

T cell-mediated Rejection: Emerging Relationships – Puzzles and Paradoxes

The ability of primed T effector cells to enter and reject an organ remains an important and incompletely understood problem in organ transplantation. Despite the decline in the incidence of T cell-mediated rejection (TCMR), the mechanisms and significance of this process continue to be central to designing and testing new immunosuppressive agents and to the differential diagnosis of many disease states affecting transplant patients. Among the many diseases that must be distinguished from TCMR are viral infections (e.g. hepatitis C, polyoma), inflammation secondary to organ injury, antibody-mediated rejection, “quilty effects” in heart transplants, and many others. Understanding TCMR is also key to understanding many primary organ diseases mediated by cognate T cell recognition of tissue antigens. Thus, a better understanding of TCMR would be most welcome. This symposium will bring together internationally renowned researchers to address current issues in TCMR and the relationships among the many factors affecting this process.

Although the pattern of TCMR in transplant patients is relatively uniform, it can be altered drastically in severely T cell-depleted patients. Overall, the patient’s immunosuppressive regimen does not affect the diagnostic criteria for TCMR. Moreover, in some drug regimens, TCMR does not necessarily affect the graft outcome. Thus, understanding the behaviour of TCMR in the presence of specific immunosuppressive agents, as well as the incidence and consequences of TCMR, is of paramount importance. These topics will be discussed in the first talk of this symposium.

The interaction of the T cell with its environment depends on the interactions of specific integrins with their ligands. This type of signalling plays a critical, and often bidirectional, role as the T cell receives and transmits information. It is therefore important to know how integrins might determine T cell behaviour. Specific examples of how these interactions might influence TCMR will be addressed in the second presentation.

The third presentation will focus on the relationship between alloimmunity and protective immunity. Given that transplant physicians must find a balance between the risk for TCMR and the risk for infections, this is a central issue that needs to be addressed daily in the clinics to ensure optimal patient management. Recent experiences with specific immunosuppressive agents and anti-inflammatory drugs in autoimmune disease have shown that some agents can make the patient vulnerable to specific infections. As experience with new protein drugs, such as costimulation blockers, in transplantation grows, the challenge of understanding how an individual agent affects the risk of specific infectious complication, often in a specific site, grows along with it.

Perhaps the central problem in organ transplantation is how the population of cognate alloreactive T cells against antigens of a specific donor learns to adapt to the persistence of antigen by clonal deletion, anergy and regulation. The clinical lessons from liver transplants are particularly instructive and will be discussed in the last talk of the symposium.

We hope that this journey through the intricacies of TCMR will provide the audience with clinical understanding and spur new research in this complex and important area.

ROTRF Luncheon Satellite Symposium

San Diego Convention Center
San Diego, USA
Room 32 AB
Saturday, May 1, 2010, 12:00 – 13:15



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Moderators: **Robert B. Colvin**, *Harvard Medical School, Boston, USA*
Philip F. Halloran, *University of Alberta, Edmonton, Canada*

12:00 – 12:10 **Introduction**
Philip F. Halloran

12:10 – 12:25 **Patterns of TCMR:
Relationships to Immunosuppression Therapies**
Allan D. Kirk, *Emory University, Atlanta, USA*

12:25 – 12:40 **Integrins and TCMR**
Gregg A. Hadley, *Ohio State University Medical Center,
Columbus, USA*

12:40 – 12:55 **The Intertwined Relationships between Alloimmunity and
Protective Immunity**
Aneesh K. Mehta, *Emory University, Atlanta, USA*

12:55 – 13:10 **Pathology of Rejection versus Acceptance –
Lessons from the Liver**
Anthony J. Demetris, *University of Pittsburgh Medical Center,
Pittsburgh, USA*

13:10 – 13:15 **Closing Remarks**
Robert B. Colvin

Please note that lunch will be provided inside the symposium room before the start of the symposium.

Presented for attendees of the American Transplant Congress.

This symposium is supported by the Roche Organ Transplantation Research Foundation (ROTRF). This is not an official function/event of the American Transplant Congress. There are no charges for admission to this symposium.

For further information on the ROTRF, please visit our **information booth # 721** at ATC 2010 or **www.rotrf.org**