MORGAN L. MAEDER, PhD

41 Spring Park Ave., Jamaica Plain, MA 02130
(617) 460-4420
morganLmaeder@gmail.com

RESEARCH EXPERIENCE

Editas Medicine, Cambridge MA

As a leading genome editing company, Editas Medicine is focused on using CRISPR/Cas9 technology to develop transformative medicines for the treatment of genetic diseases. Founded in November 2013, the company has active preclinical programs in the areas of inherited retinal disease, hemoglobinopathies and immuno-oncology.

Scientist III January 2016-Present
Scientist II January 2014-January 2016
Consultant October-December 2013

- As the LCA10 Program Lead, I played a critical role in the development of EDIT-101 for the treatment of Leber Congenital Amaurosis caused by mutations in the CEP290 gene
    - Developed editing strategy and performed in vitro proof of concept studies
    - Worked with multi-disciplinary team to develop and implement pre-clinical in vivo studies (mouse and non-human primate) to demonstrate therapeutic gene editing strategy
    - Established NGS-based assays for specificity profiling of targeted nucleases
    - Presented program, in person, at the EMA to obtain Orphan status
    - Worked with CMC to transfer research protocols and materials to enable GMP manufacturing
    - Worked with Regulatory to draft materials for, and participate in conversations with, the FDA
- In addition to the LCA10 program, my group (2 research associates and one scientist) also works to explore and develop editing strategies for additional inherited retinal diseases, test novel delivery technologies and develop complex in vitro model systems to interrogate gene editing in photoreceptors
- Inventor on many of the company's early patent filings
- As the first Scientist at the company, I was responsible for establishing the lab and was actively involved in defining the core values and growing the company from an early start-up to a mature public company

Harvard University, Massachusetts General Hospital, Charlestown, MA

Advisor: J. Keith Joung

Postdoctoral Associate May-December 2013
PhD Candidate September 2008-May 2013

- Demonstrated first ZFN-induced correction of a disease causing mutation in human induced pluripotent stem (iPS)cells. Corrected the sickle cell causing mutation in iPS cells derived from sickle cell patients.
- Demonstrated high efficacy and multiplex capabilities of TALE-activator fusions for targeted gene activation.
- Demonstrated first use of CRISPR/Cas9 system for targeted gene activation in human cells.
- Developed ZF and TALE based system for targeted DNA demethylation by engineering fusions to the Tet1 catalytic domain.

Massachusetts General Hospital, Charlestown, MA

Research Technologist June 2007 - August 2008
Research Technician June 2006 - June 2007

- Developed and validated a technology platform for engineering designer DNA-binding zinc finger proteins.
- Induced targeted alteration of endogenous genes in human cells using engineered zinc finger nucleases.
- Demonstrated use of combinatorial zinc finger transcription factor libraries for functional genomics studies in human cells.

EDUCATION

PhD in Genetics, **Harvard University**, Cambridge, MA May 2013

Graduate School of Arts and Sciences, Division of Medical Sciences

BA in Biological Sciences, **Connecticut College,** New London, CT May 2006

Phi Beta Kappa, *Magna Cum Laude*

PROFESSIONAL ACTIVITIES

- American Society of Gene and Cell Therapy, Member (2007-Present)
    - Gene Editing Committee Member (2016-Present)
    - New Investigator Committee Member (2017-Present)
- Association for Research in Vision and Ophthalmology, Member (2015-Present)
- Guest lecturer in Gene Editing course for Harvard Biological and Biomedical Sciences PhD program
- Member of *Human Gene Therapy Methods* Editorial Board
- Peer Reviewer for *Nature Biotechnology, Nature Methods, Nature Communications, Molecular Therapy, Nucleic Acids Research, Nucleic Acids Research Methods* and *PLOS One*

PATENT APPLICATIONS

Inventor on total of 16 submitted patent applications and 2 granted patents.

- Crispr/cas-related methods and compositions for treating leber's congenital amaurosis 10 (lca10). WO-2015138510-A1
- Crispr/cas-related methods and compositions for treating usher syndrome and retinitis pigmentosa. WO-2015134812-A1
- Compositions and methods for treating cep290 associated disease. WO-2018026976-A1
- Zinc finger nuclease for the CFTR gene and methods of use thereof. US-8846578-B2
- TAL-Tet1 fusion proteins and methods of use thereof. US-9890364-B2

PUBLICATIONS

Maeder ML, Gersbach CA. Genome-editing Technologies for Gene and Cell Therapy. *Molecular Therapy*. 2016 Mar;24(3):430-46.

