

## Juan Alvarez, Ph.D.

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Harvard Stem Cell and Regenerative Biology Department

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## RESEARCH INTERESTS

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I seek to understand the interplay between metabolism, circadian rhythms, and cellular maturation, using human stem cell-derived pancreatic islet organoids as a model system. This work will be important to advance replacement therapies for type 1 diabetes and for harnessing control over the function and applications of any human organoid.

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## EDUCATION

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### Harvard University

Postdoctoral Fellow, laboratory of Douglas A. Melton  
Project: Dissecting human  $\beta$ -cell differentiation regulatory networks  
Funding: HHMI Postdoctoral Fellowship (2017-2020)

2015-Present  
Cambridge, MA

### Massachusetts Institute of Technology

Ph.D. in Biology, laboratories of Harvey F. Lodish & Alexander van Oudenaarden  
Thesis: Modulation of lineage-specific cell differentiation by long non-coding RNAs  
Certificate in Graduate Student Teaching

2009-2015  
Cambridge, MA

### Princeton University

Bachelor of Arts in Molecular Biology, *Magna Cum Laude*  
Thesis: Role of self-catalytic DNA depurination in site-specific mutagenesis  
Certificate in Quantitative and Computational Biology

2005-2009  
Princeton, NJ

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## PUBLICATIONS

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**Alvarez-Dominguez, J.R.\***, and Melton, D.A. (2020). Cell maturation. *Cell* [invited review].

**Alvarez-Dominguez, J.R.\***, Donaghey, J., Rasouli, N., Kenty, J.H.R., Helman, A., Charlton, J., Straubhaar, J.R., Meissner, A., and Melton, D.A. (2020). Organoid Maturation by Circadian Entrainment. *StemJournal* 2, 7-13.

**Alvarez-Dominguez, J.R.\***, Montalvo, A.P., Kenty, J.H.R., Straubhaar, J.R., and Melton, D.A. (2020). Dec1 links circadian rhythms to pancreatic islet maturation. *Under review*.

**Alvarez-Dominguez, J.R.**, Winther, S., Hansen, J.B., Lodish, H.F., and Knoll, M. (2020). An adipocyte-specific lncRAP2 – Igf2bp2 complex enhances adipogenesis and energy expenditure by stabilizing target mRNAs. *bioRxiv* DOI:10.1101/2020.09.29.318980.

Rasouli N., Melton, D.A., and **Alvarez-Dominguez, J.R.\*** (2020). Purification of live stem cell-derived islet lineage intermediates. *Curr Protoc Stem Cell Biol*, 53, e111.

**Alvarez-Dominguez, J.R.**, Donaghey, J., Rasouli N., Kenty, J.H.R., Helman, A., Charlton J., Straubhaar, J.R., Meissner, A., and Melton, D.A. (2019). Circadian Entrainment Triggers Maturation of Human in vitro Islets. *Cell Stem Cell* 26, 108-122 e110.

Highlighted in: B. Andersen, Z. Lin (2020). Evaluation of Alvarez-Dominguez et al. *Cell Stem Cell* 26, 1, *Stem Cell Podcast*, *The Stem Cell Group*, *Topbiopapers*, *Society for Research on Biological Rhythms Outreach*.

Jiang, M., **Alvarez-Dominguez, J.R.**, Yuan, B., and Lodish, H.F. (2019). LncRNA Hoxc4-au inhibits visceral and promotes subcutaneous adipogenesis. *Under review*.

Xu, D., Xu, S., Kyaw, A.M.M., Lim, Y.C., Chia, S.Y., Chee Siang, D.T., **Alvarez-Dominguez, J.R.**, Chen, P., Leow, M.K., and Sun, L. (2017). RNA Binding Protein Ybx2 Regulates RNA Stability During Cold-Induced Brown Fat Activation. *Diabetes* 66, 2987-3000.

**Alvarez-Dominguez, J.R.\***, and Lodish, H.F. (2017). Emerging mechanisms of long noncoding RNA function during normal and malignant hematopoiesis. *Blood* 130, 1965-1975.

