POSTER #
(49)

9th ANNUAL DEPARTMENT OF PATHOLOGY YOUNG INVESTIGATORS’ DAY
POSTER SESSION
Thursday, April 5th, 2007
TURNER CONCOURSE
REGISTRATION FORM

E-mail COMPLETED Registration form and abstract to:
Stacey Morgan (smorgan9@jhmi.edu) on or before
Friday, March 16th, 2007

If you have questions or problems regarding your submission, please contact Stacey
Morgan via e-mail (smorgan9@jhmi.edu)

Applicant’s Name:  Kazunori Murata   Degree: BA
Applicant’s Division:  Immunopathology
Faculty Preceptor:  William Baldwin
(Must hold a primary appointment in Pathology)
Appointment Category:   _____House Staff  _____Clin Fellow  _____Research Fellow
                        _____Medical Student  X Graduate Student (Program: Pathobiology)
Register for:    _____ Clinical Research  ____Translational Research  X Basic Research
Full Poster Title: NON-COMPLEMENT ACTIVATING ALLOANTIBODIES CONTRIBUTE
                  TO CARDIAC ALLOGRAFT REJECTION THROUGH SYNERGISTIC ACTIVATION OF
                  COMPLEMENT

Where has the work been presented?
Meeting Name  American Transplant Congress
Meeting Date  May 5-9, 2007
Not Previously Presented  ______________________________________
Where is this work being published?  ______________________________________
Journal Name, Volume, Page, Date  ______________________________________
In Preparation  ______________________________________
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Abstract Title: NON-COMPLEMENT ACTIVATING ALLOANTIBODIES CONTRIBUTE TO CARDIAC ALLOGRAFT REJECTION THROUGH SYNERGISTIC ACTIVATION OF COMPLEMENT

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Body: The role of non-complement activating alloantibodies in humoral rejection is not completely understood. We hypothesized that non-complement activating alloantibodies synergistically activate complement in conjunction with complement activating antibodies. B10.A hearts were transplanted into immunoglobulin knock out (IgKO) mice reconstituted with high doses of monoclonal MHC class I antibodies of subclass IgG1, IgG2b, or a low dose IgG2b combined with high dose IgG1. Unreconstituted IgKO recipients did not produce antibody, and no C4d was detected in their allografts. Similarly, reconstitution with IgG1 or low dose IgG2b alloantibodies did not cause C4d deposition. However, mice injected with low dose IgG2b combined with IgG1 had heavy linear deposits of C4d on arterial and capillary endothelium. C4d deposits correlated with decreased graft survival. To replicate this synergistic activity in vitro, lymph node cells from B10.A mice were incubated with MHC class I antibodies of IgG subtypes 1, 2a, or 2b, or combinations of IgG1 with either IgG2a or IgG2b. Flow cytometry revealed that both IgG2a and IgG2b synergized with IgG1 to deposit C4d. To investigate a potential mechanism by which IgG1 increased complement activation, non-complement fixing F(ab)2 fragments directed against the light chains of the complement activating antibodies were incubated with low doses of complement activating alloantibodies. Increases in the dosage of F(ab)2 fragments corresponded with significant increases in C4d deposition, suggesting that crosslinking of MHC antigens may be responsible for the synergistic contribution of IgG1 to C4d deposition. In summary, we demonstrate that non-complement activating antibodies can synergize with complement activating antibodies to activate complement in vivo and in vitro. Furthermore, we show that crosslinking of MHC molecules is one mechanism which can result in synergistic complement activation. This suggests an additional role for non-complement activating alloantibodies in humoral rejection.