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Are we Hierarchically Definitive Multicellular Organisms or Governing Bodies Consisting of Multiple Independent Multicellular Systems?

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Editorial
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Editorial

Traditionally, a multicellular organism could be viewed as an organismal system consisting of one or more groups of cells that are specialized in different functions. Examples include commonly known circulatory, respiratory, nervous, endocrine, musculoskeletal, reproductive, and immune systems, to name a few. In this traditional point of view, each group of specialized cells acts as a dependent system within the organism as an independent whole being. Each system serves to support the well-being of the whole organism. In today's governmental system, one could parallel the organism as a country's central or national government, and each system as an individual ministry or department (e.g., education, finance, national defense, etc.). All these ministries or departments (individual systems) perform their functions to support the centralized governmental structure, which acts in turn as an umbrella over to maintain integrity and order of the country (organism as a whole). This is a top-down view of a multicellular organism, which provides well organized structure and hierarchy.

Today, I want to challenge the readers to consider a multicellular organism from a very different organizational structure perspective. In this alternative perspective, a multicellular organism can also be viewed as an organismal system consisting of many independent, pre-existing or not, multicellular systems within the organism as a whole. This is a particularly challenging perspective that each group of cells specialized in different functions (e.g., blood cells) can be viewed as an independent "peripheral" system (e.g., circulatory system) reporting to the "central" system or the governing body (i.e., organism). In today's governmental system, one could parallel the organism as the federal government, and each system as an independent state or province, reporting to the governing body in a federal-state or federal-provincial relationship. The governing body provides centralized resources (e.g., digestive system for energy intake), and peripheral systems in turn provide basic, motor, regulatory, and defense functions to support and maintain integrity and order of the central-peripheral system (e.g., breathing (basic), musculoskeletal movement (motor), endocrinal secretion (regulatory), and immune response (defense)). This is a bottom-up view of a multicellular organism, which provides a more fluidic but very adaptive structure and hierarchy.

In both views, cells with specialized functions heavily involve and play a critical role in the definition of a complex multicellular organism. Several questions remain unanswered on how these specialized cells appeared in the first place, in relationship to two different organizational structure perspectives mentioned above. First, in the top-down view, did cells adopt specific functions via "centralized specialization/differentiation program(s)" as a result of evolutionary progress, or did cells already adopt specific functions but either joined proactively into or was recruited passively into the existing multicellular organism? Second, in the bottom-up view, could these systems of specialized cells be already in a multicellular state as a community but later joined proactively into or were recruited passively into the existing multicellular organism? Last, could it be possible that these independent multicellular communities originally lived on their own but adopted specialized functions (which may or may not be the same, similar, or different from their original functions) to adapt to live in a multi-community environment such as an organism?

In this editorial, I will challenge the readers further again specifically on how the immune system can be viewed differently as an independent system working in a governing body. Immune system is a defense system comprising of various network of biological processes that protects an organism from diseases. When a pathogenic invasion occurs, immune cells are often recruited to the infection site to fight off and defend against invading pathogens. This process involves multiple biological processes, signaling cascades, biological network and pathways [1,2]. On the organismal level, some questions still remain unaddressed. First, does this recruitment of immune cells, a big immune response event, occur because?

- The governing body (directed by the "brain") detects a threat and sends immune cells to the invasion site to fight, or
- The immune system detects a threat and sends its own immune cell troops to fight, or
- The governing body detects a threat and sends order(s) to the immune system and then immune system initiates and carries out the defense mechanism (e.g., recruitment of immune cells), or lastly
- The immune system detects a threat, reports to the governing body, and then receives order(s) from the governing body to initiate and carry out the recruitment of immune cells process? Second, assuming there is a constant and/or temporary line of communication between governing body and immune (and other peripheral) systems, does the skin, which often acts as the first line of defense [2], report the pathogenic invasion directly to the governing body, which in turn assigns the defense operation to all involving parties, including the immune system as the primary defense team leader? Third, in addition to assumed central-peripheral communication, does constant and/or temporary peripheral-peripheral communication actually occur that the skin informs the immune system of the pathogenic invasion so that the immune system can either
- Report to the governing body and wait for further order(s), or
- Stage all recruited immune cell troops at the border (interfacial region between infected and uninfected tissues or cells) and be combat ready, or
- Directly mobilize all recruited immune cell troops to initiate the defense mechanism? Lastly, could the skin detect the threat and report directly to the governing body but share information simultaneously with the immune system so that it can initiate early preparation, recruitment, and mobilization of immune cells as preventive measures against unwanted delays in immune responses, much like today's various well integrated, sharable information systems?

