Stanford

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Bio

BIO

For the past 20 years Ayelet has been researching development, stem cell mediating regeneration processes, and immunology in the colonial tunicate Botryllus schlosseri. As a PHD student in the Technion and IOLR (Israel) Ayelet discovered a method to extend the life span of the Botryllus colonies and suggested that this treatment affects the stem cells of the treated colonies. She became a post-doctoral fellow at the Tunicate lab of Irv Weissman in Stanford Hopkins Marine Station and studied stem cell mediating developmental processes. She isolated the first adult stem cell niche and the first germline stem cell niche in this organism. Since 2009 Ayelet has been leading and supervising the Botryllus studies in HMS and directed the Botryllus genome project with teams from the labs of Irv Weissman, Steve Quake and several international laboratories. In processing the Botryllus genome they developed a novel method for high-throughput sequencing of repeat-rich genomes (called Moleculo / LRseq; acquired by Illumina). Having the genome in hand Ayelet and her collaborators looked for the gene that controls immune recognition in the colonies and allows or prevents fusion of blood vessels between colonies. They isolated the BHF, a single polymorphic gene that allows Botryllus colonies to distinguish self from non-self. Recently, Ayelet and her collaborators began characterizing the Botryllus hematopoietic and immune system at the cellular and molecular levels and succeeded in identifying the hematopoietic stem cells (HSCs), myeloid cell lineage progenitors, cytotoxic cells that induce cellular tissue rejection, and the hematopoietic organ.

Using the resources and tools she and others developed Ayelet continues studying the BHF, the evolution of blood borne immune system, and stem cell mediated regeneration programs.

CURRENT ROLE AT STANFORD

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EDUCATION AND CERTIFICATIONS

- Postdoctoral Fellow, Stanford University, Stanford, California , Stem Cell Biology (2006)
- Ph.D, Technion, Israel institute of technology, Haifa , Cell Biology (2001)
- M.Sc, Tel-Aviv University, Tel-Aviv, Israel , Zoology (1995)
- B.Sc, The Hebrew University of Jerusalem, Israel , Animal science (1991)

PATENTS

- Ayelet Voskoboynik; Dmitry Pushkarev, Stephen Quake. "United States Patent 61/532,882; International application No. PCT/US2012/054461 Methods for obtaining a sequence. US 61/532,882, filed September 9, 2011(Pending); International application No. PCT/US2012/054461, filled September 10, 2012 (Pending); United Kingdom patent application 1216076.8 filed September 10, 2012 (Pending)"

LINKS

- https://marinestemcell.stanford.edu/: https://marinestemcell.stanford.edu/
- Botryllus schlosseri genome browser: http://botryllus.stanford.edu/botryllusgenome/
- http://botryllus.stanford.edu/index.html: http://botryllus.stanford.edu/index.html

Professional

PROFESSIONAL INTERESTS

The B. schlosseri genome project

Urochordates like B. schlosseri are considered to be the closest living invertebrate relatives of vertebrates. Using a novel method for high-throughput sequencing of eukaryotic genomes, we sequenced and assembled 580 Mbp of the B. schlosseri genome. The genome assembly is comprised of nearly 14,000 intron-containing predicted genes, and 13,500 intron-less predicted genes, 40% of which could be confidently parceled into 13 (of 16 haploid) chromosomes. A comparison of homologous genes between B. schlosseri and other diverse taxonomic groups revealed genomic events underlying the evolution of vertebrates and lymphoid-mediated immunity. The B. schlosseri genome is a community resource for studying alternative modes of reproduction, natural transplantation reactions, and stem cell-mediated regeneration (Voskoboynik et al., 2013).

BHF and the evolution of allorecognition

This study focuses on genes, cells, and pathways that regulate allogeneic recognition and tolerance induction in B. schlosseri. Botryllus colonies have a defined vasculature with circulating blood cells. Self-recognition between compatible colonies leads to formation of parabionts with a common vasculature, whereas incompatible colonies will reject one another. As described above we identified the single gene that determine the fusion vs. rejection reaction, BHF. The BHF

sequence suggests that it is neither a membrane-bound nor secreted protein, as would be expected of a gene that controls self–nonself recognition (e.g., MHC). Therefore study of this gene will likely reveal new mechanisms of recognition. We developed BHF monoclonal antibodies and recombinant BHF proteins and are currently using flow cytometry, diverse immunological essays, whole-transcriptome sequencing, and computational methods to characterize the BHF pathway (Voskoboynik and Newman et al., 2013). Recently we began characterizing the B. schlosseri hematopoietic and immune system at the cellular and molecular levels. We did it by deploying advanced genomics, live imaging and classical immunological methods including multi-parameter flow cytometric isolation of cellular populations, cell sorting, transplantation assays as well as phagocytosis and cytotoxicity measurement. We identified the hematopoietic stem cells (HSCs), myeloid cell lineage progenitors, cytotoxic cells that induce cellular tissue rejection, and discovered the Botryllus hematopoietic niche showing that it is homologous to human hematopoietic bone marrow (Rosental and Kowarsky et al. 2018).

