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Editorial

Editorial introduction

The 10th CD1-MR1 workshop in Napa Valley gathered an exceptional group of scientists who over the past 20 years have collectively elucidated the biology of two populations of innate T lymphocytes, natural killer T (NKT) cells and mucosal associated invariant T (MAIT) cells, that sit at the interface between innate and adaptive immunity. Both cell types use unique "semi-invariant" T cell receptors which have invariantly rearranged α chains paired with a limited set of β chains. For this reason, they are hypothesized to recognize a limited set of ligands that are thought to resemble molecular patterns that signify microbial infection and perhaps also cellular stress. The second commonality of the two cell types is that the antigen presenting molecules that display their stimulatory ligands are non-classical MHC-like molecules: MR1 for MAIT cells, and CD1 for NKT cells. Both CD1 and MR1, along with NKT cells and MAIT cells are very conserved throughout mammalian evolution, indicating an essential function. A third commonality, related to the functions of MR1 and CD1, is the recognition of non-peptidic antigens by NKT cells and MAIT cells. The conference presentations also included possible evolutionary antecedants of these antigen presentation systems in amphibians and birds, and the analysis of CD1 and MR1 reactive T cells with more diverse TCRs that might more closely resemble typical CD4 and CD8 T cells.

The core group of scientists who attended the workshop has been very steady over the past 20 years and 10 inceptions of the meeting. The cohesiveness and talent of the investigators in the CD1-MR1 field has produced remarkably rapid advances in our understanding. The identification of natural ligands and structural work on the interaction of T cell receptors with MR1 and CD1 at the atomic level has been complemented by the generation of specific reagents that have allowed us to interrogate the functions of the two cell populations in great detail. These advances in understanding the basic biology of NKT cells and MAIT cells are now directly supporting efforts to develop approaches to utilize these cells for clinical applications.

Building on these advances, there are many exciting questions to be addressed with the help of the incoming younger generation who also participated actively in the confernece. For example, it appears that both NKT cells and MAIT cells may play key roles in controlling communication between the microbiota and the immune system. Indeed, both populations are enriched in organs that are in direct contact with microbes and their metabolites, liver, intestine, and lung. Both are stimulated by ligands that come from the prokaryotic world, and both can expand and contract during particular types of infections. This relationship probably endows NKT and MAIT cells with a key contribution to the first line of defense against pathogenic microbes, as well as a unique role in maintaining a state of harmony with non-pathogenic microbial colonists. However, conversely, both NKT cells and MAIT cells also utilize pathways of activation that do not require the recognition of microbial ligands and that instead rely on host-derived signals associated with inflammation and/or metabolic processes. The exact nature of these functions is still poorly understood and underpins the possibility of understanding the position of each of these two cell types in disease pathogenesis, and their potential usage in therapy. This next frontier will be addressed in the years to come and the next CD1-MR1 workshop in Oxford, U.K. and those to follow. Based on the track record, we can be optimistic that the new series of questions will be answered.

Jenny Gumperz
University of Wisconsin, Madison, WI, 53716-1521, USA

Mitchell Kronenberg
La Jolla Institute for Immunology, La Jolla, CA, 92037, USA

Luc Teyton*
The Scripps Research Institute, Department of Immunology and Microbiology, La Jolla, CA, 92037, USA
E-mail addresses: jegumperz@wisc.edu (J. Gumperz), mitch@lji.org (M. Kronenberg), lteyton@scripps.edu (L. Teyton),

* Corresponding author.

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