# Dennis B. Leveson-Gower, Ph.D.

275 Hawthorne Ave, Apt. 144
Palo Alto, CA, 94301
Phone: (650) 380-1544
Email: dleveson@gmail.com
URL: www.DennisLG.com

## SUMMARY

- Accomplished immunologist with specialization in immunoregulation and stem cell transplantation
- Experienced in the use of adoptive cellular therapy to treat cancer in vivo.
- Extensive background in protein biochemistry and molecular biology
- Proven success in establishing, leading, and executing multiple research programs with academic partners
- Experienced mentor

## EDUCATION AND RESEARCH EXPERIENCE

Research Associate and Postdoctoral Fellow, Div. of Bone and Marrow Transplantation 2006-Present
Stanford University School of Medicine
Advisor: Robert S. Negrin, MD

- Applied a powerful imaging approach to study the trafficking of NKT cells in hematopoietic stem cell transplantation (HCT) and discovered novel mechanisms by which NKT cells can regulate graft-versus-host disease (GVHD)
- Discovered that host mast cells have an immunosuppressive role and reduce GVHD after HCT
- Elucidated the mechanism by which a co-stimulatory blockade of T cells promotes the engraftment of in Embryonic and Induced Pluripotent stem cells
- Revealed the mechanisms governing the differential effects of Rapamycin on $CD4^{+}CD25^{+}$ regulatory T cells (Treg) vs. Tcon
- Currently investigating the use of NKT cells in combination with bone marrow transplantation to treat various tumors.

Ph.D., Department of Biochemistry and Molecular Biology 2005
University of British Columbia
Advisor: Victor Ling, Ph.D.

- Adapted a split-enzyme protein complementation assay to the study of ½ ABC transporters and characterized all interactions between members of the TAP family
- After discovering that TAPL protein forms homodimers, discovered its function as a lysosomal peptide transporter

Research Assistant 1999
Howard Hughes Medical Institute at University of Chicago
Advisor: M. Celeste Simon, Ph.D.

- Assisted in the generation of transgenic embryonic stem cells
- Studied the affect of various genes on the survival of cells after inducing ischemia-reperfusion injury

B.Sc. Microbiology 1999
University of Victoria
Advisors: Chris Upton and J.T. Buckley

- Produced and purified large quantities of Taq polymerase
- Performed titers of Vaccinia virus
- Determined effect of various mutations on the hemolytic activity of aerolysin

## MANUSCRIPTS

**Leveson-Gower DB,** Sega EI, Kalesnikoff J, Florek M, Galli S, Negrin RS. Mast cells suppress GVHD in a mechanism involving IL-10 production, but independent of $CD4^+CD25^+$ regulatory T cells. *In Submission.*

**Leveson-Gower DB**, Negrin RS. (2013) In vivo imaging of GVHD and GVL. In BR Blazar, G Socie (Eds.) Immune biology of allogeneic hematopoietic stem cell transplantation. Elsevier. (Book Chapter) *In press.*

Shin HJ, Baker J, **Leveson-Gower DB,** Smith A, Sega EI, Negrin RS. Rapamycin and IL-2 reduces lethal acute graft-versus-host disease associated with increased expansion of donor type $CD4^+CD25^+Foxp3^+$ regulatory T cells. Blood. 2011 Aug 25; 118(8): 2342-50. 2011.

**Leveson-Gower DB,** Olson JA, Sega EI, Luong RH, Baker J, Zeiser R, Negrin RS. Low doses of natural killer T cells provide protection from acute graft-versus-host disease via an IL-4 dependent mechanism. Blood. 2011 Mar 17; 117(11):3320-9.

Pearl JI, Lee A, **Leveson-Gower DB**, Sun N, Ghosh Z, Lan F, Ransohoff J, Negrin RS, Davis MM, Wu JC. Short-term immunosuppression promotes engraftment of embryonic and induced pluripotent stem cells. Cell Stem Cell. 2011 Mar 4;8(3):309-17.

Olson JA, **Leveson-Gower DB**, Gill S, Baker J, Beilhack A, Negrin RS. NK cells mediate reduction of GVHD by inhibiting activated, alloreactive T cells while retaining GVT effects. Blood. 2010 May 27;115(21):4293-301.

Zeiser R, Zambricki E, **Leveson-Gower DB**, Beilhack A, Negrin RS. Host derived interleukin-18 differentially impacts regulatory and conventional T cell expansion during acute graft-versus-host disease. Biology of Blood and Marrow Transplantation. 2007 Dec; 13(12):1427-38

Zeiser R, **Leveson-Gower DB**, Zambricki EA, Kambham N, Beilhack A, Loh J, Hou JZ, Negrin RS. Differential impact of mammalian target of rapamycin inhibition on $CD4^+CD25^+Foxp3^+$ regulatory T cells compared with conventional $CD4^+$ T cells. Blood. 2008 Jan 1;111(1):453-62.

