

General Information

11.15.2004

Name: Igor M. Leykin

Office Address:

Joslin Diabetes Center
Bioinformatics Core, #640B
One Joslin Place
Boston, MA 02215
Tel: (617) 713-3492

Home Address:

200 Swanton Street, #338
Winchester, MA 01890
Tel: (781) 729-5788

E:Mail: Igor.Leykin@joslin.harvard.edu

FAX: (617) 432-5619

Place of Birth: Vitebsk, Belarus

Education:

1999	Ph.D. Immunology	Weizmann Institute of Science, Israel
1984	M.D.	Vitebsk State Medical University, Belarus

Postdoctoral Training:

2004-current	Director	Bioinformatics	Joslin Diabetes Center
2000-2004	Research Fellow	Bioinformatics	Harvard School of Public Health
1999-2000	Research Fellow	Immunology	Massachusetts General Hospital
1991-1992	Clinical Resident	Psychiatry	Mental Health Center "Beer-Yakov", Israel

Licensure and Certification:

Permanent License for Medical Practice, Israel

Professional Societies:

2001	The International Society for Computational Biology	Member
------	---	--------

Awards:

2000	The Diabetes Action Research and Education Foundation (DAREF) Research Grant
------	--

Research, Teaching, and Clinical Contributions

In line with the autoimmune hypothesis of schizophrenia I have studied whether the commonly used neuroleptics can also act as systemic immunosuppressants. Conventional in vitro mitogenic stimulation of peripheral blood lymphocytes (PBL) from schizophrenic patients treated with either clozapine or haloperidol indicated a clear suppression of responsiveness of approximately 50% in all patients. Haloperidol and clozapine are also shown to inhibit stimulation of lymphocytes in vitro. Heat shock protein-60 (HSP60) is implicated in several autoimmune diseases as a triggering antigen. I have examined cellular and humoral responses against HSP60 and a series of its peptide fragments with PBL of schizophrenic patients and healthy subjects. With HSP60 and one of its peptide the average stimulation index of PBL from schizophrenic patients was significantly higher than that obtained for control subjects.

Bone marrow transplantation (BMT) from diabetes-resistant strains with complete replacement of the recipient immune system by the allogeneic donor has led to tolerance to donor islets and cure of diabetes in a mouse model of type 1 diabetes. I have demonstrated that nonmyeloablative conditioning achieves mixed hematopoietic chimerism across MHC barriers in spontaneously diabetic NOD mice. This conditioning preserves alloreactive and autoreactive diabetogenic host NOD T-cells, but when mixed chimerism was established, diabetic NOD mice accepted donor-type allogeneic islet grafts and were cured of diabetes, despite a significant recipient T-cell contribution. Furthermore, induction of mixed chimerism permitted acceptance of NOD islet grafts, demonstrating reversal of autoimmunity. Allogeneic BMT was critical for tolerization of diabetogenic and alloreactive host T-cells. Thus, mixed hematopoietic chimerism induces tolerance to donor islets and reverses established autoimmunity in diabetic NOD mice.

A common and fundamental problem in promoter analysis is determination of transcription start sites. In my approach, I have defined the transcription start sites of human and mouse genes based on the Ensembl EST GeneBuilder, which maps ESTs to the genome and then processes by merging the redundant ESTs. I have selected a subset of 5'-reliable resulting transcripts using stringent criteria for more accurate transcription start site predictions and then extracted upstream sequence for such transcripts. Using such a subset I have constructed databases of promoter sequences useful for understanding the transcriptional regulation of genes. I have developed software for analysis of corresponding promoter regions of co-regulated genes. For numerous projects I have identified significant binding sites (and their combinations) using the weight matrices of known transcription factors.

The identification of disease-associated genes using single nucleotide polymorphisms (SNPs) has been reported. In particular, Affymetrix Mapping 10K oligonucleotide SNP microarray (10K SNP array) platform uses one PCR primer to determine the genotype of more than 11,000 SNPs in the human genome. I have developed the accessory software for automated formatting 10K SNP array data and calling multi-point linkage analysis software Merlin, GeneHunter and Allegro, and visualizing the results in dChip in the context of genes and cytobands. I have analyzed several families with focal segmental glomerulosclerosis where I have confirmed one of the previously identified loci in chromosome 1 and identified a novel locus on chromosome 3.

Current Research Activities:

Microarray Data Analysis	Project Leader
Promoter Analysis of Co-Regulated Genes	Project Leader
Software Developing for Multi-Point Linkage Analysis	Project Leader

Teaching:

2000 – 2004	Supervisor for graduate students and fellows	Harvard School of Public Health
-------------	--	---------------------------------

Invited Presentations:

1998	Seminar	Yale University School of Medicine
1998	Seminar	Albert Einstein College of Medicine
1998	Seminar	Massachusetts General Hospital/ Harvard Medical School
2001	Invited Lecture	Specialized Program of Research Excellence in Breast Cancer
2002	Seminar	Torrey Mesa Research Institute (Syngenta Biotechnology Inc.)
2002	Invited Lecture	Millennium Pharmaceuticals, Inc.
2003	Invited Lecture	Repromedix Corporation

Clinical Activities:

1991-1992 Clinical Resident in Psychiatry at Mental Health Center "Beer - Ya'akov", Israel. Introduced new biochemical-based diagnostic methods for schizophrenia and obsessive-compulsive disorder.

