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The Mucosal Immunology – Much is Done but the Most is Forthcoming

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For the past 4-5 decades, the field of mucosal immunology research has made tremendous progress. Mucosal immunology, as an essential component of the immune system, shows many differences. It is essential to take into the consideration that the different parts of the mucosal immune system work as one remarkable machine. Moreover, the mucosal immune system is a global organ that influences the immune development strongly not only in the mucosa but the whole organism. The process of understanding how this system operates also includes understanding the pivotal relationship with the microbiota. Unfortunately, the local environment is still critical and may darken the present models instead of broadening the knowledge how the mucosal immune system functions. However, the mucosal immunology research does not stop here. The next years of research will be devoted not only to further aiding to the better understanding of the known but to gather the knowledge and facilitate the development of future studies and taking new directions.

The most significant findings regarding the mucosal immunology, have been understood from relatively recent studies, such as oral tolerance, immune deficiencies and associated diseases, inflammatory bowel disease and gluten enteropathy, even approaches for designing of effective vaccines [1]. The concept of using the relationship with commensal flora as a tool for designing therapies exploring the microbial counterparts is slowly coming to the forefront. The idea that crosstalk between mucosal compartments is critical for mucosal immune functions is now finally beginning to be appreciated [1]. Collectively, such studies suggest that the mucosal immune system is one extensive associated network and that the specific components are very efficient at distributing information distally.

Characterization of the behavior and function of immune cells in peripheral tissues is an exciting research frontier in biology, especially in the mucosal immunology research. Recent studies report using a novel organ culture system that will enhance our ability to dissect the challenging interactions between commensal microbes and host intestinal tissue networks due to the complexity and inaccessibility of the system [2]. The technologies include cell line based methods (Gut-on-a-chip), primary cell-based (intestinal organoids), and organ based (Gut-in-a-dish). These methods allow *ex vivo* modeling of epithelial cell development, intestinal flow, or interactions between defined components, including intestinal microbes and epithelial cells [3]. The next step is forming tissue microarchitecture to study cell recruitment, migration, and interactions between many cellular components and gut bacteria. The ability to maintain whole intestinal segments *ex vivo* for an extended period can be used to examine cell migration and functional responses to various treatments. A new study now reports a distinct intestinal organ culture system and shows how it can enable such experimentation [3]. The system developed by Yissachar et al. represents the first organ culture system of the gut. As with any first method, the system has limitations. The gut explants can currently only be cultured for no more than forty hours without wasting tissue integrity. However, the developed organ culture system brings a new dimension to the study of gut biology and a new tool to mucosal immunologists, who now seem well equipped to dissect the complex networks controlling immune responses in this fascinating organ [3].

The advances in mucosal immunology research promise also to hasten the construction and examination of new mucosal vaccines against diseases such as HIV/AIDS. Unquestionably, policies for the development of efficient mucosal vaccines need to reflect the broad and continuous response to the antigens of the microbiota. A given vaccine antigen competes for the attention of the mucosal immune system. Moreover, the delivery of vaccine antigens by microbes has been tried in various forms [4]. Other limitations are the preexisting of systemic immunity provoked by prior infection or systemic immunization, the possibility of inducing mucosal tolerance by locally administered vaccines is little. Also, the choice and order of vaccination routes (systemic priming supported by following mucosal boosting), dose of antigen, delivery method, and use of adjuvants or cytokines, may change the extent and quality of the immune response toward the wanted outcome. Finally, different mucosal places of initial antigen exposure (oral cavity, intestinal tract, nasal mucosa, and lungs, or female genital tract), is not equally effective in the induction of mucosal and systemic responses or tolerance [4].

Over the next decades, the researchers in the field of mucosal immunology have to shift the focus to make further progress. Study of the mucosal immune system as one organ, rather than as a group of unique elements, will help to identify and characterize the relationships between different mucosal sites. Future research should examine also how the separate parts of the mucosal immune system influence each other and how the crosstalk is achieved between distinct components and between diverse mucosal sites where could be unappreciated levels of communication between mucosal compartments. Understanding the relation between mucosal sections is vital to the next phase of disease characterization and vaccine development. Regarding the microbiome research, future studies are needed to identify the members of the microbiota that affect the development of the immune system.

In conclusion, the next decade of mucosal immunology research should not only focus on examining the new concepts outlined above but also revisit established models, taking into consideration recent advances. For example, strong concepts such as the hygiene hypothesis and even tolerance may benefit from greater analysis.

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