Profile Yehudit Bergman

Place of birth: Tel Aviv, Israel
Scientific training: Ph.D. -Weizmann Institute of Science, Rehovot, Israel; Post-doc -Stanford University, Stanford, CA, USA; Post-doc -M.I.T., Boston, MA, USA.
Former supervisors: Ron Levy, Stanford, CA, USA, David Baltimore, Caltech, CA, USA.
Present affiliation: The Hebrew University Medical School, Jerusalem, Israel
Email: yberg@md.huji.ac.il
Website: http://cancer-research.huji.ac.il/AcademicStaff/Bergman/index.html
Laboratory: 8 students and 2 post-docs

Brief CV -Yehudit Bergman

Yehudit Bergman is a professor at the Hebrew University Medical School in Jerusalem where she holds the Morley Goldblatt Chair for Cancer Research. She is an elected representative of the medical school to the Hebrew University senate and is a member of the University's standing committee. Dr. Bergman is also a member of EMBO. She completed her Ph.D. studies in immunology at the Weizmann Institute of Science in Rehovot, Israel in 1980. She then trained as a post-doc in immunology at Stanford and as a post-doc in molecular biology at M.I.T. Dr. Bergman's current research focuses on the epigenetic mechanisms controlling immunoglobulin allelic exclusion and the cancer-related activity of the Oct-3/4 transcription factor.

Research Focus: Epigenetic Mechanisms Controlling Immunoglobulin Allelic Exclusion

Monoallelic gene expression, or allelic exclusion, is critical to the functioning of the immune system as it allows each lymphocyte to elaborate a single type of antigen receptor. Chaos in immune system regulation might ensue if, for example, a B cell expressed both an antibody that responded to a pathogen and a second antibody that would cause damage to a certain host system. It has been proposed that the major pathway for implementing this choice involves a feedback mechanism, which prevents rearrangement on the remaining germ line allele. While this mechanism may certainly play a maintenance role in inhibiting rearrangement on the second allele, our studies provide evidence suggesting that the process of allelic exclusion may actually begin early in development, at about the time of implantation, when the antigen receptor genes begin asynchronously replicating in each cell. This pattern is established randomly in each cell, is maintained in a clonal manner and may serve as the basis for the initially choice of one copy that will undergo subsequent epigenetic changes and rearrangement. Furthermore, we have shown that during B cell development, the Igk locus undergoes a programmed process, which releases multiple layers of repression in a step-wise manner and culminates in the increased accessibility of recombination signal sequences to the rearrangement machinery. Our aim is to decipher the molecular events that translate the timing of asynchronous replication into subsequent epigenetic changes that allow rearrangement on one allele.

Oct-3/4, Embryonal Stem (ES) Cells and Cancer

We are studying the molecular genetic and epigenetic mechanisms that regulate Oct-3/4 expression. Oct-3/4 is a member of the POU homeodomain family of

transcription factors that are critical to embryonic development. Oct-3/4 is involved in maintaining the pluripotent state of ES cells. We have shown that the Oct-3/4 gene undergoes a novel multi-step program of inactivation following implantation. Transcriptional repression is followed by a dramatic increase in histone H3 methylation of Lysine 9 that is mediated by the SET-containing protein, G9a. This step sets the stage for local heterochromatinization through the binding of HP1 and is required for subsequent de novo methylation at the promoter by the enzymes Dnmt3a/3b. Genetic studies have shown that these epigenetic changes actually play an important role by inhibiting Oct-3/4 re-expression, thereby preventing reprogramming. We have also shown that Oct-3/4 is expressed in all human testicular germ cell tumors (GCTs) examined, even in the early pre-malignant component. We have demonstrated that Oct-3/4 dictates ES cells' oncogenic potential in a dose-dependent manner; it is a dose-dependent oncogene.

Publications – Last 3 years -Yehudit Bergman

1: Schlesinger Y, Straussman R, Keshet I, Farkash S, Hecht M, Zimmerman J, Eden E, Yakhini Z, Ben-Shushan E, Reubinoff BE, Bergman Y, Simon I, Cedar H. Polycombmediated methylation on Lys27 of histone H3 pre-marks genes for de novo methylation in cancer. Nat Genet. 2007 Feb;39(2):232-6.

2: Fraenkel S, Bergman Y. Variability and exclusion in host and parasite: epigenetic regulation of Ig and var expression. J Immunol. 2006 Nov 1;177(9):5767-74.

3: Feldman N, Gerson A, Fang J, Li E, Zhang Y, Shinkai Y, Cedar H, Bergman Y. G9amediated irreversible epigenetic inactivation of Oct-3/4 during early embryogenesis. Nat Cell Biol. 2006 Feb;8(2):188-94.

4: Goldmit M, Ji Y, Skok J, Roldan E, Jung S, Cedar H, Bergman Y. Epigenetic ontogeny of the Igk locus during B cell development. Nat Immunol. 2005 Feb;6(2):198-203.

5: Bergman Y, Cedar H. A stepwise epigenetic process controls immunoglobulin allelic exclusion. Nat Rev Immunol. 2004 Oct;4(10):753-61.

6: Goldmit M, Bergman Y. Monoallelic gene expression: a repertoire of recurrent themes. Immunol Rev. 2004 Aug;200:197-214.

Selected Publications in Immunology:

Mostoslavsky, R., Singh, N., Tenzen, T., Goldmit, M., Gabay, C., Elizur, S., Qi, P., Reubinoff, B. E., Chess, A., Cedar, H. and Bergman, Y. (2001) Asynchronous replication and allelic exclusion in the immune system. Nature 414:221-225.

Highlight on #37. Bell, J. (2001) Out of sync. Nature Reviews Immunology 1:169.

Dispatch on #37. Rada, C. and Ferguson-Smith, A. C. (2002) Epigenetics: monoallelic expression in the immune system. Current Biology 12:R108-R110.

Selected Publications in Stem Cell Biology:

Gidekel, S., Pisov, G, Bergman, Y. and Pikarsky, E. (2003) Oct-3/4 is a dose-dependent oncogenic fate determinant. Cancer Cell 4:361-370. (Featured Article)

Preview on #43. Abate-Shen, C. (2003) Homeobox genes and cancer: New OCTaves for an old tune. Cancer Cell 4:329-330.

News on #43. Holding C. (2003) Embryos and cancer -Early embryonic pluripotency gene controls malignant phenotype in germ cells. The Scientist December 3, 2003.

Highlight on #43. Greenwood E. (2003) Oncogenes -Determining fate. Nature Reviews Cancer (in press).