Publications

PUBLICATIONS

- **Sexual and asexual development: two distinct programs producing the same tunicate.** *Cell reports*
  Kowarsky, M. n., Anselmi, C. n., Hotta, K. n., Burighel, P. n., Zaniolo, G. n., Caicci, F. n., Rosental, B. n., Neff, N. F., Ishizuka, K. J., Palmeri, K. J., Okamoto, J. n., Gordon, T. n., Weissman, et al
  2021; 34 (4): 108681

- **Complex mammalian-like haematopoietic system found in a colonial chordate.** *Nature*
  Rosental, B. n., Kowarsky, M. n., Seita, J. n., Corey, D. M., Ishizuka, K. J., Palmeri, K. J., Chen, S. Y., Sinha, R. n., Okamoto, J. n., Mantalas, G. n., Manni, L. n., Raveh, T. n., Clarke, et al
  2018

- **Identification of a colonial chordate histocompatibility gene.** *Science*
  Voskoboynik, A., Newman, A. M., Corey, D. M., Sahoo, D., Pushkarev, D., Neff, N. F., Passarelli, B., Koh, W., Ishizuka, K. J., Palmeri, K. J., Dimov, I. K., Keasar, C., Fan, et al
  2013; 341 (6144): 384-387

- **Repeated, Long-Term Cycling of Putative Stem Cells between Niches in a Basal Chordate** *DEVELOPMENTAL CELL*
  Rinkevich, Y., Voskoboynik, A., Rosner, A., Rabinowitz, C., Paz, G., Oren, M., Douek, J., Alfassi, G., Moiseeva, E., Ishizuka, K. J., Palmeri, K. J., Weissman, I. L., Rinkevich, et al
  2013; 24 (1): 76-88

- **The genome sequence of the colonial chordate, Botryllus schlosseri.** *eLife*
  Voskoboynik, A., Neff, N. F., Sahoo, D., Newman, A. M., Pushkarev, D., Koh, W., Passarelli, B., Fan, H. C., Mantalas, G. L., Palmeri, K. J., Ishizuka, K. J., Gissi, C., Griggio, et al
  2013; 2

- **Identification of the Endostyle as a Stem Cell Niche in a Colonial Chordate** *CELL STEM CELL*
  Voskoboynik, A., Soen, Y., Rinkevich, Y., Rosner, A., Ueno, H., Reshef, R., Ishizuka, K. J., Palmeri, K. J., Moiseeva, E., Rinkevich, B., Weissman, I. L.
  2008; 3 (4): 456-464

- **Striving for normality: whole body regeneration through a series of abnormal generations** *FASEB JOURNAL*
  Voskoboynik, A., Simon-Blecher, N., Soen, Y., Rinkevich, B., De Tomaso, A. W., Ishizuka, K. J., Weissman, I. L.
  2007; 21 (7): 1335-1344

- **Botryllus schlosseri as a Unique Colonial Chordate Model for the Study and Modulation of Innate Immune Activity.** *Marine drugs*
  Goldstein, O., Mandujano-Tinoco, E. A., Levy, T., Talice, S., Raveh, T., Gershoni-Yahalom, O., Voskoboynik, A., Rosental, B.
  2021; 19 (8)

- **Stem Cells and Innate Immunity in Aquatic Invertebrates: Bridging Two Seemingly Disparate Disciplines for New Discoveries in Biology.** *Frontiers in immunology*
  Ballarin, L., Karahan, A., Salvetti, A., Rossi, L., Manni, L., Rinkevich, B., Rosner, A., Voskoboynik, A., Rosental, B., Canesi, L., Anselmi, C., Pinsino, A., Tohumcu, et al
  2021; 12: 688106

- **Evolutionary perspective on the hematopoietic system through a colonial chordate: allogeneic immunity and hematopoiesis.** *Current opinion in immunology*

Rosental, B., Raveh, T., Voskoboynik, A., Weissman, I. L.
2020; 62: 91–98

- **Sixty years of experimental studies on the blastogenesis of the colonial tunicate Botryllus schlosseri** *DEVELOPMENTAL BIOLOGY*
  Manni, L., Anselmi, C., Cima, F., Gasparini, F., Voskoboynik, A., Martini, M., Peronato, A., Burighel, P., Zaniolo, G., Ballarin, L.
  2019; 448 (2): 293–308