**Leveson-Gower DB,** Michnick SW, Ling V. Detection of TAP Family Dimerizations by an *In Vivo* Assay in Mammalian Cells. Biochemistry. 2004 Nov 9; 43(44):14257-64.

## SELECTED PRESENTATIONS

Emanuela I Sega, **Dennis B Leveson-Gower**, Mareike Florek, and Robert S Negrin. The Inhibitory Receptor LAG-3 is not Essential for Regulatory T Cell Function but Influences Donor T Cell Potency in Acute Graft-Versus-Host Disease. Blood (ASH Annual Meeting Abstracts), Dec, 2011; in press.

Mareike Florek, Emanuela I Sega, Antonia MS Mueller, **Dennis B Leveson-Gower**, Judith A Shizuru, and Robert S Negrin. A Novel Model of Pre-Emptive ECP Treatment Shows Significant Reduction of GVHD-Related Mortality in Mice. Blood (ASH Annual Meeting Abstracts), Dec, 2011; in press.

Lucrezia Colonna, Mareike Florek, **Dennis B Leveson-Gower**, Emanuela I Sega, and Robert S Negrin. IL-17 Gene Ablation Does not Impact Treg-Mediated Suppression of Graft-Versus-Host Disease Following Bone Marrow Transplantation. Blood (ASH Annual Meeting Abstracts), Dec, 2011; in press.

**Dennis B Leveson-Gower**, Emanuela I Sega, Janet Kalesnikoff, Mareike Florek, Stephen J. Galli, and Robert S Negrin. Mast Cells Suppress GVHD in a Mechanism Independent of $CD4^+CD25^+$ Regulatory T cells. ASBMT 2011 BMT Tandem Meetings. BBMT Vol.17 (2) S328.

Mareike Florek, Emanuela I Sega, **Dennis B Leveson-Gower**, Saar Gill, Antonia MS Meuller, and Robert S Negrin. Single Dose Administration of ECP Treated Cells Prior to Transplantation Significantly Increases Survival in a MHC-Mismatched Model of Acute GVHD. ASBMT 2011 BMT Tandem Meetings. BBMT Vol.17 (2) S337-S338.

**Invited Speaker, Dennis B Leveson-Gower**, Emanuela I Sega, Janet Kalesnikoff, Mareike Florek, Stephen J. Galli, and Robert S. Negrin. Mast Cells Reduce GVHD Severity In Allogeneic Transplantation by Reducing the Proliferation of Conventional T Cells. Blood (ASH Annual Meeting Abstracts), Nov, 2010; 116: 243.

Adrianne E. Vasey, Jeanette B. Baker, **Dennis B Leveson-Gower**, and Robert S. Negrin, MD. Similarities in the Initial Events of Murine GVHD Development in a Minor, as Compared to a Major, Mismatch Model of Transplantation. (ASH Annual Meeting Abstracts), Nov, 2010; 116: 3750.

Emanuela I. Sega, **Dennis B Leveson-Gower**, Vu H. Nguyen and Robert S. Negrin. Ex-vivo expanded and freshly isolated $CD4^+CD25^+Foxp3^+$ regulatory T cells suppress murine acute GVHD with different potency. ASBMT 2010 BMT Tandem Meetings. BBMT Vol.16 (2) S163.

**Invited Speaker, Dennis B Leveson-Gower**, Janelle Olson, Emanuela I Sega, Jeanette Baker, Robert Zeiser, and Robert Negrin. GVHD Severity Is Regulated by the Adoptive Transfer Low Numbers of NKT Cells by a Mechanism Distinct From $CD4^+CD25^+$ Regulatory T Cells. Blood (ASH Annual Meeting Abstracts), Nov 2009; 114: 229

Ho-Jin Shin, Jeanette Baker, **Dennis B Leveson-Gower**, Emanuela I Sega, and Robert Negrin. Rapamycin and IL-2 Prevents Lethal Acute Graft-Versus Host Disease by Expansion of Donor Type $CD4^+CD25^+Foxp3^+$ Regulatory T Cells. Blood (ASH Annual Meeting Abstracts), Nov 2009; 114: 1334.

**Invited Speaker, Dennis B Leveson-Gower**, Janelle A Olson, Emanuela I Sega, Jeanette Baker, Robert Zeiser, and Robert Negrin. Adoptive transfer of NKT cells reduces GVHD severity via an IFN-γ and IL-4 dependent mechanism. ASBMT 2009 BMT Tandem Meetings. BBMT Vol.15 (2) S13.

**Invited Speaker, Dennis B Leveson-Gower** "Visualizing Immune Cells in Hematopoietic Stem Cell Transplantation" Small Animal Imaging Workshop at Stanford University, November, 2008.

Janelle A Olson, **Dennis B Leveson-Gower**, Jeanette Baker, Andreas Beilhack, and Robert Negrin. NK Cells Suppress GVHD by Directly Inhibiting Activated Alloreactive T Cells through An NKG2D-Mediated Mechanism. Blood (ASH Annual Meeting Abstracts), Nov 2008; 112: 61.