Friedland AE, Baral R, Singhal P, Loveluck K, Shen S, Sanchez M, Marco E, Gotta GM, **Maeder ML**, Kennedy EM, Kornepati AV, Sousa A, Collins MA, Jayaram H, Cullen BR, Bumcrot D. Characterization of Staphylococcus aureus Cas9: a smaller Cas9 for all-in-one adeno-associated virus delivery and paired nickase applications. *Genome Biol*. 2015 Nov 24;16:257.

Gori JL, Hsu PD, **Maeder ML**, Shen S, Welstead GG, Bumcrot D. Delivery and Specificity of CRISPR-Cas9 Genome Editing Technologies for Human Gene Therapy. *Hum Gene Ther*. 2015 Jul;26(7):443-51.

Rahman SH, Kuehle J, Reimann C, Mlambo T, Alzubi J, **Maeder ML**, Riedel H, Fisch P, Cantz T, Rudolph C, Mussolino C, Joung JK, Schambach A, Cathomen T. Rescue of DNA-PK Signaling and

T-Cell Differentiation by Targeted Genome Editing in a prkdc Deficient iPSC Disease Model. *PLoS Genet*. 2015 May 22;11(5):e1005239.

Zuris JA, Thompson DB, Shu Y, Guilinger JP, Bessen JL, Hu JH, **Maeder ML**, Joung JK, Chen ZY, Liu DR. Cationic lipid-mediated delivery of proteins enables efficient protein-based genome editing in vitro and in vivo. *Nature Biotechnology*. 2015 Jan;33(1):73-80.

Liu Y, Kretz CA, **Maeder ML**, Richter CE, Tsao P, Vo AH, Huarng MC, Rode T, Hu Z, Mehra R, Olson ST, Joung JK, Shavit JA. Targeted mutagenesis of zebrafish antithrombin III triggers disseminated intravascular coagulation and thrombosis, revealing insight into function. *Blood*. 2014 Jul 3;124(1):142-50.

Kiskinis E, Sandoe J, Williams LA, Boulting GL, Moccia R, Wainger BJ, Han S, Peng T, Thams S, Mikkilineni S, Mellin C, Merkle FT, Davis-Dusenbery BN, Ziller M, Oakley D, Ichida J, Di Costanzo S, Atwater N, **Maeder ML**, Goodwin MJ, Nemesh J, Handsaker RE, Paull D, Noggle S, McCarroll SA, Joung JK, Woolf CJ, Brown RH, Eggan K. Pathways disrupted in human ALS motor neurons identified through genetic correction of mutant SOD1. *Cell Stem Cell*. 2014 Jun 5;14(6):781-95.

Maeder ML*, Angstman JF*, Richardson ME, Linder SJ, Cascio VM, Tsai SQ, Ho QH, Sander JD, Reyon D, Bernstein BE, Costello JF, Wilkinson MF, Joung JK. Targeted DNA demethylation and activation of endogenous genes using programmable TALE-TET1 fusion proteins. *Nature Biotechnology*. 2013 Dec;31(12):1137-42.

Hwang WY, Fu Y, Reyon D, **Maeder ML**, Kaini P, Sander JD, Joung JK, Peterson RT, Yeh JR. Heritable and precise zebrafish genome editing using a CRISPR-Cas system. *PLoS One*. 2013 Jul 9;8(7):e68708.

Maeder ML, Linder SJ, Cascio VM, Fu Y, Ho QH, Joung JK. CRISPR RNA-guided activation of endogenous human genes. *Nature Methods*. 2013 Oct;10(10):977-9.

Reyon D, **Maeder ML**, Khayter C, Tsai SQ, Foley JE, Sander JD, Joung JK. Engineering Customized TALE Nucleases (TALENs) and TALE Transcription Factors by Fast Ligation-Based Automatable Solid-Phase High-Throughput (FLASH) Assembly. *Curr Protoc Mol Biol*. 2013 Jul;Chapter 12:Unit12.16.