- **Natural Chimerism and Tolerance Induction in a Colonial Chordate** *Advances in Comparative Immunology*
  Voskoboynik, A., Newmab, A. M., Kowarsky, M., Weissman, I. L.
  Springer .2018: 18

- **Developmental cell death programs license cytotoxic cells to eliminate histocompatible partners** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Corey, D. M., rosental, B., Kowarsky, M., Sinha, R., Ishizuka, K. J., Palmeri, K. J., Quake, S. R., Voskoboynik, A., Weissman, I. L.
  2016; 113 (23): 6520-6525

- **Characterization of Ambra1 in asexual cycle of a non-vertebrate chordate, the colonial tunicate Botryllus schlosseri, and phylogenetic analysis of the protein group in Bilateria** *MOLECULAR PHYLOGENETICS AND EVOLUTION*
  Gasparini, F., Skobo, T., Benato, F., Gioacchini, G., Voskoboynik, A., Carnevali, O., Manni, L., Valle, L. D.
  2016; 95: 46-57

- **Botryllus schlosseri, an emerging model for the study of aging, stem cells, and mechanisms of regeneration** *INVERTEBRATE REPRODUCTION & DEVELOPMENT*
  Voskoboynik, A., Weissman, I. L.
  2015; 59: 33-38

- **Guidelines for the Nomenclature of Genetic Elements in Tunicate Genomes** *GENESIS*
  Stolfi, A., Sasakura, Y., Chalopin, D., Satou, Y., Christiaen, L., Dantec, C., Endo, T., Naville, M., Nishida, H., Swalla, B. J., Volff, J., Voskoboynik, A., Dauga, et al
  2015; 53 (1): 1-14

- **Botryllus schlosseri, an emerging model for the study of aging, stem cells, and mechanisms of regeneration.** *Invertebrate reproduction & development*
  Voskoboynik, A. n., Weissman, I. L.
  2015; 59 (sup1): 33–38

- **Ontology for the Asexual Development and Anatomy of the Colonial Chordate Botryllus schlosseri** *PLOS ONE*
  Manni, L., Gasparini, F., Hotta, K., Ishizuka, K. J., Ricci, L., Tiozzo, S., Voskoboynik, A., Dauga, D.
  2014; 9 (5)

- **Ascidian Mitogenomics: Comparison of Evolutionary Rates in Closely Related Taxa Provides Evidence of Ongoing Speciation Events** *GENOME BIOLOGY AND EVOLUTION*
  Griggio, F., Voskoboynik, A., Iannelli, F., Justy, F., Tilak, M., Xavier, T., Pesole, G., Douzery, E. J., Mastrototaro, F., Gissi, C.
  2014; 6 (3): 591-605

- **Chimerism a natural ability to tolerate kin, evolutionary traits connecting mammalian and protochordates** *ISJ-INVERTEBRATE SURVIVAL JOURNAL*
  Voskoboynik, A.
  2009; 6 (1): S9-S20

- **Stem Cells, Chimerism and Tolerance: Lessons from Mammals and Ascidians** *Stem Cells in Marine Organisms*
  Voskoboynik, A., Rinkevich, B., Weissman, I. L.
  Springer Netherlands.2009: 281–308

- **A conserved role of the VEGF pathway in angiogenesis of an ectodermally-derived vasculature** *DEVELOPMENTAL BIOLOGY*
  Tiozzo, S., Voskoboynik, A., Brown, F. D., De Tomaso, A. W.
  2008; 315 (1): 243-255

- **BS-Cadherin in the colonial urochordate Botryllus schlosseri: One protein, many functions** *DEVELOPMENTAL BIOLOGY*
  Rosner, A., Rabinowitz, C., Moiseeva, E., Voskoboynik, A., Rinkevich, B.
  2007; 304 (2): 687-700

- **fester, a Candidate allorecognition receptor from a primitive chordate** *IMMUNITY*

Nyholm, S. V., Passegue, E., Ludington, W. B., Voskoboynik, A., Mitchel, K., Weissman, I. L., De Tomaso, A. W.
2006; 25 (1): 163-173

- **Macrophage involvement for successful degeneration of apoptotic organs in the colonial urochordate Botryllus schlosseri** *JOURNAL OF EXPERIMENTAL BIOLOGY*
  Voskoboynik, A., Rinkevich, B., WEISS, A., Moiseeva, E., Reznick, A. Z.
  2004; 207 (14): 2409-2416

- **Rejuvenescence and extension of an urochordate life span following a single, acute administration of an anti-oxidant, butylated hydroxytoluene** *MECHANISMS OF AGEING AND DEVELOPMENT*
  Voskoboynik, A., Reznick, A. Z., Rinkevich, B.
  2002; 123 (9): 1203-1210