BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Landfear, Scott M.	University Professor
eRA COMMONS USER NAME (credential, e.g., agency login) LANDFEARS	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Chicago	A.B.	06/72	Chemistry
Harvard University	A.M.	03/74	Chemistry
Harvard University	Ph.D.	06/78	Biochemistry
MIT	Postdoc	06/82	Molecular Biology
Harvard School of Public Health	Postdoc	06/85	Molecular Parasitology

A. Personal Statement

For many years my laboratory has studied membrane transport proteins that play central roles in import of critical nutrients for *Leishmania* and the African trypanosomes. We have cloned and functionally expressed genes for hexose transporters, *myo*-inositol transporters, purine nucleoside and nucleobase transporters, etc. in various species of parasites. The laboratory has developed considerable expertise in functional analysis of transporters, using heterologous systems such as yeast and *Xenopus* oocytes as well as complemented knock out lines of the parasites. We have employed many molecular genetic and biochemical approaches for studying transporters, including gene knockout technology, site-directed mutagenesis, antibody generation for subcellular localization, electrophysiology, etc. We have employed mass spectrometry to identify proteins whose expression is modulated in glucose transporter null mutants of *L. mexicana*, and we have used TAP-tagging and mass spectrometry to identify the KHARON1 protein that interact with the flagellar targeting domain of a flagellar glucose transporter and with other flagellar membrane proteins. We routinely employ the murine model for cutaneous leishmaniasis to evaluate the virulence phenotypes of various Leishmania mutants and add back lines. I have successfully obtained and administered NIH grants since 1987 and have led my research group since that time. In addition to primary research publications, I have been invited to write a variety of review articles on permeases in parasitic protozoa and their role in pathogenesis. I have been a member of the NIH Eukaryotic Pathogens Study Section and continue to review grants for NIH and other funding organizations.

B. Positions and Honors

Positions and Employment

1982-1984 Instructor, Biology of Parasitism, Marine Biological Laboratories, Woods Hole, MA (summers)
7/85-1/87 Research Associate in Tropical Public Health, Harvard School of Public Health, Boston, MA
2/87-6/93 Assistant Professor of Microbiology, Oregon Health & Science University, Portland, OR
7/93-6/99 Associate Professor of Microbiology, Oregon Health & Science University, Portland, OR
7/99-10/08 Professor of Molecular Microbiology and Immunology, Oregon Health & Science University, Portland, OR
11/08- University Professor, Oregon Health & Science University, Portland, OR

Other Experience and Professional Memberships

10/97-10/99 Ad hoc Member, Tropical Medicine and Parasitology NIH Study Section
02/00-06/05 Permanent Member, Tropical Medicine and Parasitology/Eukaryotic Pathogens NIH Study Section
05/06-06/09 Ad hoc Member, NIH Special Emphasis Study Sections

10/08-06/09 Ad hoc Member, Drugs and Drug Resistance NIH Study Section
04/10- American Heart Association Microbiology BSc2 Study Section

Honors

10/72-06/76 Predoctoral Trainee, NIH Training Grant, Harvard University
07/78-06/80 Postdoctoral Fellowship, American Cancer Society, National
07/80-06/82 Postdoctoral Fellowship, American Cancer Society, Massachusetts Division
07/82-06/84 Postdoctoral Fellowship, The Medical Foundation
05/92, 05/93 Graduate Program Excellence in Teaching Award
06/90-05/94 Burroughs Wellcome New Investigator Award in Molecular Parasitology
08/93-07/98 NIH Career Development Award, NIAID
07/97-06/02 Burroughs Wellcome Molecular Parasitology Scholar Award
11/08- University Professor, Oregon Health & Science University, Portland, OR

