March 2008

Keystone Symposium on the 'Biology of Natural Killer and Natural Killer T Cells'

My interest in going to this Keystone meeting lies in the direction that my project seems to be taking. I am studying how T cells develop in the thymus early during life. For this purpose, we use tadpoles of the frog, *Xenopus laevis*, as our model organism because we can easily access and manipulate its thymus very early in development (as early as 3-days post-fertilization). In immunology classes, we are taught that CD8 T cells require recognition of classical MHC class Ia (class Ia) molecules to successfully develop in the thymus. The puzzling peculiarity about our animal model is that tadpoles are deficient in class Ia protein expression in the thymus but have CD8+ T cells. So, if tadpoles do not have class Ia, how is it that their T cells develop?

Well, it turns out that there are many different flavors of T cells. Besides the 'conventional' T cells that we learn about in class, it has recently become clear that there are several so called 'innate T cells,' which have completely different developmental programs, phenotypes and effector functions. The Keystone meeting dealt with one of these types of T cells – Natural Killer T (NKT) cells – and the ligand that its T cell receptor (TCR) recognizes – CD1, a nonclassical MHC class Ib (class Ib) molecule. The exciting thing about this field for my project is that 'innate T cells' don't need class Ia for their development, but rather class Ib. Therefore the possibility exists that tadpole T cells also develop through interactions with class Ib, rather than with class Ia.

I was fascinated to hear talks about CD1 lipid antigen presentation and how it differed from class Ia peptide antigen presentation. After one of the plenary sessions, I waited around to get a chance to ask the speaker, Dr. Albert Bendelac from the University of Chicago, some questions. As a result of our conversation, he put me in contact with another scientist, Dr. Erin Adams, also from the University of Chicago, and mentioned that she had done work crystallizing the TCR of an alternative T-cell type in complex with a class Ib molecule. Dr. Bendelac mentioned that I should talk to Dr. Adams because she is always looking for new ligands to crystallize. Dr. Adams and I had a productive exchange of ideas that may very well lead to a collaboration.

The poster session was also very fruitful. I had several visitors who really wanted to learn more about our animal model. Dr. Thomas Herrmann (University of Wurzburg in Germany), asked questions about the reagents we use, or the lack of reagents (currently no antibodies are available against TCR, class Ib, etc.), and he mentioned that he has just finished making several monoclonal antibodies against rat CD1. Some of these antibodies cross-react with mouse, and he was willing to let us borrow some to try on products of the class Ib genes I am studying. Another thing that came out of my poster session is a collaboration with Dr. Ram Savan, who works at the NIH, and is also interested in comparative studies of immunity. He asked if we had characterized certain immune genes in the frog, and I noted that we have been struggling to finish getting the sequence of one of the genes he mentioned. It turns out he has lots of experience with this gene and is willing to help us get the remaining portion of the sequence. We are sending him RNA samples so he can detect expression of the gene and clone it.

In summary, I am very grateful to the Graduate Women in Science group at the University of Rochester for funding my trip to this meeting. I was able to meet new people with whom collaborations have been established as well as 'catch-up' on ongoing projects with long-time collaborators. I also got a fresh perspective on the development, function and evolution of a new and exciting type of immune recognition strategy, that of innate T cells with class Ib molecules.

Goyos