



# Quisquis Amat Valeat! (Whoever Loves, May He be Well) Why Love and Passion Are Important for the Well-Being of the Immune System

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“*Quisquis amat valeat; pereat qui non-scit amare; bis tanti pereat, quisquis amare vetat*”—(Whoever loves, may he be well; may he perish who does not know how to love; may he perish twice as much whoever forbids loving). This graffiti was found in the old city of Pompei. The author is unknown. Possibly a poet but quite possibly an ordinary citizen who in the spur of their passion wanted to share with everyone a pearl of wisdom. *Amare* in Latin is “to love” and, as in English, it is not just about sex or romance, but also about passion for a cause or an ideal. The Latins knew that to be in love, to have a passion, is to be healthy in the body and as well as in the mind. In this article, I hypothesize that the lack of passion and love in life is one of the main causes of modern diseases and specifically immune/inflammatory diseases. I will explore in layman terms the limitations of specifically focusing on controlling bodily functions without considering the social and emotional dimensions of one’s life. Lastly, I will highlight the importance of cooperative research, engagement with the public and education as the way forward for a more effective and democratic model for new socially inclusive therapies.

**Keywords:** immune system, passion, love, well-being, psychoneuroimmunology

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## PHILOSOPHY AND IMMUNOLOGY: SIMILARITIES AND OVERLAPS

Immunology is a relatively new biomedical discipline that has expanded exponentially in the last decades (Cohn, 2017). Even in popular science, the immune system has become a major driver of the quality of our daily living and directly connected to our well-being. Looking at social and daily media we learn that stress is “*bad for the immune system*” (about 144,000,000 results when typed in Google)—or that an incredibly vast variety of minerals and nutrients are needed “*to keep the immune system strong*” (about 96,500,000 results when typed in Google)—and, based on very recent evidence, even falling in love has been proposed to be an “immunological process” (Murray et al., 2018).

The reason behind this popularity should not be surprising. Indeed, few people realize that we project onto Immunology the same functions that our pre-decessors gave to Philosophy. Indeed, Immunology and Philosophy are greatly similar and have been proposed to be interconnected (Tauber, 1994; Pradeu, 2010, 2019; Pradeu et al., 2013; Anderson, 2014). Philosophy is a creation of the mind that we use as “*a way of thinking about the world, the universe, and society.*” Philosophy is what we have used every day to cope with the challenges of daily living and to understand better who we are.

Similarly, Immunology is the “*language*” our physical body uses to relate to the outside world and to adjust to it. Thanks to the immune system we can deal with a myriad of pathogens that are invisible to the naked eye. Both Philosophy and Immunology are concerned with “*the inside and outside realities.*” Both Philosophy and Immunology are concerned with the Self (Grabar, 1974; Vaz and Varela, 1978; Howes, 1998; Ohashi, 2002), i.e., “*the conditions of identity that make one subject of experience distinct from all the other.*”

Why has this switch from Philosophy to Immunology happened? And most importantly, how has this impacted the way we look at well-being? To answer these questions, it might be essential to take a few steps back in human history. The rise of specialized and reductionist research of the twentieth century has rendered speculative disciplines like Philosophy vague and unreliable. The main pre-occupation of a philosophical enquiry is the search and understanding of one’s philosophical Self, i.e., one’s personality, lifestyle and social conditions and emotional intelligence. This journey of self-discovery (*know thyself*; cit. Socrates) and management of one’s well-being was often very painful and uncertain. There was no system of reference, and it required a very high degree of self-reliance. Instead, we have opted for more measurable and “numerical” disciplines like Immunology as these give objective measures about ourselves with minimum effort on our behalf. When we measure bodily functions, we rely on numbers produced by a machine rather than human participation. Through these numbers we ascertain if we are happy or sad, in need of some rest, fit or overweight.

The increased popularity of Genomics (Wall and Tonellato, 2012) is probably one of the best by-products of this new outlook to life. Many scientists are busy searching for a cure for defective genes responsible for obesity (Clément, 2006; Apalasyam and Mohamed, 2015) but few reflect on the fact that these genes do create a problem only when the subject carrying them is following an unhealthy lifestyle or an over caloric diet (Barrès and Zierath, 2016; Wang et al., 2018). As in the case of the search for a stronger and better immune system, we seek outside for something that is missing or malfunctioning inside. We do not take responsibility for what is happening to us or try to understand why we are having these health problems.

