimmune body are even more materially restricting or subjectivizing in a non-affirmative manner, and yet, they point to a form of embodiment that is not

necessarily negative in the traditional biopolitical sense or in the sense of Lemke's biopolitical reformulation of a "molecular politics" (Lemke, 2011: 170), as the power or force causing this form of subjectification or disadjustment comes partially or fully from the body's own doing, rather than from an external force that has some sort of "grip on the body" (Lemke, 2011: 171). Thus, to think of the technologies of the autoimmune body in such a way also challenges normalized notions of what immune and autoimmune, normal and pathological, self and other can mean. This power or force of the ambivalently constituted subject —like that of the katéchon— is a form of 'doing' or embodiment, which is neither negative nor affirmative, and at times is violently undone by its own destabilizing and destructive life force.

In such a sense, the whole notion of governmentality as problematized from an autoimmune embodied perspective is subverted. The removal or undoing of such an embodiment of the katéchon that restrains or inhibits individual and social life would not in fact allow/result in the possibility of imagining social life beyond any political notions formulated along the 'logical' coordinates of sovereignty as Agamben's biopolitics imagines. The complexity raised by the notion of inhibition as I have developed it here, together with Virno's reading of the katéchon, and against or together with Foucault's concept of governmentality, is that it is not at all clear who or what is the agent that inhibits, and thus prefers, allows or encourages, one process from occurring (governing in a certain direction), while preventing or postponing another one from taking place. Importantly, the agent or entity that prefers, allows, or encourages one process to happen, as it inhibits another process from taking place, is itself self-undermining, self-destructive and self-inhibited. This 'evolution' of the concept of inhibition will shortly be put to work in my analysis of the biochemical object of TNF inhibitors. In my analysis, I understand the concept of inhibition from an autoimmune perspective, as a continual ontological process that embodies an empty ontological category that is even resistant to itself and does not dictate or direct a teleological desire for or of domination.

2.4 Mutation-as-inhibition

It is here that I would like to speculate on how the concept of mutation can come to fulfil the 'agential' entity behind such a reading of the concept of inhibition. Mutation-as-inhibition could also potentially be understood through Rosi Braidotti's notion of "the split temporality of the present as both

what we are ceasing to be and what we are in the process of becoming" (Braidotti, 2019). In this "no-man's-land of that which exists no more and that which does not yet exist" (Lavaert and Gielen, 2009) new rules or mutations can be created and take root. Mutation in that sense is an inhibition of both what it ceases to be and what it still is in the process of becoming and individuating. Mutation in that sense is an inhibition of an inhibition, in that it is both always 'on the path' to becoming something it is not, and not yet being there or where it was before. The process of mutation is the process that is resistant to any such inhibitory measures and simply thrives as an ever-evolving conatus. Importantly, I do not read mutation in the Darwinian sense of random, accidental or uncontrolled linear and 'progressive' development or selection for fitness, but rather a mutation that is self-mutant, unrecognizable and not even in control of its new state of becoming. In that sense the autoimmune body which has chronically 'mutated' from its previous immune state is just as well inhibited by its new self-undermining restrained 'condition'. At the same time, it is an uninhibited body that is not in control or capable of governing itself yet maintains a creative/destructive capacity of/for life, as Virno (2018) explores in his radically open and incomplete notion of the katéchon.

Mutation could also be understood as a form of inhibition, when considered along the lines of Virno's account of the katéchon, as it embodies a "bio-anthropological" (Virno, 2008: 57) tendency to inhibit the inhibition from self-destruction, as it allows a certain amount of self-destructiveness to flourish. The katéchon embodies this double inhibition as a constraint, a constraint that is capable of altering or mutating as new conditions for it to thrive are created. The notion of mutation-as-inhibition can also help extend Samantha Frost's "biocultural" (Frost, 2016: 98) notion of a protein or gene having a "direction without intention" (Frost, 2016: 84), in how it helps formulate a more specific kind of agency of such proteins or genes. Here the 'unintentional' act of an inhibitor could be understood as an action that withholds (inhibits) a finite or definite action, or as an 'action' understood as a continual ontological process or series of actions, capable of creating infinitely possible responses to a biological, anthropological or cultural environment that is itself not finite. In that sense, when the process of mutation-as-inhibition is ever-evolving and becoming, 'intention' itself and 'mutation' in the traditional Darwinian sense of random indeterminate mutations lose their meaning. This notion of agency also connects well with the synthesized notion of the 'healthy individual' I traced in the theoretical introduction to this article as the creative individual,