Bibliography

Original Articles:

1. Deckmann M, Shinitzky M, Leykin I, Cheng D, Guy J. Humoral and cellular response against autologous platelets in schizophrenia - clinical and pathophysiological implications. *Italian Journal of Psychiatry and Behavioural Sciences* 1996;6:29-34.
2. Levine J, Gutman J, Feraro R, Levy P, Kimhi R, Leykin I, Deckmann M, Handzel ZT, Shinitzky M. Side effect profile of azathioprine in the treatment of chronic schizophrenic patients. *Neuropsychobiology* 1997;36:172-6.
3. Leykin I, Mayer R, Shinitzky M. Short and long term immunosuppressive effects of clozapine and haloperidol. *Immunopharmacology* 1997;37:75-86.
4. Peled A, Leykin I, Deckmann M, Shinitzky M. Evaluation of immune memory of human lymphocytes engrafted in SCID mice. *Immunobiology* 1999;201:145-50.
5. Leykin I, Spivak B, Weizman A, Cohen IR, Shinitzky M. Elevated Cellular Immune Response to Human Heat-Shock Protein-60 in Schizophrenic Patients. *European Archive of Psychiatry and Clinical Neuroscience* 1999;249:238-46.
6. Waner T, Leykin I, Shinitzky M, Sharabani E, Buch H, Keysari A, Bark H, Harrus S. Detection of platelet-bound antibodies in beagle dogs after artificial infection with *Ehrlichia canis*. *Veterinary Immunology and Immunopathology* 2000;77:145-50.
7. Storch K-F, Lipan O, Leykin I, Viswanathan N, Davis FC, Wong WH, Weitz CJ. Extensive and divergent circadian gene expression in liver and heart. *Nature* 2002;417:78-83.
8. Koeller KM, Haggarty SJ, Perkins B, Leykin I, Wong JC, Kao M-CJ, Schreiber SL. Chemical genetic modifier screens: small molecule trichostatin suppressors as probes of acetylation in transcription, cell cycle progression, and stability of the cytoskeleton. *Chemistry and Biology* 2003;10:397-410.

9. Nikolic B, Takeuchi Y, Leykin I, Fudaba Y, Smith RN, Sykes M. Mixed Hematopoietic Chimerism Allows Cure of Autoimmune Diabetes Through Allogeneic Tolerance and Reversal of Autoimmunity. *Diabetes* 2004;53:376-83.
10. Leykin I, Hao Ke, Meyer N, Cheng J, Pollak M, Smith R, Wong WH, Rosenow C, Li C. dChipLinkage: Parametric Linkage Analysis and Visualization of High-Density Oligonucleotide SNP Array Data. *Submitted to BMC Genetics*, 2004.
11. Leykin I, Kao M, Wong WH. *HumanUpstream* and *MouseUpstream*, a Databases of Promoter Sequences in the Human and Mouse Genomes, for the Identification of *cis*-Regulatory Elements and Their Combinations. *Submitted to OMICS*, 2004.

Proceedings of Meetings:

1. Leykin I, Nikolic B, Sykes M. Mixed Bone Marrow Chimerism as a Treatment for Autoimmune Diabetes. Proceedings of the International Society of Transplantation Meeting; 2000 Aug 27 – Sept 1; Rome, Italy. *Transplantation Proceedings* 2001;33:120.

Chapters:

1. Shinitzky M, Leykin I, Deckmann M. Autoimmunity against platelets in schizophrenia. In: Y. Shoenfeld, editor. *The Decade of Autoimmunity*. Elsevier, 1999. p. 277-84.

Clinical Communications:

1. Levine J, Susnovski M, Handzel ZT, Leykin I, Shinitzky M. Treatment of schizophrenia with an immunosuppressant. *Lancet* 1994;344:59-60.

Thesis:

1. Leykin I. Characterization of autoimmune elements in the pathogenesis of schizophrenia. PhD Thesis. Weizmann Institute of Science, Israel. 1999.

Patents:

1. Leykin I, Shinitzky M, Deckmann M, inventors. Peptides derived from heat shock protein 60 for the diagnosis of schizophrenia. PCT WO 97/01959. 1997.
2. Shinitzky M, Cohen IR, Leykin I, inventors. Use of a peptide derived from heat shock protein 60 for treatment of schizophrenia. PCT Int. Appl. PCT/IL2000/035. 2000

Abstracts:

1. Igor Leykin, Ming-Chih Kao and Wing Hung Wong. Identification of *cis*-regulatory Elements and Their Combination in Mammalian Promoter Sequences. *Currents in Computational Molecular Biology* 2002;p117.