C. Selected Peer Reviewed Publications (Selected from a total of 86)

1. Burchmore, R.J.S., Rodriguez-Contreras, D., McBride, K., Merkel, P., Barrett, M.P., Modi, G., Sacks, D., and **Landfear, S.M.** Genetic characterization of glucose transporter gene function in *Leishmania mexicana*. Proc. Natl. Acad. Sci. U.S.A. (2003) **100**:3901-3906. PMID: 12651954
2. Valdés, R., Vasudevan, G., Conklin, D., and **Landfear, S.M.** Transmembrane domain 5 of the LdNT1.1 nucleoside transporter is an amphipathic helix that forms part of the nucleoside permeation pathway. Biochemistry (2004) **43**:6793-6802. PMID: 15157113
3. Rodriguez-Contreras, D. and **Landfear. S.M.** Metabolic changes in glucose transporter-deficient *Leishmania mexicana* and parasite virulence. J. Biol. Chem. (2006) **281**:20068-20076. PMID: 16707495
4. Valdés, R., Liu, W., Ullman, B., and **Landfear. S.M.** Comprehensive examination of charged intramembrane residues in a nucleoside transporter. J. Biol. Chem. (2006) **281**:22647-22655. PMID: 16799726
5. Ortiz, D., Sanchez, M.A., Pierce, S., Herrmann, T., Kimblin, N., Bouwer, H.G.A., and **Landfear, S.M.** Molecular genetic analysis of purine nucleobase transport in *Leishmania major*. (2007) Molecular Microbiology **64**:1228-1243. PMID: 17542917
6. Ortiz, D., Sanchez, M.A., Quecke, P., and **Landfear, S.M.** Two novel nucleobase/pentamidine transporters from *Trypanosoma brucei*. Mol. Biochem. Parasitol., **163**:67-76 (2009). PMC2630410
7. Feng, X., Rodgriguez-Contreras, D., Buffalo, C., Bouwer, A., Kruvand, E., Beverley, S.M., and **Landfear, S.M.** Amplification of an alternate transporter gene suppresses the avirulent phenotype of glucose transporter null mutants in *Leishmania mexicana*. Mol. Microbiol., **71**:369-381 (2009). PMC2729070
8. Ortiz, D., Sanchez, M.A., Koch, H., Larsson, P., and **Landfear, S.M.** An acid-activated nucleobase transporter from *Leishmania major*. J. Biol. Chem., **284**:16164-16169 (2009). PMC2713545
9. Valdés, R., Arastu-Kapur, S., **Landfear, S.M.**, and Shinde, U. An *ab initio* structural model of a nucleoside permease predicts functionally important residues. J. Biol. Chem., **284**:19067-19076 (2009). PMC2707223
10. Carter, N.S., Yates, P.A., Gessford, S.K., Galagan, S.R., **Landfear, S.M**., and Ullman, B. Adaptive responses to purine starvation in *Leishmania donovani*. Mol. Microbiol., 78:92-107 (2010). PMC2964060
11. Ortiz, D. Valdés, R., Sanchez, M.A., Hayenga, J., Elya, C., Detke, S., and **Landfear, S.M.** Purine restriction induces pronounced translational upregulation of the NT1 adenosine/pyrimidine nucleoside transporter in *Leishmania major*. Mol. Microbiol., **78**:108-118 (2010). PMC2971681
12. Feng, X., Feistel, T., Buffalo, C., McCormack, A., Kruvand, E., Rodriguez-Contreras, D., Akopyants, N.S., Umasankar, P.K., David, L., Jardim, A., Beverley, S.M., and Landfear, S.M. Remodeling of protein and mRNA expression in *Leishmania mexicana* induced by deletion of glucose transporter genes. Mol. Biochem. Parasitol., **175**:39-48 (2011). PMC2974008
13. Tran, K., Rodriguez-Contreras, D., Shinde, U., and **Landfear, S.M.** Both sequence and context are important for flagellar targeting of a glucose transporter. J. Cell Sci. **125**:3293-3298 (2012). PMC3516375
14. Tran, K.D., Rodriguez-Contreras, D., Vieira, D.P., Yates, P.A., David, L., Beatty, W., Elferich, J., and **Landfear, S.M.** KHARON1 mediates flagellar targeting of a glucose transporter in *Leishmania mexicana*

and is critical for viability of infectious intracellular amastigotes. J. Biol. Chem. **288**:22721-22733 (2013) PMC2376651.
15. Valdés, R., Elferich, J. Shinde, U., and **Landfear. S.M.** Identification of the intracellular gate for a member of the equilibrative nucleoside transporter (ENT) family. J. Biol. Chem. **289**:8799-8809 (2014). PMC24497645.

