BIOGRAPHICAL SKETCH

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NAME: Horb, Marko

eRA COMMONS USER NAME: markohorb

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 Illinois at Urbana-Champaign	B.Sc.	05/1993	Cell & Structural Biology
Stony Brook University, Stony Brook, NY	Ph.D.	08/1998	Cell & Developmental Biology
University of Bath, Bath, UK	Postdoc	06/2003	Developmental Biology

A. Personal Statement

In 2011, I was appointed Director of the newly established National *Xenopus* Resource (NXR), and Senior Scientist, in the Bell Center for Regenerative Biology and Tissue Engineering at the MBL. My current position as Director of the NXR is to manage the on-site facilities at all levels. This includes staff oversight, budget planning and maintenance, course organization, communication with the community, transgenic production, breeding, frog sales, husbandry, interactions with summer researchers and establishment of new technological advancements in the field. In addition to NXR functions, I have developed a strong research program focused on improving genome editing in *Xenopus*. Since 2015, we have created over 125 different *Xenopus* mutants and I am now proposing to continue this project and establish the NXR as a central hub for the *Xenopus* community to ensure that researchers can easily come to the MBL and use NXR resources. With our expertise in breeding and maintaining *Xenopus*, the work proposed in this grant is perfectly suited for the NXR and ensures that the reagents produced are quickly made available for the entire *Xenopus* community. My lab's expertise in genome editing, combined with NXR resources, are perfect for the development of new resources for the wider community. In addition, each year we host visiting scientists who come to the NXR to use its many resources, including the various transgenic and mutant lines.

a. **Horb M**, Wlizla M, Abu-Daya A, McNamara S, Gajdasik D, Igawa T, Suzuki A, Ogino H, Noble A; Centre de Ressource Biologique Xenope team in France, Robert J, James-Zorn C, Guille M. (2019). *Xenopus* resources: Transgenic, inbred, and mutant animals, training opportunities, and web-based support. Front Physiol. 10:387. eCollection 2019. Review. PMCID: PMC6497014

b. Corkins, M.E., Hanania, H.L., Krneta-Stankic, V., DeLay, B.D., Pearl, E.J., Lee, M., Ji, H., Davidson, A.J., **Horb, M.E.** and Miller, R.K. (2018) Transgenic *Xenopus laevis* line for in vivo labeling of nephrons within the kidney. *Genes* 9, 197 PMCID: PMC5924539

c. Wlizla M., McNamara S., **Horb M.E.** (2018) Generation and Care of *Xenopus laevis* and *Xenopus tropicalis* Embryos. Methods Mol Biol. 1865:19-32. PMCID: PMC6396978

d. McNamara S., Wlizla M., **Horb M.E.** (2018) Husbandry, General Care, and Transportation of *Xenopus laevis* and *Xenopus tropicalis*. Methods Mol Biol. 1865:1-17. PMCID: PMC6421069

B. Positions and Honors

Professional Positions

2003-2009 Assistant Research Professor, Institut de Recherches Cliniques de Montréal (IRCM)
2004-2010 Chercheur Adjoint, Department of Medicine, Université de Montréal
2004-2011 Associate Member, Department of Anatomy & Cell Biology, McGill University
2004-2011 Associate Member, Division of Experimental Medicine, McGill University
2006-2011 Member, Montreal Diabetes Research Center
2009-2011 Associate Research Professor, IRCM

2010-2011 Chercheur Agrégé, Department of Medicine, Université de Montréal
2011-2017 Associate Professor (MBL), Department of Molecular Biology, Cell Biology and Biochemistry, Brown University
2011-2017 Associate Scientist, Marine Biological Laboratory
2011- Director, National *Xenopus* Resource
2017- Senior Scientist, Marine Biological Laboratory

Other Experience and Professional Memberships

2003- Member, Society for Developmental Biology
2010 Co-organizer, 13th International *Xenopus* Conference
2012- Member, Strategy Board for European *Xenopus* Resource Center
2013, 2015 Co-organizer, *Xenopus* PI Meeting
2014 Co-author NIH community *Xenopus* White Paper
2014-2015 Ad hoc member, NIH Animal/Biological Resource Facilities study section
2015-2017 Co-chair NIH Animal/Biological Resource Facilities study section
2017, 2019 Co-organizer, *Xenopus* Resources and Emerging Technologies Meeting
2017- Chair, MBL Institutional Animal Care and Use Committee
2018 Organizer, 9th Aquatic Models of Human Disease Conference