which is in a continual ontological process of evolving from its previous 'pre-individual' states, individuates and becomes with/against its environment, is capable of continuing to adapt to its environment's ever-changing norms of life. Importantly, the notion of mutation-as-inhibition also opens up a space of resistance/mutation/inhibition that suspends the hasty and naturalized transition from ontology to a teleology of domination.

To summarize, and before going on to analyse the biochemical object of TNF inhibitors, the peculiar notion of agency the concept of inhibition provokes is not one that actively suppresses or destroys another entity or process, but rather suspends it by indirectly slowing it down. In that sense it is different from traditional notions of agency that are more about interfering in the here and now in order to bring about a change or a particular action. The action/non-action of that which inhibits is more projected towards the future, though that future is not goal-orientated in a strictly teleological sense.

3. A DIFFERENT FORM OF EMBODIMENT WHICH IS NEITHER AFFIRMATIVE NOR NEGATIVE, AND YET STILL REMAINS RESISTANT EVEN TO ITSELF

3.1 Tumour Necrosis Factor (TNF) Inhibitors

I would now like to put to work the ambivalent concept of inhibition as I have developed it so far in the theoretical proposal for this article. Here I will explore how the concept of immune inhibition plays out in the material-discursive object of TNF inhibitors as a pharmaceutical drug that aims to inhibit the "over-reactive" or "dysregulated" (Steeland, Libert and Vandenbroucke, 2018: 1) process of TNF immune responsiveness in the case of autoimmune diseases, a process also known in scientific literature as a "cytokine stor" (Tisoncik et al., 2012). In my object analysis I will mainly focus on exploring further how the concept of inhibition is used in tandem with the TNF inhibitor drug to dominantly define what cure and medicine can mean in the context of autoimmune bodies, whether defined as normal or pathological, healthy or diseased, immunocompetent or immunocompromised. In short, I seek to problematize the too hasty and unnuanced transition from ontological foundations that are unstable and questionable, while setting in motion a naturalized and dominating teleology that, in the case of autoimmune bodies, tries to inhibit, regulate or dominant the body's own physiological processes.

In the case of the TNF inhibitor for autoimmune diseases, I will try to problematize, inhibit or suspend how, once a 'pathological' autoimmune human body is diagnosed to be stricken by an autoimmune disease and thus is not 'normally' itself, the normative and prescriptive notions of what ought to be done with this body on a medical-pharmaceutical level rush in. I would like to explore how the ontological foundations that guide the dominant pharmaceutical application of TNF inhibitors for autoimmune diseases can be turned on their heads and themselves inhibited. I aim to do this within a new ontological framework for understanding immunity that seeks to develop differently embodied forms of agency in a manner which empowers "subjects to take over and modify scientific interpretations of life for their own conduct" (Lemke, 2011: 178). Here I depart from my own experience of living with an autoimmune disease and the TNF inhibitor medication HUMIRA® (adalimumab) I was recommended by clinical immunologists to regulate my 'over-excessive' immune system and put it 'back in balance', a medical treatment I eventually refused.