D. RESEARCH SUPPORT

Ongoing Research Support

R01 AI44138-11 PI: Landfear, S.M. 04/01/10-05/31/15
Purine Nucleoside/Nucleobase Transporters in *Leishmania*
The major goals of this grant are to study nucleoside and nucleobase transporters (NTs) in *L. donovani* and *L. major*. Detailed structure-function studies will be performed on the NT1 nucleoside transporter and the NT4 nucleobase transporter. The role of the NT4 transporter, a permease that is activated in the acidic environment of the macrophage phagolysome, in promoting survival of the parasite within the mammalian host will be investigated. The mechanism controlling the adaptive upregulation of purine transporter expression during purine starvation will be examined.
Role: PI

1R21AI102874-01 PI: Landfear, S.M. 02/01/13-01/31/15
Selective Inhibitors of the Hexose Transporter from African Trypanosomes
The principal objective of this grant is to screen a large library of chemical compounds for selective inhibitors of the essential hexose transporter of bloodstream form African trypanosomes. Hits from the screen will be evaluated for anti-trypanosomal activity and for potential for development of novel anti-trypanosomal drugs.
Role: PI

T32 AI007472 PI: Landfear, S.M. 09/01/11-08/31/15
Interactions at the Microbe/Host Interface
This training grant supports graduate students and postdoctoral fellows within the interdepartmental microbial pathogenesis program at OHSU. There are 25 preceptors from 4 departments and one research institute, and support is provided for 5 predoctoral and 3 postdoctoral fellows.
Role: PI

Completed Research Support

5 U54 AI081680-02 PI: Nelson, J. 04/20/09 – 02/28/14
Pacific Northwest Regional Center of Excellence in Biodefense and Emerging Infectious Diseases
The first goal of the PNWRCE is to identify age-related immune system defects to develop new vaccines and supplemental therapies to enhance protection of individuals to NIAID Category A-C pathogens. A second goal of this center is to use systems genetic, chemical, and proteomics approaches to identify therapeutic targets for biodefense and emerging diseases.
Role: Director of Career Development Program

W81XWH-09-1-0429 PI: Landfear, S.M. 07/01/09-06/30/13
Screening for Inhibitors of Essential *Leishmania* Glucose Transporters
The major objective of this grant is to screen large libraries of chemical compounds for those that selectively inhibit the glucose transporters of *Leishmania mexicana*. Positive hits from these screens will be potential leads for development of novel anti-leishmanial drugs.
Role: PI

R01 AI44138-10 PI: Landfear, S.M. 06/01/04-05/31/09
Nucleoside/Nucleobase Transporters in *Leishmania major*

The major goals of this grant are to study nucleoside and nucleobase transporters (NTs) in *L. major*. The genes encoding the 4 members of this family will be deleted one at a time and in all possible combinations to determine the biological consequences of gene deletions. One model nucleoside transporter, NT2, will be studied by mutagenesis to identify residues essential for transport. The recently identified fourth member of the NT family, NT4, will be thoroughly characterized regarding biochemical function and substrate specificity.

R01 AI25920-24 PI: Landfear, S.M. 06/01/06-05/31/11
Functional Characterization of *Leishmania* Transporters
The current application is a Competitive Renewal of this grant. The major objectives of this grant are to study the biochemical, cellular, and physiological effects of knocking out glucose transporters in *Leishmania mexicana*. Results of these experiments should elucidate why the parasites require glucose transporters in their infectious stage. In addition, we will prepare null mutants of each of the 3 individual glucose transporter genes and examine their phenotypes to determine the specific functions of each glucose transporter isoform.
Role: PI

R01 AI079092 PI: Landfear, S.M. 07/01/08-06/30/11
Development of Assay for High Throughput Screen of Parasite Glucose Transporters
The major objective of this grant is to develop an assay for high throughput screening of chemical libraries for inhibitors of parasite glucose transporters, especially the essential malaria glucose transporter PfHT. A fluorescence cell growth assay is being adapted to screen for such inhibitors in a medium to high throughput manner.
Role: PI