- Alvarez-Dominguez, J.R.\***, Knoll, M., Gromatzky, A.A., and Lodish, H.F. (2017). The Super-Enhancer-Derived lincRNA-EC7/Bloodline Potentiates Red Blood Cell Development in *trans*. *Cell Reports* 19, 2503–2514.  
Highlighted in: Espinosa, J.M. (2017). On the Origin of lincRNAs: Missing Link Found. *Trends Genet* 33, 660-662.
- Alvarez-Dominguez, J.R.\***, Zhang, X., and Hu, W. (2017). Widespread and dynamic translational control of red blood cell development. *Blood* 129, 619-629.  
Highlighted in: Warren, A.J. (2017). Decoding erythropoiesis. *Blood* 129, 544-545.
- Atianand, M.K., Hu, W., Satpathy, A.T., Shen, Y., Ricci, E.P., **Alvarez-Dominguez, J.R.**, Bhatta, A., Schattgen, S.A., McGowan, J.D., Blin, J., et al. (2016). A Long Noncoding RNA lincRNA-EPS Acts as a Transcriptional Brake to Restrain Inflammation. *Cell* 165, 1672-1685.  
Highlighted in: Lu, C. (2016). Curb Your Inflammation. *Cell* 165, 1553-1555, *Science Daily*, and *Newswise*.
- Alvarez-Dominguez, J.R.\***, and Lodish, H.F. (2016). Unravelling of the role of long noncoding RNAs in haematopoiesis. *ISBT Science Series* 11, 188-195.
- Russell, M.R., Penikis, A., Oldridge, D.A., **Alvarez-Dominguez, J.R.**, McDaniel, L., Diamond, M., Padovan, O., Raman, P., Li, Y., Wei, J.S., et al. (2015). CASC15-S Is a Tumor Suppressor lincRNA at the 6p22 Neuroblastoma Susceptibility Locus. *Cancer Research* 75, 3155-3166.
- Amosova, O., **Alvarez-Dominguez, J.R.\***, and Fresco, J.R. (2015). Why the DNA self-depuration mechanism operates in HB-beta but not in beta-globin paralogs HB-delta, HB-varepsilon1, HB-gamma1 and HB-gamma2. *Mutation Research* 778, 11-17.
- Alvarez-Dominguez, J.R.**, Bai, Z., Xu, D., Yuan, B., Lo, K.A., Yoon, M.J., Lim, Y.C., Knoll, M., Slavov, N., Chen, S., et al. (2015). De Novo Reconstruction of Adipose Tissue Transcriptomes Reveals Long Non-coding RNA Regulators of Brown Adipocyte Development. *Cell Metabolism* 21, 764-776.  
Highlighted in: *Futurity* (2015). RNA catalogue reveals key to brown fat.
- Smith, J., **Alvarez-Dominguez, J.R.**, Kline, N., Huynh, N., Geisler, S., Hu, W., Coller, J., and Baker, K.E. (2014). Translation of small open reading frames within unannotated RNA transcripts in *Saccharomyces cerevisiae*. *Cell Reports* 7, 1858-1866.  
Highlighted in: *Science Daily* and *Biome*.
- Alvarez-Dominguez, J.R.**, Hu, W., Gromatzky, A.A., and Lodish, H.F. (2014). Long noncoding RNAs during normal and malignant hematopoiesis. *Int J Hematol* 99, 531-541.
- Alvarez-Dominguez, J.R.**, Hu, W., Yuan, B., Shi, J., Park, S.S., Gromatzky, A.A., van Oudenaarden, A., and Lodish, H.F. (2014). Global discovery of erythroid long noncoding RNAs reveals novel regulators of red cell maturation. *Blood* 123, 570-581.  
Highlighted in: Gallagher, P.G. (2014). Long noncoding RNAs in erythropoiesis. *Blood* 123, 465-466. Coetzer, T. (2014). Red Cells, RNA, and Regulation: The Plot Thickens. *The Hematologist* 11, 10
- Caudy, A.A., Guan, Y., Jia, Y., Hansen, C., DeSevo, C., Hayes, A.P., Agee, J., **Alvarez-Dominguez, J.R.**, Arellano, H., Barrett, D., et al. (2013). A new system for comparative functional genomics of *Saccharomyces* yeasts. *Genetics* 195, 275-287.
- Alvarez-Dominguez, J.R.\***, Amosova, O., Fresco, J.R. (2013). Self-catalytic DNA depuration underlies human beta-globin gene mutations at codon 6 that cause anemias and thalassemias. *J Biol Chem* 288, 11581-11589.
- Hu, W., **Alvarez-Dominguez, J.R.**, and Lodish, H.F. (2012). Regulation of mammalian cell differentiation by long non-coding RNAs. *EMBO Rep* 13, 971-983.

### Book chapters

- Alvarez-Dominguez, J.R.**, Hu, W., and Lodish, H.F. (2013). Regulation of Eukaryotic Cell Differentiation by Long Noncoding RNAs. *Molecular Biology of Long Non-coding RNAs*, 15-67. (New York: Springer Science).
- Fresco, J.R., Amosova, O., Wei, P., **Alvarez-Dominguez, J.R.**, Glumcher, D., and Torres, R. (2011). Site-Specific Self-Catalyzed DNA Depuration, the Basis of a Spontaneous Mutagenic Mechanism of Wide Evolutionary Significance. *Evolutionary Biology: Concepts, Biodiversity, Macroevolution and Genome Evolution*, 3-19. (Springer-Verlag Berlin).

