

Participant 4. UIO-Prof. Bent Rolstad University of Oslo, Norway

Prof. Rolstad has a scientific basis in cellular and molecular immunology. He has published ca. 100 original articles and reviews in the fields of basic immunology with emphasis on lymphocyte migration in vivo, graft-vs.-host (GvH) reactions, and in particular in the immunobiology of natural killer (NK) cells, and their role in bone marrow allotransplantation. Focus has been on mechanisms of NK cell recognition of foreign cells and molecular characterisation of receptors mediating NK recognition of MHC class I molecules on haematopoietic cells. He has developed a rat model for bone-marrow allotransplantation after myeloablative treatment and shown that the requirement for successful allografting across an MHC barrier is dependent on alloreactive NK cells. In the present project this model will be exploited in the study of how NK cells of bone marrow donor and host origin and MHC antigens interact after ABMT and the role in graft adaptation and GvL using a rat model for AML, the BNML.

Dr. Rolstad has held several training scholarships or positions in immunology (Florey Fellowship from Queen's College, Oxford, Senior Fogarty grant NIH, MD, USA, visiting Professor VA Medical Centre UCSF, CA, USA). He has been a president of the Norwegian Society for Immunology, and has held a grant from *Human Frontier Science Program (HFSP)* as well as several grants from the Norwegian Research Council and the Norwegian Cancer Society, including a program grant from the Research Council. He is a member of *Norwegian Academy of Science and Letters* and committee leader of *Anders Jahre's Foundation for the Promotion of Science*, medical section. He has been an invited speaker at several conferences in immunology, is a scientific reviewer for several leading immunological journals, and has reviewed Ph.D. theses in immunology and applications for professorships in Norway, Sweden, England and the United States.

The group employs a PhD research fellow.

In this proposal the Oslo group will benefit particularly from mutual exchange of information and personnel between the Göttingen and Newcastle groups. It is suggested that one person will be trained in the rat models for ABMT, GvH and GvL in Oslo, and use these models to examine the effects on MHC-expression patterns in affected tissues (skin, spleen, liver, bone marrow) in Göttingen and to which extent a rat model to be set up for the skin explant assay (UNEW) predicts a role of NK cell receptors in AMBT, GVHD or GVL. Possible translation to humans can be obtained from comparisons of candidate rat NK receptor or MHC genes detected in these assays to orthologous human genes.

Network Team:

Dr John Torgils Vaage is a medical doctor at the Institute of Immunology, Rikshospitalet University Hospital, where he is engaged with clinical immunology in the field of transplant medicine. He has developed all the cellular and molecular methods necessary the characterisation of NK receptors and ligands. He has his training from Oslo, Hanover, Germany, and UCSF-CA-USA. He won the *King's gold medal* for best thesis at the University of Oslo in 1996, and has supervised a number of medical students and Ph.D. students. During the period 1999-2002 six candidates have completed their PhD theses from the group, of which Dr Vaage has been the main supervisor of three. He is now with Rolstad leading a group of 8 people at the Dept. of Anatomy, all working in the area of natural immunity. He has been the driving force in the, genetic, functional and molecular characterisation of rat NK cell receptors for MHC antigens.

Dr. Ke-Zheng Dai is a postdoc. in Dept. Anatomy. He is an expert in all molecular techniques regarding NK cell receptor cloning, expression and functional testing of transfectants against target cells expressing defined MHC haplotypes.

Dr. Christian Naper is a postdoc. in Dept Anatomy. He is the person in charge of all the genetic and molecular work on inbred and MHC recombinant rat strains and has done seminal work on the importance of MHC polymorphisms and NK receptor repertoires in determining survival or rejection of haematopoietic allografts. This knowledge has laid the ground for selection of BM donor - recipient rat strain combinations where BM allografts survive and the effect of BM allografting on GVL and GVH can be studied systematically.

Together Prof. Rolstad and Vaage have built up an international network of collaborators in the field of Natural Immunity, with participants from USA (Dr J Ryan and W Seaman, VA Medical Center UCSF San Francisco), England (Dr G. Butcher, the Babraham Institute, Cambridge), Germany (Dr L. Walter and E. Günther, Göttingen, and Dr K. Wonigeit, Hanover). The group has solid experience in all aspects of modern biotechnology, from genetic and genomic work, bioinformatics to search and analyse sequence information made available through genome and EST sequencing projects, gene expression techniques and in-depth analysis of molecular function in vivo.

Relevant references

1. Rolstad B, Naper C, Løvik G, Vaage JT, Ryan JC, Backman-Petersson E et al. Rat NK cell receptor systems and recognition of MHC-I molecules. **Immunol Rev** 2001; 181:149-157.
2. Naper C, Hayashi S, Kveberg L, Niemi EC, Lanier LL, Vaage JT et al. Ly49s3 is a promiscuous activating rat NK receptor for nonclassical MHC class I-encoded target ligands. **J. Immunol.** 169, 22-30. 2002.

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