Specifically, my analysis focuses on how the biochemical object of TNF inhibitors can come to perform two completely opposing forms of immunity and embodiment that are neither entirely affirmative nor negative. As the TNF inhibitors work by lowering the over-excited or dysregulated amounts of TNF production, they place the bodies that are administered these drugs at a higher risk of becoming infected with infectious diseases, including the risk of developing various forms of cancer, as their immunity threshold is 'lowered'. However, if inflammation goes uncontrolled, the body may also develop various forms of cancer and risk of infection from infectious diseases increases (Solomon, Mercer and Kanavaugh, 2012). Ambivalently, these high-risk TNF inhibitor drugs stabilize and put back in a 'healthy state' the 'pathological' autoimmune body with its 'over-excessive' amount of TNF production, which is said to be harmful to bodily tissues. Furthermore, the autoimmune bodies that are not administered these TNF inhibitor drugs remain in an 'over-excessive' and heightened immune state of TNF production, keeping them —from the medical-pharmaceutical perspective of the TNF inhibitor drugs/medication— in a pathological and unhealthy state that is self-destructive and harmful to itself.

Somewhat echoing the logic of the Greek word for drug (pharmakon) as a medication or cure that is at the same time a harmful and toxic poison, this resonance with the notion of the pharmakon as drug is negatively defined. It is not, as in the traditional philosophical readings of the concept of the pharma-

kon (Derrida, 1981), that a 'cure' can at one and the same time also mean and function as a 'poison'. Instead, from the perspective of the drug or the pharmakon, a negative or empty notion of a 'non-cure' (which is not the same as poison) emerges, which can also be the state of being non-medicated or not being given a cure. In this 'non-cure' or non-medicated state, the autoimmune body that is unmedicated or uninhibited comes to be defined or labelled as unhealthy or in a chronically ill state. In that sense, cure and poison are ambivalently entangled, as to turn away from or resist being medicated negatively implies that one is or remains in an unhealthy or risky state.

This 'inverted biopolitical logic' also resembles Foucault's notion of governmentality I previously explored, where inhibition can be understood as the act that, at one and at the same time, prefers, allows, or encourages one process to happen, whilst preventing or postponing another process from taking place. This inverted form of biopolitics further elucidates Lemke's (2011) analysis of how some "forms of physical and psychological suffering receive political, medical, scientific, and social attention and are understood as intolerable, relevant to research, and in need of therapy— [while others] are ignored or neglected" (Lemke, 2011: 177). In this case the TNF inhibitor drugs are offered as a form of governmentality of a protection of life from its own harmful tendencies; a life that needs to be protected and inhibited with the administration of the immune inhibition drugs. As I problematized above through an alternative notion of a 'healthy' state of an individual (Canguilhem, 1991), life that is creative/destructive can also be violent to itself. And yet as the autoimmune body is a body that undermines its own agency and resists itself, it is not entirely clear what form of cure or treatment, medical or non-medical, can be an appropriate form of healing or care for the uninhibited autoimmune. Furthermore, if disease is understood to have a conatus or 'life of its own', it is not always clear what 'drives' this form of life and what in it needs to be or can at all be suspended or inhibited to put the diseased individual back in an undiseased 'healthy' state. If TNF is seen as the driver or 'in control' of the autoimmune disease, and the autoimmune body is not in control of its over-excessive TNF production, it is hard to disentangle the disease that is 'harboured' within the autoimmune body from the diseased autoimmune body that 'attacks itself'. Autoimmune disease in this case is indeed seen as a 'condition' that chronically conditions or governs the body in a certain direction while parts of its own material physical body (TNF) are negatively defined as not 'its own'. TNF is othered and becomes an objectified non-self entity that needs to be controlled, governed, and inhibited.