To make the problem worse, we have adopted a “Frankenstein” view of our living. The body is just a patchwork of tissues and organs glued together. One is obese because a metabolic gene is not expressed at the required physiological level (Skrypnik et al., 2017; Thaker, 2017)—obesity-associated depression comes from an imbalance of mediators in the brain (Pereira-Miranda et al., 2017)—obesity-driven activation of the immune inflammatory system is the primary determinant of the undesirable appearance of cellulite (de la Casa Almeida et al., 2013). Everything is compartmentalized, and for every single problem there is a prescribed best solution. God forbid thinking there are possible connections between these different issues.

Put together, the compartmentalization of problems and the release from any responsibility for one’s health and well-being, has created our current twentieth century crisis in both body and mind well-being. This crisis has been experienced by all including the police (Winters et al., 2015; Chidgey et al., 2018). We keep

moving from one solution to another hoping that the “new research” will get it right this time. We have become like a car (all with the same engine and body parts) that one needs to take care of by adding the right lubricants, petrol, and tires. Similar to a car, we can measure what is missing and top it up to bring everything back to “normal” with a single action and solution.

## THE EXPANSION OF IMMUNOLOGY

Substituting the holistic view of well-being offered by Philosophy with the numbers and measures of reductionist science has not always gone too far. Few non-narrow-minded scientists have started to realize that the problem of well-being needs to be seen in a “transversal way.” A phase of zooming out instead of the reductionist zooming in has been set in motion. System biology, i.e., the holistic view of the functioning of different cells and tissues as part of something bigger, has gradually become popular. In Immunology, new areas of research have emerged such as Behavioral Immunology (Hucklebridge, 2002; Larson, 2002; Gassen et al., 2018) or Eco-Immunology (Ottaviani et al., 2008; Downs et al., 2014; Bowden et al., 2017). In both these cases, researchers have been trying to investigate how the Immune System of a single individual is influenced by the person’s specific behavior and by their external environment. As I have already mentioned in my previous writings on this topic (Brod et al., 2014; D’Acquisto et al., 2014; D’Acquisto, 2017), there is now compelling evidence that the immune system is very “plastic” (Perobelli et al., 2015; Gronke et al., 2016; Laurent et al., 2017; Smith et al., 2017) and continually adjusting to whatever we are experiencing at the moment (Dhabhar, 1998, 2003, 2014). This includes a state of anxiety and fear (Salim et al., 2012; Ray et al., 2017) or happiness (Barak, 2006) and laughter (Yim, 2016).

Interestingly, we have just started to appreciate that well-being and living conditions are not only important and relevant to human beings but also other living creatures. Plants can suffer from social isolation (Gagliano et al., 2012; Gagliano and Renton, 2013), trees can talk to each other (Gorzalak et al., 2015), fish can be depressed (Brennan, 2011) or suffer from addictions (Ninkovic and Bally-Cuif, 2006; Klee et al., 2011; Mathur et al., 2011) and rats can be “pro-social” and help other rats in difficulties despite having different fur color (Ben-Ami Bartal et al., 2014).

## CURRENT CHALLENGES IN THE MANAGEMENT OF WELL-BEING

We live in a world where we are constantly told what to do and what we need to achieve. If we were to follow “*what is recommended*” in everything we do from the food that we eat, a healthy number of hours of sleep, amount of physical exercise and “*mental activities*” we would be occupied 24 h a day 7 days a week. There would be no time or space to make a single and simple decision because experts who “*know better*” has already decided on our behalf.

The irony of this situation is that these *experts* have never met us in person and do not seem to be in touch with reality. They

might not know that eating just three of the recommended five-a-day (<https://www.nhs.uk/live-well/eat-well/5-a-day-what-counts/>) will cost a fortune in certain parts of the world. Instead, one can opt for a much more filling (and cheaper) meal with bad proteins, bad fat and 100% artificially flavored drinks. Equally the experts seem to ignore that mineral water costs substantially more than addictive drinks and that the recommended 30 min of daily exercise or 10,000 steps per day (Tudor-Locke et al., 2011) in a heavily polluted city is more likely to cause lung cancer (Fashi et al., 2015; Guillerm and Cesari, 2015; Kantipudi et al., 2016; Bhopal et al., 2019) (<https://www.theguardian.com/cities/2017/feb/13/tipping-point-cities-exercise-more-harm-than-good>) than generate a better control of blood glucose. In simple terms, this costly research that is made behind the four closed walls of a lab carries the risk of being utterly irrelevant to the individual (Lowenstein and Castro, 2009; Hwang et al., 2016; Fogel, 2018) that is genuinely trying to improve his/her life and well-being.