Honors

1993 Graduation with Distinction, Dept. of Cell & Structural Biology, University of Illinois
1997 Sigma Xi Excellence in Research Award, Stony Brook Chapter
2004-2006 Bourse de chercheur boursier Junior 1
Fonds de recherche en santé du Québec (FRSQ)
2006-2010 Bourse de chercheur boursier Junior 2
Fonds de recherche en santé du Québec (FRSQ)
2011-2013 Bourse de chercheur boursier Senior (declined)
Fonds de recherche en santé du Québec (FRSQ)
2015 Hermann Foundation Award, Marine Biological Laboratory

C. Contribution to Science

1. **Establishment of the National *Xenopus* Resource.** In 2011, I was appointed the first Director of the National *Xenopus* Resource (NXR), which was a newly established P40-funded NIH animal resource center. The NXR was founded at the Marine Biological Laboratory (MBL) and I moved there to set up the facility. There were no frogs at the NXR when I arrived, and I was required to establish stocks of over 100 different lines for both *Xenopus laevis* and *Xenopus tropicalis*. The NXR not only serves as a repository for the *Xenopus* community, but also provides a service for creating and breeding custom transgenic and mutant animals. In addition, the NXR offers advanced training workshops for the community and has a research "hotel" service for individual researchers to come to the NXR for an extended visit and use its resources to enhance their own research program. NXR users are funded by 10 NIH institutes and 47 other funding sources, including NSF and HHMI. In the last year, the NXR has become the focal point for genome editing in *Xenopus*. This important resource for the community helps to expand and enhance the research capabilities of NIH-funded investigators because most *Xenopus* researchers do not have the facilities to create and maintain transgenic and mutant lines at their home institution.
    a. Pearl E, Morrow S, Noble A, Lerebours A, **Horb M**, Guille M. (2017) An optimized method for cryogenic storage of *Xenopus* sperm to maximise the effectiveness of research using genetically altered frogs. Theriogenology. 92, 149-155. PMCID: PMC5340284
    b. Wlizla, M, Falco, R, Peskin, L., Parlow, A and **Horb, ME** (2017) Luteinizing Hormone is an effective replacement for hCG to induce ovulation in *Xenopus*. *Developmental Biology* 426, 442-448. PMCID: PMC5135639
    c. Wlizla, M, McNamara, S, & **Horb, ME** (2018). Generation and Care of *Xenopus laevis* and *Xenopus tropicalis* Embryos. In K. Vleminckx (Ed.), *Xenopus: Methods and Protocols* (pp. 19-32). New York, NY: Springer New York. PMCID: PMC6396978

d. McNamara, S, Wlizla, M, & **Horb, ME** (2018). Husbandry, General Care, and Transportation of Xenopus laevis and Xenopus tropicalis. In K. Vleminckx (Ed.), *Xenopus: Methods and Protocols* (pp. 1-17). New York, NY: Springer New York. PMCID: PMC6421069

2. **Development of genome editing and transgenic technology in *Xenopus*.** Starting in 2014 when CRISPR-Cas and TALENS first became available, I established a pipeline to create new mutant animals for the *Xenopus* community. In the last five years we have created over 117 different mutants. This has become an important resource for the community, and we work closely with *Xenopus* researchers to provide access to these mutants. Individual researchers are now coming to the NXR to take advantage of our expertise and are ordering custom mutant animals through the NXR. These new mutants will enhance the research capabilities of other scientific collaborators.
    a. Ratzan, W, Falco, R, Salanga, C, Salanga, M and **Horb, ME** (2017). Generation of a *Xenopus laevis* F1 albino J strain by genome editing and oocyte host-transfer. *Developmental Biology* 426, 188-193. PMCID: PMC5025372
    b. Tandon, P, Conlon, F, Furlow, D and **Horb, ME** (2017). Expanding the genetic toolkit in *Xenopus:* approaches and opportunities for human disease modeling. *Developmental Biology* 426, 325-335. PMCID: PMC5074924
    c. Delay, BD, Corkins, M.E., Hanania, HL, Salanga, M, Deng, JM, Sudou, N, Taira, M, **Horb, M** and Miller, RK (2017). Tissue-specific gene inactivation in *Xenopus laevis*: knockout of lhx1 in the kidney with CRISPR/Cas9. *Genetics* 208, 673-686. PMCID: PMC5788530
    d. Naert T, Tulkens D, Edwards NA, Carron M, Shaidani NI, Wlizla M, Boel A, Demuynck S, **Horb ME**, Coucke P, Willaert A, Zorn AM, Vleminckx K (2020). Maximizing CRISPR/Cas9 phenotype penetrance applying predictive modeling of editing outcomes in *Xenopus* and zebrafish embryos. Sci. Rep. 10:14662. PMCID: PMC7473854