Fu Y, Foden JA, Khayter C, **Maeder ML**, Reyon D, Joung JK, Sander JD. High-frequency off-target mutagenesis induced by CRISPR-Cas nucleases in human cells. *Nature Biotechnology*. 2013 Jun 23.

Osborn MJ, Starker CG, McElroy AN, Webber BR, Riddle MJ, Xia L, Defeo AP, Gabriel R, Schmidt M, Von Kalle C, Carlson DF, **Maeder ML**, Joung JK, Wagner JE, Voytas DF, Blazar BR, Tolar J. TALEN-based Gene Correction for Epidermolysis Bullosa. *Molecular Therapy*. 2013 Jun;21(6):1151-9.

Maeder ML, Linder SJ, Reyon D, Angstman JF, Fu Y, Sander JD, Joung JK. Robust, synergistic regulation of human gene expression using TALE activators. *Nature Methods*. 2013 Mar;10(3):243-5.

Hwang WY, Fu Y, Reyon D, **Maeder ML**, Tsai SQ, Sander JD, Peterson RT, Yeh JR, Joung JK. Efficient genome editing in zebrafish using a CRISPR-Cas system. *Nature Biotechnology*. 2013 Mar;31(3):227-9.

Hermann M, **Maeder ML**, Rector K, Ruiz J, Becher B, Bürki K, Khayter C, Aguzzi A, Joung JK, Buch T, Pelczar P. Evaluation of OPEN zinc finger nucleases for direct gene targeting of the ROSA26 locus in mouse embryos. *PLoS One*. 2012;7(9):e41796.

Sebastiano V*, **Maeder ML***, Angstman JF, Haddad B, Khayter C, Yeo DT, Goodwin MJ, Hawkins JS, Ramirez CL, Batista LF, Artandi SE, Wernig M, Joung JK. In situ genetic correction of the sickle cell anemia mutation in human induced pluripotent stem cells using engineered zinc finger nucleases. *Stem Cells*. 2011 Nov;29(11):1717-26.

Lee J, Hirsh AS, Wittner BS, **Maeder ML**, Singavarapu R, Lang M, Janarthanan S, McDermott U, Yajnik V, Ramaswamy S, Joung JK, Sgroi DC. Induction of stable drug resistance in human breast cancer cells using a combinatorial zinc finger transcription factor library. *PLoS One*. 2011;6(7):e21112.

Sander JD, Dahlborg EJ, Goodwin MJ, Cade L, Zhang F, Cifuentes D, Curtin SJ, Blackburn JS, Thibodeau-Beganny S, Qi Y, Pierick CJ, Hoffman E, **Maeder ML**, Khayter C, Reyon D, Dobbs D, Langenau DM, Stupar RM, Giraldez AJ, Voytas DF, Peterson RT, Yeh JR, Joung JK. Selection-free zinc-finger-nuclease engineering by context-dependent assembly (CoDA). *Nature Methods*. 2011 Jan;8(1):67-9.

Sander JD*, **Maeder ML***, Joung JK. Engineering designer nucleases with customized cleavage specificities. *Curr Protoc Mol Biol*. 2011 Oct;Chapter 12:Unit12.13.

Rahman SH, **Maeder ML**, Joung JK, Cathomen T. Zinc-finger nucleases for somatic gene therapy: the next frontier. *Hum Gene Ther*. 2011 Aug;22(8):925-33. Review.

Sander JD, Reyon D, **Maeder ML**, Foley JE, Thibodeau-Beganny S, Li X, Regan MR, Dahlborg EJ, Goodwin MJ, Fu F, Voytas DF, Joung JK, Dobbs D. Predicting success of oligomerized pool engineering (OPEN) for zinc finger target site sequences. *BMC Bioinformatics*. 2010 Nov 2;11:543.

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Sander JD, **Maeder ML**, Reyon D, Voytas DF, Joung JK, Dobbs D. ZiFiT (Zinc Finger Targeter): an updated zinc finger engineering tool. *Nucleic Acids Res*. 2010 Jul 1;38.