This division and lack of communication between the experts and society is also evident in a clinical setting. Compliance and adherence to pharmacological therapies are the most difficult challenges for the health system. Patient distrust in the medical sector as well as in research has never been this high (Schenker et al., 2012; Shoff and Yang, 2012; Grande et al., 2013). From the patient's perspective, it has become almost normal to be told one thing on a Monday and the polar opposite on Friday. And even when the therapies are followed, there are aspects of the disease that are either not considered at all or simply disregarded. This is especially true if those aspects cannot be measured. The best example of this is in the context of immune diseases is fatigue. Rheumatoid arthritis or multiple sclerosis patients (both diseases seriously impair one's overall mobility) can gain enormous benefits from current therapies. However, one common unsolved problem is fatigue or severe depression. Even more aggravating, these patients often refrain from reporting these problems (see for instance this very poignant video titled "*Behind the smile*" by the National Rheumatoid Arthritis Society <https://www.facebook.com/nationalrheumatoidarthritisociety/videos/10154652264647300/>) afraid to be perceived as being never satisfied although they "look just fine."

Another example of incomplete understanding of patient's perspective is a study I have conducted on dream in patients suffering from autoimmune diseases ([www.dreamingautoimmunity.com](http://www.dreamingautoimmunity.com)). The sufferers of these conditions experience very vivid dreams that they would reluctantly share with their GP or consultant amid their fear of been referred to a psychiatrist. The simple sharing of these experiences provides them with an enormous emotional and sometimes physical relief (F. D'Acquisto, unpublished data) at no cost or impact on standard pharmacological therapies.

These extreme cases pose the question of what should be really considered as well-being and what can be done in maintaining it. Thus far, I have highlighted that people want to actively control their life, and that when they are not allowed to, they lose interest (and passion)—they become completely disengaged from science and research.

## EDUCATION AND THE IMMUNE SYSTEM

For the non-biomedical readers of this article, it might come as a surprise that immune cells are educated—and that this has a pivotal role in well-being. Evolved and complex species such as humans have a specific type of immune cell called "adaptive." The name comes from the fact that these cells can adjust themselves and become specialized to respond to a wide range of problems (from viral infection to bacteria and worms). How do they do this? How do they know how to behave best when facing an immense diversity of potential threats that the outside world poses?

The answer is their education. Both T and B cells (two types of adaptive immune cells) undergo an elaborate programme of selection called positive and negative selection whereby they learn one fundamental lesson: to recognize what is "good" and what is "bad" (Santori, 2015; Takaba and Takayanagi, 2017). What is "good" is the cells and tissues of our own body (the immunological Self) and what is "bad" is everything else we consider as non-belonging to us, e.g., bacteria, viruses, and similar. This process of knowing and experiencing what is good or bad for the immune system has been slowly disappearing from our daily life as we have become more and more "clean" and dependent on what the above-mentioned experts sanctioned as "good."

The lack of contact with the "dirt" (physical and emotional) of the outside world has been deleterious for our well-being and immune system as highlighted by the "hygiene hypothesis" (Stiemsma et al., 2015; Leong et al., 2016; Ege, 2017; Alexandre-Silva et al., 2018). According to this theory, "*the decreasing incidence of infections in western countries and more recently in developing countries is at the origin of the increasing incidence of both autoimmune and allergic diseases*" (Okada et al., 2010). In layman terms, the reduced chances of the immune system to be educated to fighting infections (or difficult life experiences) have made it unable to distinguish the Self from non-Self. As a consequence of this, there has been an increase of autoimmune diseases, i.e., pathologies where immune cells start to attack self-tissues and self-organs. Many of my colleagues in the immunology field have invested a great deal of their research time in assessing the impact of the hygiene hypothesis in a variety of immune disorders, but very few have tried to understand the psychosocial origin of this phenomenon.