3. **Establishment of *Xenopus* as a model system for pancreas development**. When I first started my postdoc in 1998 the use of *Xenopus laevis* for research on pancreas development was almost nonexistent. In the past 19 years I have focused my research efforts to place *Xenopus* among the key model organisms for studying pancreas development. Inparticular I have shown that, in addition to early pancreas development, *Xenopus* can also be used to study the transdifferentiation of liver to pancreas. As an example of my leadership in this field is the fact that I was invited to write the first comprehensive review on *Xenopus* pancreas development for a special issue on *Xenopus* development in the journal Developmental Dynamics published in 2009.
    a. Pearl, EJ, Bilogan, CK, Mukhi, S, Brown, DD and **Horb, ME** (2009) *Xenopus* pancreas development. *Developmental Dynamics* 238, 1271-1286. PMCID: PMC2921176
    b. Jarikji, ZH, Horb, LD, Shariff, F, Mandato, CA, Cho, KWY and **Horb, ME** (2009) The tetraspanin tm4sf3 is localized to the ventral pancreas and regulates fusion of the dorsal and ventral pancreatic buds. *Development* 136, 1791-1800. PMCID: PMC2680106
    c. Pearl, EJ, Jarikji, Z and **Horb, ME** (2011) Functional analysis of RFX6 and mutant variants associated with neonatal diabetes. *Developmental Biology* 351, 135-145 PMCID: PMC3042741
    d. Oropeza, D and **Horb, ME** (2012) Transient expression of Ngn3 in *Xenopus* endoderm promotes early and ectopic development of pancreatic beta and delta cells. *Genesis* 50, 271-285 PMCID: PMC3294191

4. **Transdifferentiation of Liver to Pancreas.** I showed that a modified form of a single transcription factor is sufficient to bring about the conversion of liver to pancreas. The importance of this result is that it raises the hope that differentiated cells may one day be used for the treatment of diabetes. This work suggests a novel means for producing beta cells for diabetics. The importance of this result is shown in the fact that numerous newspapers and science journals from around the world highlighted the paper in their respective publications. More recently, we have shown that Pdx1-VP16 can convert rat liver cells to insulin-producing cells that are capable of curing diabetes in a mouse model. If this technique can be applied to the clinic this

would allow more diabetics to be treated than those currently treated with islet transplants. I followed up this study and showed that another factor, Ptf1a can also convert liver to pancreas.

a. **Horb, ME,** Shen, CN, Tosh, D and Slack, JMW (2003) Experimental conversion of liver to pancreas. *Curr Biology* 13, 105-115

b. Cao, LZ, Tang, DQ, **Horb, ME**, Li, SW and Yang, LJ (2004) High Glucose is Necessary for Complete Maturation of Pdx1-VP16-Expressing Hepatic Cells into Functional Insulin-Producing Cells. Diabetes 53, 3168-317

c. Jarikji, ZH, Vanamala, S, Beck, CW, Wright CVE, Leach, SD and **Horb, ME** (2007) Differential ability of Ptf1a and Ptf1a-VP16 to convert stomach, duodenum and liver to pancreas. *Developmental Biology* 304, 786-799

5. **The role of T-box genes.** During my graduate studies at SUNY at Stony Brook, my research focused on isolating and characterizing two T-box genes, VegT and Tbx5. Both genes are essential during normal development and helped strengthen the idea that T-box genes are critical determinants of cell fate. In particular, VegT is a critical regulator of mesodermal and endodermal cell fate in *Xenopus* embryos, while Tbx5 is important for heart development. My research into the function of both these transcription factors helped to open up the whole field of T-box genes, since initially only two T domain transcription factors had been isolated prior to VegT. Now there are more than 20 different T-box genes that are expressed in a wide range of tissues.

