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Education:

- B.A., 1990, Hunter College
- Ph.D., 1996, Stanford University
- Postdoc., 1996-2000, University of California Berkeley

Research Interest:

Gene regulation and genetic engineering of T cells

T cells are the major organizers of the adaptive immune response, and a target of viruses such as HIV and HTLV-1 that cause currently incurable diseases. T cells can also be targeted to eliminate cancer cells in an organism by equipping them (through genetic engineering) with known antigen receptor genes. Such known receptors now exist targeting various cancers including those of prostate, skin and blood cell origin. T cells develop from hematopoeitic stem cells that reside in the bone marrow. This process is governed by incompletely understood gene regulatory mechanisms that execute the T cell genetic program. Our laboratory investigates gene regulation during T cell development. We use both in vivo transgenic mouse models as well as newly developed technology for in vitro T cell development from embryonic stem cells. Our focus has been on the regulation of the gene locus encoding the alpha chain of the T cell receptor (TCRa), particularly its locus control region (LCR). Appropriately regulated expression of the TCRa gene is essential for the development of virtually all of the circulating T cells in the body. The TCRa LCR has powerful properties that provide a linked gene with a predictable pattern of gene expression, in terms of level, developmental timing and cell-type distribution. It also bears a strong, but poorly understood, insulation capacity that provides LCR-linked transgenes with integration site-independence when inserted into the genome. Our work to date has identified numerous sub-sequences of the TCRa LCR that support its various properties. Molecular investigations of these sequence elements (and their interactions) are expected to reveal components required for generating proper TCRa gene regulation in vivo and completion of T cell development. Through our translational research collaborations, our work will also provide tools to establish robust, predictable and specific therapeutic gene expression in T cells via eventual gene therapy applications targeted at specific cancer cell types and T cell viral diseases. Our lab's reagents and technologies have enabled us to additionally contribute to collaborations with other groups investigating important aspects of T cell development and function.

Selected Publications

- Kucerová-Levisohn M, Knirr S, Mejia RI and Ortiz BD. (2015) The 3'-J-alpha region of the TCR-alpha locus bears gene regulatory activity in thymic and peripheral T cells. PLoS ONE
10(7):e0132856.

- Lahiji A, Kucerová-Levisohn M, Holmes R, Zúñiga-Pflücker JC and Ortiz BD. (2014) Adapting *in vitro* embryonic stem cell differentiation to the study of locus control regions.

J. Immunol. Methods. 407:135-45.

- Kucerová-Levisohn M, Lovett J, Lahiji A, Holmes R, Zúñiga-Pflücker JC and Ortiz BD. (2014) Derivation of T cells in vitro from mouse embryonic stem cells. J. Vis. Exp. (JoVE).92.doi:10.3791/52119.

- Ortiz, BD. (2014) Recent advances in approaches to the study of gene locus control regions. In: Toni B, ed. *New Frontiers of Multidisciplinary Research in Science, Technology, Engineering, Agriculture, Mathematics and Health.*
Springer Proceedings in Mathematics and Statistics
.
90:189-204.

- Lahiji A, Kucerová-Levisohn M, Lovett J, Holmes R, Zúñiga-Pflücker JC and Ortiz BD. (2013) Complete TCR-alpha gene locus control region activity in T cells derived *in vitro* from embryonic stem cells.
J. Immunol
. 191:472-9.

- Arsov I, Adebayo A, Kucerova-Levisohn M, Haye J, Macneil M, Papavasiliou FN, Yue Z, Ortiz BD. (2011) A Role for Autophagic Protein Beclin 1 Early in Lymphocyte Development. J Immunol. 186:2201-9.
- Knirr S, Gomos-Klein J, Andino BE, Harrow F, Erhard KF, Kovalovsky D, Sant'Angelo DB, Ortiz BD. (2010) Ectopic T cell receptor-alpha locus control region activity in B cells is suppressed by direct linkage to two flanking genes at once. PLoS One. 5(11):e15527.

- Kovalovsky D, Pezzano M, Ortiz BD, Sant'Angelo DB. (2010) A novel TCR transgenic model reveals that negative selection involves an immediate, Bim-dependent pathway and a delayed, Bim-independent pathway. PLoS One. 5(1):e8675
- Gomos-Klein J, Harrow F, Alarcón J, Ortiz BD (2007) CTCF-independent, but not CTCF-dependent, elements significantly contribute to TCR-alpha locus control region activity.
J. Immunol
. 179:1088-95.

- Harrow F, Ortiz BD. (2005) The TCR-alpha locus control region specifies thymic, but not peripheral, patterns of TCRalpha gene expression. J. Immunol. 175:6659-67.
- Harrow F, Amuta JU, Hutchinson SR, Akwaa F, Ortiz BD. (2004) Factors binding a non-classical Cis-element prevent heterochromatin effects on locus control region activity.
J. Biol. Chem
. 279:17842-9.

- Ortiz BD, Harrow F, Cado D, Santoso B, Winoto A. (2001) Function and factor interactions of a locus control region element in the mouse T cell receptor-alpha/Dad1 gene locus. J. Immunol
. 167:3836-45.