If Aristotle were still with us, he would suggest that we have completely misunderstood his teaching and have confused being "clean and tidy" as being virtuous. Fearful of the possible disastrous consequences of being infected, we carry with us sanitizing gels for our hands 24/7. The market for hand sanitizers has increased from \$28 million in 2002 to \$402 million in 2015 (<https://www.theguardian.com/society/2012/may/13/do-we-really-need-hand-sanitisers>). Another classic example of this change of attitude is the "5 s rule" (<https://www.independent.co.uk/news/science/five-second-rule-food-dropped-floor-germs-scientists-professor-anthony-hilton-aston-university-a7629391.html>) according to which "*if food is removed from a contaminated surface quickly enough, the microorganisms on the surface won't have time to transfer, or jump, onto the food.*"

This closing up to experiencing the external world together with a lack of being in touch with ourselves has negatively impacted on both our immune systems and on our minds. As I mentioned before, well-being has become something we have no control over. It has become a prescription that even when followed does not hold the promise we have been given. How is this relevant to education and how can educators apply this scientific perspective to the context of learning? Rather than relying on pre-set answers and prescribed truths, students need to engage with dialogues and processes that can be challenging, dangerous and difficult. They need to understand that education is about developing their own truth rather than conforming to what has been prescribed, exactly as the immune system develops in a unique way in response to challenges in life. As educators, how do we foster this process of self-discovery? The answer might be to encourage students to be passionate about challenges in learning as this could be pivotal for their well-being.

## PASSION, WELL-BEING, AND THE IMMUNE SYSTEM

The idea that passion is good for someone's health and well-being is not new (St-Louis et al., 2016; Lalande et al., 2017). History has shown that passionate people are resilient in body and mind and deal with problems (emotional and physical) in a much better and constructive way compared to those that lack motivation. This is of course also very true in the context of the immune response. According to several studies of Steven Cole—eudaimonic people (Fredrickson et al., 2013, 2015; Cole et al., 2015; Davis et al., 2015) respond better to infections compared to hedonic.

The argument that eudaimonia—i.e., one's fulfillment and a meaningful life—is the future cure for the weakening of the immune system and today's poor well-being is not far-fetched and not just a thought-construction that I am trying to make here. The critical point is that eudaimonia supports the concept of personal fulfillment. It recognizes that we are all different and that we are in the first place responsible for keeping our body healthy. This is hugely relevant in the context of an immune response. As I have mentioned before we are all immunologically different and the very same seasonal flu can affect some people and not others, and it can be very harmful to some or very mild for others. When one starts to look at all these individuals not as bodies but in their fullness, i.e., their social connections, economic status, personality type and overall attitude to life, patterns emerge. Those who are “full of life” make their own choices, have a pursuit in life and actively engage with their surroundings by adjusting to it, are much better off at maintaining a status of well-being (Zozulya et al., 2008; Ožura et al., 2012; Mirmics et al., 2013; Jandackova et al., 2017; Masafi et al., 2018).

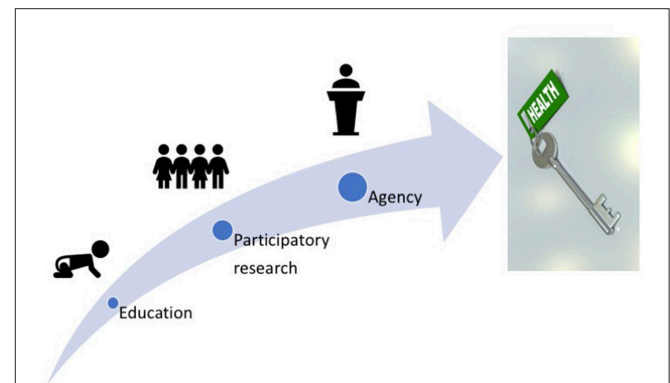
The immune system is one of the sensor organs of well-being. As I stated in my previous work (D'Acquisto, 2017), the immune response is the mirror of our emotional state and lifestyle. One best example that supports this statement is that short bouts of stress cause the immediate mobilization of immune cells in blood as a way to get us ready to “fight the danger” (causing our stress) (Dhabhar et al., 2012). A sustained level of continuous stress

leads to a state of immunosuppression that ultimately creates many problems from flu to recurrent infection and pre-mature aging (Dohms and Metz, 1991; Cannizzo et al., 2011; Adamo, 2017; Sharif et al., 2018; Sun and Zhou, 2018). An individual with a eudaimonic approach to life would not engage in activities that cause long-term stress and would most certainly address the causes of their stress rather than counting calories, walking endlessly, or looking at the colors of vegetables.