   a. **Horb, ME** and Thomsen, GH (1997) A vegetally localized T-box transcription factor in *Xenopus* eggs specifies mesoderm and endoderm and is essential for embryonic mesoderm formation. *Development* 124, 1689-1698

   b. **Horb, ME** and Thomsen, GH (1999) Tbx5 is essential for heart development. *Development*, 126, 1739-1751

   c. **Horb, ME** and Slack, JMW (2001) Endoderm Specification and Differentiation in *Xenopus* Embryos. *Developmental Biology* 236, 330-343

   d. Steimle JD, Rankin SA, Slagle CE, Bekeny J, Rydeen AB, Chan SS, Kweon J, Yang XH, Ikegami K, Nadadur RD, Rowton M, Hoffmann AD, Lazarevic S, Thomas W, Boyle Anderson EAT, **Horb ME**, Luna-Zurita L, Ho RK, Kyba M, Jensen B, Zorn AM, Conlon FL, Moskowitz IP. (2018) Evolutionarily conserved Tbx5-Wnt2/2b pathway orchestrates cardiopulmonary development. PNAS 115(45):E10615-E10624 PMCID: PMC6233116

Complete list of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1vwdUHk5-8VAd/bibliography/48240025/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

NIH P40 OD010997-11 (PI: Horb) 08/12/10-04/30/25
NIH/NICHD and OD
National Xenopus Resource Center
This grant is funded to create and build a National *Xenopus* Resource Center. The grant is focused on establishing the housing systems for *Xenopus laevis* and *Xenopus tropicalis*, to create new workshops for the community, to produce transgenic animals and to serve as repository for different *Xenopus* lines created by individuals in the *Xenopus* field.
Role: Contact PI

NIH R24OD030008 (PI: Horb) 07/01/20-06/30/24
NIH/OD
Xenopus Mutant Resource
This grant is funded to generate a new resource for the Xenopus community focused on mutants in *Xenopus*. The goals of the grant are to create new mutants for the community using CRISPR-Cas and to generate new transgenic and knock-in models. The *Xenopus* Mutant Resource will also be a centralized research hub for

scientists to come and collaborate while working on many different mutants, as well as obtain training in working with *Xenopus tropicalis*, the species most amenable to genetic manipulation.
Role: PI

Completed Research Support

NIH R21OD023810 (PI: Horb) 04/01/19-03/31/21
NIH/OD
Enhancing CRISPR-Cas for disease modeling in Xenopus
This pilot grant has two main aims. To discover new low temperature Cas9 variants from psychrophilic bacteria and identify their preferred target sites. The second is to develop CRISPR EATING as a reliable method for generating mutants in genes with many exons.
Role: PI

NIH R01HD084409 (PI: Horb) 07/15/15-04/30/21
NIH/NICHD
Xenopus models of human disease by targeted genome editing
This grant proposes to create 200 mutant frogs in human disease-related genes for the *Xenopus* community. These mutants will be created using the new genome editing technologies, CRISPR-Cas and TALENs, in both *Xenopus laevis* and *Xenopus tropicalis*. In addition, the work will focus on developing new methodologies and techniques with genome editing, including knock-in technology and the use of oocyte host transfer.
Role: PI

NSF IOS-1645105 (PI: Gorbsky and Horb) 07/15/17-06/30/21
NSF Division of Integrated Organismal Systems
IOS EDGE: Rapid and Efficient Gene Editing of Amphibians Through Nuclear Transfer from Engineered Cell Lines
The long-term goal of the project is to make *Xenopus* and other amphibians vastly more powerful systems by simplifying the generation of precisely defined mutants. The overall objectives of this application are to develop reliable methods for generating *X. laevis* and *X. tropicalis* cell lines with specific mutations that can be fully characterized and stored frozen. These cells will then be used to generate F0 mutant Xenopus embryos.
Role: co-PI

NIH 3P40 OD010997-08S2 (Multi PI: Horb and Grainger) 07/18/17-04/30/20
NIH/NICHD and OD
Research Supplements to Promote Diversity in Health-Related Research (Admin Supp)
National Xenopus Resource Center
This grant is funded to provide support for a minority candidate to work in the National *Xenopus* Resource as a research assistant. The focus of the project is to provide training for the candidate to gain experience in the laboratory.
Role: Contact PI

NIH 5 R01 HD073104 (PI: Kirschner) 09/01/17-05/31/19
NIH/NICHD
Systems analysis of cell type differentiation in Xenopus development
This grant is to apply and develop modern genomic tools focused the embryonic development of cell types in the vertebrate embryo with the goal of understanding and ultimately controlling pathways for cell differentiation. Such studies could facilitate the development of procedures to direct cell differentiation in ways that would ultimately contribute to regenerative medicine in the treatment of important human diseases.
Role: subaward PI

NIH R13 OD026559 (PI: Horb) 08/03/18-07/31/19
NIH/NICHD
9th Aquatic Models in Human Disease Conference
This grant provided funds to host a conference to explore the recent developments in technology, study design and data analysis and the latest applications of aquatic animals in the study of human diseases.
Role: PI