3.2 Tumour Necrosis Factor (TNF)

Discovered in 1984 (Aggarwal et al.), TNF is a proinflammatory cytokine which is a signalling protein that a variety of immune cells release in inflammatory processes of the immune system as they deliver messages between cells of the body when they encounter infectious pathogens in various viral diseases. An excess of TNF production is "associated with a number of chronic and inflammatory autoimmune diseases" (Tisoncik et al., 2012). In that sense and seen from a perspective of disease having a conatus or 'life of its own', (excessive) TNF acts as the 'driver' of such diseases. On the other hand, it has also been shown that TNF production "is sometimes needed to inhibit or control autoimmunity" (Steeland, Libert and Vandenbroucke, 2018: 6). In other words, TNF is ambivalently both a proinflammatory 'agent' of disease, and an anti-inflammatory 'agent' of a well-balanced 'healthy' immune system. For example, in the case of immunodeficient diseases such as cancer, "TNF is a double-dealer. On one hand, TNF could be an endogenous tumour promoter, because TNF stimulates cancer cells' growth and proliferation [...]. On the other hand, TNF could be a cancer killer" (Wang and Lin, 2008). As TNF already plays an ambivalent or double proinflammatory and anti-inflammatory role in immune responsivity, it is not surprising that the administration of TNF inhibitor drugs can also lead to at times contradictory effects or forms of embodiment.

Furthermore, the 'normal' functioning of the body also inhibits excess TNF naturally. So, the body in any case also disciplines or inhibits itself. In this case the TNF inhibitor drugs act as an assistant or supplement to the body that stopped inhibiting the TNF. Contrastingly, even the TNF protein itself acts or communicates as a negatively regulating inflammatory agent rather than one that promotes or excites inflammation. In any case, the ambivalent and at times paradoxical framework or paradigm of TNF production and TNF inhibitor medication can help imagine alternative formulations of anti-anti-immunity or doubly inhibited or negated forms of embodiment, which I will expand upon further below. In that sense, by embodying an empty, negative, or inverted notion of 'non-cure', or not being medicated (which is not the same as poison), or by affirmatively and biochemically inhibiting such already immune inhibitory processes (which I will expand upon below), the very idea of a dialectics of immune inhibition and/or uninhibited 'excessive' immune response is somewhat subverted. Through the subversion of such a dialectics a

different form of embodiment can come about which is neither affirmative nor negative, and yet still remains resistant even to itself.

At the same time a somewhat more affirmative notion of a doubly inhibited or doubly negated form of TNF-mediated immunotherapy (Montfort et al., 2019) led to the scientists behind its discovery, James P. Allison and Tasuku Honjo, being awarded the 2018 Nobel-prize in Physiology or Medicine (Nobel Prizes, 2018). Interestingly, the advanced revolutionary cancer immunotherapy called 'immune checkpoint therapy', works along similar double-negation lines, and seems to produce a more affirmative 'positive' outcome in treating cancer patients without compromising their immune system as other treatments do. Previous cancer treatments were designed either to attack the cancer cells themselves by surgery, radiotherapy or anti-cancer drugs, or to stimulate or enhance the immune response against the cancer cells, and at the same time compromise the immune system's own defences, thus leading to further complications and disorders. Immune checkpoint therapy similarly seeks to harness the body's own immune system to attack cancerous cells, but it does so in a slightly different way: not by stimulating or enhancing the immune system but rather by inhibiting it. In short, cancer cells proliferate in the body by co-opting the built-in ability of the body's immune checkpoint inhibitors to maintain tolerance to its own tissues, thus also inhibiting the ability of the immune system from being fully activated as it encounters these cancer cells. In other words, cancer cells manage to hijack and subvert the immune system's own inhibitory checkpoints for their own proliferation and by doing so, prevent the immune system's surveillance apparatus from attacking infectious pathogens. In pointing back to the formulation of disease I explored in the beginning of this article as having a conatus or 'life of its own', disease/cancer finds ways to evolve, mutate, and adapt to the current environment and circumstances it proliferates and thrives in. When disease is misunderstood or misread as lacking its own constructive and innovative force, therapy —as previous less successful immunotherapy for cancer that targets cancer cells has done— attempts to directly revalorize or compensate the ill or "evil" (Canguilhem, 1991: 275) diseased state. The idea of a 'cure' in this sense is also not a final or fixed result of a teleology geared towards total elimination of disease, but a process in which both an organism and its external or internal environment are continuously changing and becoming adaptive to one another.