To date, we do not have sufficient evidence to demonstrate that the governing body (directed by the brain) actually commands the immune system. For example, the immune system has to "receive" an order from the governing body before they could send immune cells to act on an infection, although one could argue that the governing body actually indirectly commands the immune system as it controls the synthesis of hormones and other immunomodulator, both known and unknown ones, to stimulate or suppress the sensitivity of the immune system in response to a pathogenic attack. In addition, while the infection "signature" (combination of antigens) is often detected passively, we do not have knowledge on whether there is any (sentry) signal sent actively from a "potential" infection site (e.g., when sentry cells detect that pathogens enter a wound site, localize, and prepare to proliferate) to either or both governing body and immune system to trigger subsequent immune responses. Similarly, we do not have information to confirm the existence of sentry (cells or molecules), nor could we deny their existence. Furthermore, when an infection becomes more severe, we do not have complete understanding on whether the immune system makes the decision to elevate the response on its own or reports to the governing body to proceed with a more large-scale, coordinated elevated response from the immune system and potentially other systems, assuming that an elevated response (not a de-escalation) is true when an infection becomes more severe.

When an immune response is triggered, a network of biological processes is oftentimes activated. Generally, these biological processes may involve many other systems, e.g., endocrine, circulatory, respiratory, to name a few. Similarly, many questions remain unanswered on how these systems work together to reach a common goal prevents the host from getting sick. First, do these systems receive order(s) from the governing body (directed by the brain) to carry out specific tasks individually or do these systems work collaboratively? Second, within the system itself, does the system divide and assign tasks, or do individual subgroups/teams share tasks? For example, repair and regeneration normally come after an insult. Does the immune system assign these repair tasks to specific groups of cells or is there a (preassembled) "repair team" of cells that autonomously respond as a (emergency) unit at a later stage of an immune response to initiate repair processes after other defense units fight off pathogens? Lastly, if latter is true, does this "repair team" report to the immune system or directly to the governing body to demonstrate successful tissue repair? with or without sharing information with the immune system?

This brings us into another big concept question. If the team-based work is true for the immune system (and other systems alike), are these teams prebuilt (i.e., trained to perform specific tasks) or rather recruited for specific purposes in the course of the event (e.g., tissue repair, as an efficient tissue repair requires several crucial aspects such as the plasticity of immune cells as well as the balance between pro and anti-inflammatory signals)?. If these teams can be prebuilt, can these be preassembled as well? In addition, if plasticity is so important, it would also be difficult to exclude the speculation that cells could learn, adapt and/or be trained to work in different functions to support different team objectives.

On a final note, here I want to provoke the readers much further with one even more daring concept all systems are independent from each other on the same hierarchical order, but they are simply in symbiotic relationship. If this relationship is not well balanced and maintained, the organism cannot function properly and falls apart. This concept hypothesizes that in one or multiple historical biological event(s), there was possibly a need for a single cell to acquire a symbiotic relationship with another cell of a different function in order to survive evolutionary pressure, and this pressure may well also be the driving force for a small community of cells (e.g., the 2-cell community mentioned above) to communicate with other cells and/or community/ies of cells of different functions, simultaneously or separately in either temporal and/or spatially distinct event(s), to join together as a group symbiotically in order to survive ongoing rounds of evolutionary selection. To take this hypothesis further, one could view these systems as individual multicellular organisms in symbiotic relationship in a bigger organismal system, but each with specialized functions as a result of evolutionary selection pressure. Questions regarding the organizational structure of a living organism act like a key to a Pandora box. Once the box is opened, more and more questions will arise for us to seek answers for many years to come, but it should not be an obstacle to stop us from imagining all different possibilities. We need to continue thinking outside the box and this is the driving force for science to reach another ground-breaking discovery, both on the organizational structure of multicellular organisms and other questions of interest to different scientific researchers and communities.

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