\*Corresponding author

## PRESENTATIONS

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### Invited Talks

- The New York Stem Cell Foundation Annual Conference, Virtual (2020). *Organoid Maturation by Circadian Entrainment*.
- United Scientific Group Biomedical Engineering and Instrumentation Summit, Virtual (2020). *Circadian Control of Organoid Physiology*.
- Harvard Stem Cell Institute Annual Retreat: Translating Science to the Clinic, Virtual (2020). *Organoid Maturation by Circadian Entrainment*.
- Society for Research on Biological Rhythms Biennial Conference, Virtual (2020). *Circadian Entrainment Triggers Maturation of Human Islet Organoids*.
- International Society for Stem Cell Research Annual Meeting, Los Angeles, CA (2019). *Epigenome Dynamics Reveal New Insights into Human Islet Differentiation and Maturation*.
- International Society of Blood Transfusion Regional Congress, London, UK (2015). *Unraveling of the Role of Long non-coding RNAs in Haematopoiesis*.
- Cold Spring Harbor Laboratory Regulatory & Non-coding RNAs Meeting, Cold Spring Harbor, NY (2014). *Regulation of Red Blood Cell Development by LncRNAs*.

## FELLOWSHIPS & AWARDS

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### Fellowships

- Intersections Science Fellow, Intersections Science Fellows Program (2020)
- Howard Hughes Medical Institute Postdoctoral Fellowship, Life Sciences Research Foundation (2017-2020)
- NIGMS Center for Quantitative Biology Undergraduate Research Fellowship, Princeton University (2006-2009)

### Academic Recognition

- Vanda Pharmaceuticals Excellence Award, Society for Research on Biological Rhythms (2020)
- Zhong Mei Chen Yong Award for Scientific Excellence. International Society for Stem Cell Research (2020)
- Merit Award, International Society for Stem Cell Research (2019 and 2020)
- Senior Thesis Prize, Department of Molecular Biology, Princeton University (2009)

### Travel Awards

International Society for Stem Cell Research Annual Meeting, Los Angeles, CA (2019)

## TEACHING & MENTORING

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### Teaching Assistant, MIT

Responsibilities included developing lecture and recitation class materials, leading recitation class discussions, developing and grading assignments and exams, and giving a guest lecture.

- Introductory Biology, introductory undergraduate course (2013)
- Molecular and Engineering Aspects of Biotechnology, advanced undergraduate seminar (2011)

### Mentoring

I have mentored high school, undergraduate, and master's students. Five wrote a thesis with me:

- Ana Montalvo, Harvard undergraduate student (2019-2020)
- Niloofar Rasouli, Harvard undergraduate student (2017-2019)
- Austin A. Gromatzky, MIT undergraduate student (2013-2015)
- Alec Garza-Galindo, MIT master's student (2013-2014)
- Staphany S. Park, MIT undergraduate student (2013-2014)

### Tutoring

- Graduate Resident tutor, MIT (2011-2015)
- Resident Computing Consultant, Princeton University (2006-2007)

## OUTREACH & SERVICE

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### Diversity Leadership

I believe that disenfranchisement and unconscious bias must be counteracted through deliberate and continued efforts to nurture diversity, equity, and inclusion. I act on these values through personal example:

- Intersections Science Fellows Symposium: Harvard SCRB Department postdoctoral representative (2020-)
- Harvard SCRB Department Diversity, Inclusion, and Belonging Committee (2020-)
- New England Future Faculty Workshop (2020)
- Guatemaltecos Ilustres Orator of the Year (2019)
- Recruitment of summer high school students from low-income backgrounds (2014-)
- Princeton International Students Association Social Chair (2006-2007)

### Social Service

I live up to ideals of lifelong service by volunteering in underserved and immigrant communities:

- Community Servings, Jamaica Plain (2016-)
- Ethos, Jamaica Plain (2011-2015)
- People Making a Difference, Boston (2009-)
- Habitat for Humanity, Guatemala (2006) and US (2009-2014)
- Princeton Medical Center Translation Services (2007-2009)
- UWC Adriatic Social Service Activity, Italy (2004-2005)
- Mazatenango National Hospital, Guatemala (2003 and 2005)

### Professional Service

- Society for Research on Biological Rhythms (2020-)
- International Society for Stem Cell Research (2016-)
- American Association for the Advancement of Science/Science Program for Excellence in Science (2012-)
- New England RNA Data Club (2011-)
- Sigma Xi, (2009-)

### Editorial Advisory Board

2020 StemJournal

### Ad hoc Reviewer

2020 Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, Mechanisms of Development  
 2019 Molecular Medicine  
 2018 Blood, Haematologica  
 2017 Non-Coding RNA, Oxidative Medicine and Cellular Longevity  
 2014 BMC Genomics, Frontiers in Genetics  
 2013 FEBS Open Bio

## REFERENCES

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### Douglas A. Melton, Postdoctoral Advisor

Xander University Professor, Harvard University; Investigator, Howard Hughes Medical Institute  
 Phone: 617-495-1812  
 Email: dmelton@harvard.edu

### Harvey F. Lodish, Doctoral Advisor

Professor of Biology and Professor of Bioengineering, Massachusetts Institute of Technology; Whitehead Institute  
 Phone: 617-258-5216  
 Email: lodish@wi.mit.edu

### Alexander van Oudenaarden, Doctoral Co-Advisor

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