“Keep calm and carry on” is no-longer a reassuring motto and has now become the leading cause of suppressed frustrations and most likely one of the causes for the increase in allergies and immune disorders. Forcing people to fit into boxes created by bench-based research fosters these frustrations while luring people into thinking that their life might get better if they follow what they have been told. Not for a moment we are told to pay attention to what caused the flaring of symptoms and if there is anything that can be done about it.

This been said, the way we treat diseases is improving as we have started to consider all the unique elements of one's complex living conditions. Social prescribing is the best examples for these changes (Husk et al., 2016; Bickerdike et al., 2017) as it is based on using social interactions to treat diseases. According to the NHS, social prescribing is “*helping patients to improve their health, well-being and social welfare by connecting them to community services which might be run by the council or a local charity*” (<https://www.england.nhs.uk/contact-us/privacy-notice/how-we-use-your-information/public-and-partners/social-prescribing/>).

In my view, this is the most crucial aspect of management of well-being. Each individual should be educated to make a decision and take responsibility for it, listened to, and be supported in making their own decision in regards to treatment (Figure 1). Therapies should be participatory and be based



**FIGURE 1 |** The future management of well-being. An effective system of management of well-being that can be applied to all human beings should be based on an effective system of education that empowers people to distinguish the good from the bad. Participatory research between the lay public and researchers in all fields of science should address health problems that are concerns for the whole society. Finally, the results of these studies should allow individuals to make conscious and independent choices of what needs to be done to keep a state of health and well-being that is unique as we all are.



on an active input on behalf of the individual. In a recent TV documentary on the mechanisms behind the effects of placebo (<https://www.bbc.co.uk/news/health-45721670>) it was shown that even when the people enrolled in the study were told that they had been given a placebo, they opted for continuing taking the “drug” as this was found very beneficial to treat their pain. This suggests that when we are actively involved in an activity we are passionate about it, something in our body changes.

If this holds true, what would be the implications for the future? I think that most of the health research on well-being we are currently doing should be participatory and more specifically driven by the public. Participatory research (Aungst et al., 2017; Salsberg et al., 2017; English et al., 2018; Kwon et al., 2018) is more informative, more accurate and of high translational value compared to lab-based research. Asking the lay public what they think would improve their health or what is missing in their life might provide us with an immense source of useful data that otherwise would never reach the bench in the lab. Going back to the hygiene hypothesis, in a recent study by Lorimer et al. (Hodgetts et al., 2018), a sample of families within a defined area around the University of Oxford were consulted to provide samples of surface swab from their kitchen choosing in particular areas they thought would be either very clean or very dirty. All the participating families attended group meetings to share the results and to maximize the impact of the findings. From the choice of the sampling method and the objects used for sampling to the motivations behind it this research project with few families has revealed much more information than a classical multicentric studies with thousands of participants around the world. If we were to find a new effective way to

tackle the problems caused by the hygiene hypothesis or the ever-growing antibiotic resistance (e.g., the lack of effective antibiotics to treat infections) this would be the most likely to succeed.

Besides the strengths and limitation of participatory design (that will not be discussed here), the simple fact that people were willing to be involved in the research and were happy to lead on it should give us valuable insight in how to best tackle the issue of well-being. Being open to meet and work with the public also offer scientists to explain better and in a more pragmatic way the results of basic research. For my perspective as an immunologist, this type of research that includes an element of education would solve many pressing problems with the treatment of immune disorders. This includes the high risk of mental disorders in patients suffering from immune diseases and the role of emotions and living conditions in the fine-tuning of the inflammatory response.

I welcome and praise initiatives such as the current collection as a system to foster this culture of changes in the lay and scientific communities. It is indeed this kind of work that constitutes the stepping stone to the next level: governmental policy changes in the management of the health system. To achieve this goal, we need to capitalize and invest on education because as one of my colleagues (Prof. Jolanta Opacka-Juffry, University of Roehampton) often says: “*there is no legislation without education*”.

## AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

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**Conflict of Interest Statement:** The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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