Emanuela I Sega, **Dennis B Leveson-Gower**, Vu H. Nguyen, and Robert Negrin. Functional Comparison of Freshly Isolated and Ex-Vivo Expanded $CD4^+CD25^+Foxp3^+$ Regulatory T Cells in Suppressing Murine Acute GVHD. Blood (ASH Annual Meeting Abstracts), Nov 2008; 112: 812.

Robert Zeiser, **Dennis B. Leveson-Gower**, Elizabeth A. Zambricki, Jing Z. Hou, and Robert S. Negrin. Differential Impact of mTOR inhibition on $FoxP3^+$ regulatory T cells as compared to conventional T cells after allogeneic bone marrow transplantation. ASBMT 2007 BMT Tandem Meetings. BBMT Vol.13 (2) S17.

**Invited Speaker, Dennis B. Leveson-Gower**, Janelle A. Olson, Jeanette Baker, Robert Zeiser, Andreas Beilhack, and Robert Negrin. NKT Cells Are Potent Regulators of GVHD Following Adoptive Transfer in Allogeneic BMT. Blood (ASH Annual Meeting Abstracts), Nov 2007; 110: 353.

Janelle A. Olson, **Dennis B. Leveson-Gower**, Andreas Beilhack, and Robert S. Negrin. NK Cells Induce Alloreactive Donor T Cell Apoptosis and Decrease Proliferation in GVHD Induction. Blood (ASH Annual Meeting Abstracts), Nov 2007; 110: 2162.

**Invited Speaker,** Robert Zeiser, **Dennis B. Leveson-Gower**, Elizabeth A. Zambricki, Jing-Zhou Hou, and Robert Negrin. Impact of mTOR Inhibition on $FoxP3^+$ Regulatory T Cells as Compared to Conventional T Cells after Allogeneic Bone Marrow Transplantation. Blood (ASH Annual Meeting Abstracts), Nov 2006; 108: 448.

Andreas Beilhack, Robert Zeiser, Stephan Schulz, Janelle A. Olson, Ryosei Nishimura, **Dennis B. Leveson-Gower**, and Robert S. Negrin. Predictive Markers for Acute Graft-Versus-Host Disease in the Peripheral Blood - Surface Receptor Profile Defines Alloreactive T Cells *In Vivo*. Blood (ASH Annual Meeting Abstracts), Nov 2006; 108: 622.

**Dennis Leveson-Gower** and Victor Ling.
Identifying Interactions Between Half ABC Transporters Using an *IN VIVO* Method
Poster at the: British Columbia Cancer Agency Annual Cancer Conference 2003

**Invited Speaker, Dennis Leveson-Gower** and Victor Ling.
An *In Vivo* approach for Identifying Partners of Half ABC Transporters
Short Talk at the: 4th FEBS Advanced Lecture Course. ATP-Binding Cassette (ABC) Proteins: From Multidrug Resistance to Genetic Disease. Gosau, Austria, 2003, page 90

## SKILLS

- Bone marrow transplantation across multiple mouse strains and graft-versus-host disease induction
- Multi-Color Flow Cytometry sorting and analysis: LSRII, FACS ARIA; surface and intracellular staining, etc.
- Serum cytokine analysis by cytometric bead array (CBA) and luminex systems
- In vivo and ex vivo bioluminescence imaging of T cells, tumors, and stem cells.
- Bone Marrow-Derived Mast Cell generation
- In vitro mixed-leukocyte reactions and other in vitro cell-based assays
- Animal Handling: breeding, injections (i.p., i.v., i.m.), anesthesia, etc.
- Animal dissections, H&E staining and histology
- Protocol writing for approval From Animal Care and Use Committee
- Transfection of Mammalian cells, drug selection of colonies, etc.
- Molecular Biology: DNA/RNA purification, cloning (including vector and primer design), PCR, RT-PCR, restriction digests, preparation of competent cells, etc.
- Creation of retrovirus and transduction of insect cells
- Sucrose gradient isolation of lysosomal end ER membranes
- Radiolabelled peptide transport assays with analysis of transport kinetics
- Electrophoresis: SDS-PAGE, Agarose
- Blotting Techniques: Western, E.C.L.
- Cell Culture: Mammalian, Bacterial, and Insect
- Mouse genotyping by Southern Blot and PCR
- Transfection and culture of murine embryonic stem cells
- Ischemia-reperfusion injury of cultured cells.
- Protein Expression and Purification
- Virus titer counts (PFU)
- Hemolytic assays
- Computer Skills: FlowJo, BD Diva and CellQuest, GraphPad Prism, Living Image, MS Office

## AWARDS

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| ASH Travel Award | 2010 |
| ASBMT Travel Grant | 2009 |
| ASH Travel Award | 2009 |
| ASH Travel Award | 2007 |

## REFERENCES AVAILABLE UPON REQUEST