Zhang F, **Maeder ML**, Unger-Wallace E, Hoshaw JP, Reyon D, Christian M, Li X, Pierick CJ, Dobbs D, Peterson T, Joung JK, Voytas DF. High frequency targeted mutagenesis in Arabidopsis thaliana using zinc finger nucleases. *Proc Natl Acad Sci*. 2010 Jun 29; 107(26):12028-33.

Thibodeau-Beganny S, **Maeder ML**, Joung JK. Engineering single Cys2His2 zinc finger domains using a bacterial cell-based two-hybrid selection system. *Methods Mol Biol*. 2010;649:31-50.

Foley JE, **Maeder ML**, Pearlberg J, Joung JK, Peterson RT, Yeh JR. Targeted mutagenesis in zebrafish using customized zinc-finger nucleases. *Nature Protocols*. 2009; 4(12):1855-67.

Maeder ML, Thibodeau-Beganny S, Sander JD, Voytas DF, Joung JK. Oligomerized pool engineering (OPEN): an 'open-source' protocol for making customized zinc-finger arrays. *Nature Protocols*. 2009; 4(10):1471-501.

Zou J, **Maeder ML**, Mali P, Pruett-Miller SM, Thibodeau-Beganny S, Chou BK, Chen G, Ye Z, Park IH, Daley GQ, Porteus MH, Joung JK, Cheng L. Gene targeting of a disease-related gene in human induced pluripotent stem and embryonic stem cells. *Cell Stem Cell*. 2009 Jul 2; 5(1):97-110.

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Maeder ML, Megley C, Eastman DA. Differential expression of the Enhancer of split genes in the developing Drosophila midgut. *Hereditas*. 2009 Feb; 146(1).

Foley JE, Yeh JR, **Maeder ML**, Reyon D, Sander JD, Peterson RT, Joung JK. Rapid mutation of endogenous zebrafish genes using zinc finger nucleases made by Oligomerized Pool ENgineering (OPEN). *PLoS One*. 2009;4(2).

Fu F, Sander JD, **Maeder M**, Thibodeau-Beganny S, Joung JK, Dobbs D, Miller L, Voytas DF. Zinc Finger Database (ZiFDB): a repository for information on C2H2 zinc fingers and engineered zinc-finger arrays. *Nucleic Acids Research.* 2008.

Maeder ML, Thibodeau-Beganny S, Osiak A, Wright DA, Anthony RM, Eichtinger M, Jiang T, Foley JE, Winfrey RJ, Townsend JA, Unger-Wallace E, Sander JD, Müller-Lerch F, Fu F, Pearlberg J, Göbel C, Dassie JP, Pruett-Miller SM, Porteus MH, Sgroi DC, Iafrate AJ, Dobbs D, McCray PB Jr, Cathomen T, Voytas DF, Joung JK. Rapid "open-source" engineering of customized zinc-finger nucleases for highly efficient gene modification. *Mol Cell*. 2008 Jul 25; 31(2):294-301.

Pruett-Miller SM, Connelly JP, **Maeder ML**, Joung JK, Porteus MH. Comparison of zinc finger nucleases for use in gene targeting in mammalian cells. *Mol Ther.* 2008 Apr;16(4):707-17.

Maeder ML, Polansky, BJ, Robson, BE, Eastman, DA. Phylogenetic Footprinting Analysis in the Upstream Regulatory Regions of the Drosophila *Enhancer of Split* Genes. *Genetics.* 2007

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SELECTED PRESENTATIONS

Efficient *In Vivo* Gene Editing of Inherited Retinal Disease Genes in Mice and Non-Human Primates. Oral Abstract. American Society of Gene and Cell Therapy 20th Annual Meeting. Washington DC. May 2017.

Envisioning a Gene Editing Approach to Treat Inherited Blindness. Invited Speaker. ProRetina Society Annual Meeting. Potsdam, Germany. April 2017.

Envisioning a Gene Editing Approach to Treat Inherited Blindness. Invited Speaker. FASEB Research Conference – Genome Engineering: Cutting Edge Research and Applications. Lisbon, Portugal. June 2016.

Therapeutic Correction of an LCA-Causing Splice Defect in the CEP290 Gene by CRISPR/Cas-Mediated Genome Editing. Oral Abstract. American Society of Gene and Cell Therapy 18th Annual Meeting. Washington, DC. May 2015.