In the case of immune checkpoint therapy, the same immune checkpoints which are inhibitory regulators "hardwired into the immune system [and are

necessary for] maintaining self-tolerance and modulating the duration and amplitude of physiological immune responses [...] in order to minimize collateral tissue damage" (Pardoll, 2012) are themselves inhibited. As a result of the double inhibition of the immune checkpoint therapy, the immune system's inhibitory 'breaks' are released or inhibited, allowing the immune system to attack the cancerous cells. The cancer cells are thus defeated by harnessing and inhibiting the immune system's own ability to inhibit itself; an inhibition of the immune system's own 'negative' regulatory processes. As such, the new immunotherapy for cancer also provides new ontological grounds for rethinking how a healthy or diseased, normal or pathological, immune system is co-constituted in the diseased body. It also provides further grounds for understanding how the immune system's own regulatory mechanisms of inhibition can be harnessed or themselves inhibited to provide (in this case) a more affirmative outcome of disease.

Nevertheless, immune checkpoint therapy for cancer still has its adverse side effects, such as overproduction of TNF, which also makes the body more likely to develop further autoimmune disorders, as the immune checkpoints that are inhibited are also responsible for inhibiting the immune system from attacking the body's own tissues. Therefore, the most effective form of biochemical immunotherapy for cancer today still includes a combination of immune checkpoint inhibition drugs together with TNF inhibitor medication that tries to strike a balance in promoting and inhibiting TNF production to improve the efficiency of immunotherapy for tumour progression (Montfort et al., 2019). The logic of double negation (inhibition of an inhibitor) or anti-anti-immunity (blocking the immune block) of the revolutionary cancer immunotherapy, are helpful in subverting the very idea of a dialectics of immune inhibition and/or uninhibited 'excessive' immune response. This allows us to imagine a more spacious and nuanced theorisation of the body and the concept of immune inhibition I try to further in this article.

4. CONCLUSIONS

In conclusion and to tease out the main results of my analysis of the concept of immune inhibition and the object of TNF inhibitors, I first put forward an ambivalent formulation of disease, one that, in line with Canguilhem's problematization of the notions of the pathological and the normal, asks us to consider disease's own agency in specific autoimmune bodies. Doing so al-

lowed me to slow down, ambivalently negate or inhibit the dominant ontological pathologization of diseased bodies as less healthy or unhealthy, a state of affairs that tends to be biomedically teleologically revalorized by an external governing entity or force in the form of medication to put the disease body back on its path to a 'healthy state'. I have shown through a reading of the concepts of the katéchon, governmentality and mutation, how a different state of understanding bodily affairs is possible, one that ambivalently acknowledges and makes room for the destructive forces within autoimmune bodies to flourish, while also inhibiting absolute self-destruction by keeping disease with its own empty and mutating ontological foundations at bay while they adapt to their environment in creative and innovative ways. Importantly, my analysis of the concept of inhibition as a governmentality of the self, whether 'done' from outside the body or from within it, goes beyond Foucault's affirmative formulation of the technologies of the self, as the anarchic autoimmune body itself escapes and disrupts even its own form of governmentality and technological self-regulation. In the end, what I am proposing in my analysis is an alternative or more nuanced form of 'doing'/non-agency or a form of embodiment, which is neither negative nor affirmative, and at times is violently undone by its own destabilizing and destructive life force. Lastly, in trying to apply such an alternative understanding of immune inhibition as I read it from an autoimmune perspective, the biochemical object of TNF inhibitors predominantly dictate and perform in a myriad of at time contradictory ways, a form of embodiment for autoimmune bodies, thereby limiting the ontological and teleological space for manoeuver of autoimmune bodies themselves. In that sense, my onto-teleological operation has been to suspend such a hasty and dominating conceptualization of immune inhibition by turning it on its head and considering how the concept of immune inhibition itself can be inhibited and how the biochemical interaction of TNF inhibitors with autoimmune bodies can either be resisted, problematized or thought anew.

5. ACKNOWLEDGEMENTS

I would like to thank Joost de Bloois for his feedback on earlier versions of this article and Emma Gómez Nicolau from *Recerca. Revista de Pensament i Anàlisi* and the reviewers of the article for their feedback and encouragement.

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