THOMAS J CRADICK, Ph.D.

SUMMARY

16 years experience in Genome Editing ■ Assaying & Improving Specificity
Protein Engineering ■ Molecular Biology

RESEARCH & MANAGEMENT EXPRERIENCE

CRISPR Therapeutics, Cambridge, MA 2015-present
Head of Genome Editing

Georgia Tech, Atlanta, GA 2011-2015
Research Faculty and Director of Protein Engineering Facility

- Developed bioinformatics for specificity studies and improvements in ZFN, TALEN and CRIPSR.
- Discovered CRISPR bulge tolerance between guide and target site, and developed web tool to identify similar, putative off-target genomic sites.
- Established digital PCR for absolute quantification of gene editing.
- Developed high-throughput automation for nuclease assembly and testing.

Molecular Biology Consultant, San Francisco 2010-2011

University of Iowa, Iowa City, IA 2004-2010
Postdoctoral Fellow (2009-2010)
Biosciences PhD Student (2004-2009)

- Designed & validated Zinc Finger Nucleases (ZFNs) cleaving Hepatitis B DNA.
- Devised the (widely used) Surveyor assay for measuring DNA edits.
- Co-wrote successful R01 grant with Dr. Anton McCaffrey.
- Developed bioinformatics for ZFN design and ZFN-site tool for off-target prediction and assays.

Sangamo Therapeutics, CA 2000-2004
Associate Scientist II

- Created hundreds of DNA-binding domains as part of Zinc Finger (ZF) design and selections group.
- Selected ZFs that specifically bound 50+ DNA triplets using bacterial 2-hybrid screens.
- Developed methods for robust high-throughput assembly (prior to Golden Gate method), and SOPs for validating and testing ZFs and ZFNs.
- Established ZF & ZFN assembly pipelines containing internal and acquired library of selected ZFs.

Tularik Corporation, South San Francisco, CA 1998-1999
Research Associate

- Constructed series of different phage display libraries for high-throughput cellular assays.

University of California, San Francisco, CA 1993-1998
PhD Student Research, Microbiology & Immunology

- Developed novel phage-based selection for proteolytic antibodies against HIV gp120 (Advisor, Dr. Matthias Wabl).
- Assembled and screened very large Phage Display Antibody Libraries, both naïve and from mice
  immunized with transition-state analogs.

Repligen Corporation, Cambridge, MA 1989-1993
Associate Scientist

- Brought in-house, developed and optimized phage display library systems, mapping the binding domains of the company's lead anti-HIV antibodies and proteins: B7s, CD28 and CTLA4.
- Protein engineering and phage expression for structure/function analysis of these and other protein domains for small molecule drug discovery.

Joslin Diabetes Center, Research Associate, 1988-1989
Bioseparations Laboratory, M.I.T., Undergrad Research Opportunity 1988
Emory University Eye Center, Research Associate, 1987
Controlled Drug Release / Langer Lab, M.I.T., Research Associate 1986

EDUCATION

PhD Molecular & Cell Biology, 2009
University of Iowa, Ames, IA

MA, Microbiology & Immunology, 1998A
University of California, San Francisco, CA

BS, Life Sciences, 1998
Massachusetts Institute of Technology, Cambridge, MA

PUBLICATIONS (4687+ citations as of March 2019)

28. C Antoniani, V Meneghini, A Lattanzi, T Felix, O Romano, E Magrin, L Weber, G Pavani, S Hoss, R Kurita, Y Nakamura, **TJ Cradick**, AS Lundberg, M Porteus, M Amendola, W Nemer, M Cavazzana, F Mavilio, A Miccio (2018) Induction of fetal hemoglobin synthesis by CRISPR/Cas9-mediated editing of the human β-globin locus. Blood 13(7)1960-1973.

27. **TJ Cradick** (2016) Cellular Therapies: Gene Editing and Next-Gen CAR T Cells. Chapter in Novel Immunotherapeutic Approaches to the Treatment of Cancer. Springer.
26. EJ Fine, **TJ Cradick**, and G Bao. (2016) Strategies to Determine Off-Target Effects of Engineered Nucleases. Chapter in Genome Editing. Springer. pp 187-222.

25. CM Lee, **TJ Cradick**, E Fine and G Bao. (2016) Nuclease Target Site Selection for Maximizing Ontarget Activity and Minimizing Off-target Effects in Genome Editing. Molecular Therapy, 24(3):475-87.
24. CM Lee, **TJ Cradick** and G Bao. (2016) The Neisseria meningitidis CRISPR/Cas9 System Enables Specific Genome Editing in Mammalian Cells. Molecular Therapy, doi: 10.1038/mt.2016.8.
23, M Müller, CM. Lee, G Gasiuna, TH Davis, **TJ Cradick**, V Siksnys, G Bao, T Cathomen and C Mussolino. (2015) Highly specific human gene editing with the Streptococcus thermophilus CRISPR/Cas9 systems. Molecular Therapy, 24(3):636-44.
22. J Zhao, I Akinsanmi, D Arafat, **TJ Cradick**, CM Lee, S Banskota, G Bao and G Gibson. (2015) A Burden of Rare Variants Associated with Extremes of Gene Expression in Human Peripheral Blood. Am J Hum Genet, 98(2):299-309.
21. S Suzuki, G Sargent, A Esmaeili –Shandiz, M Yezzi, A Lee, Y Yang, S Kim, P Renz, B Illek, H Fisher, Z Qi, J Yu, MO Muench, AI Beyer, AO Guimarães, L Ye, J Chang, EJ Fine, **TJ Cradick**, G Bao, M Rahdar, MH Porteus, T Shuto, H Kai, YW Kan, DC Gruenert. (2016) TALENs Facilitate SDF Correction of F508del CFTR in Airway Epithelial Cell-derived CF-iPSCs. Molecular Therapy – Nucleic Acids, 5, e273.
20. M Mahfouz, M Aouida, A Eid, Z Ali, **TJ Cradick**, C Lee, H Deshmukh, A Atef, D Abusamra, S Gadhoum, J Merzaban, G Bao. (2015) Efficient fdCas9 Synthetic Endonuclease with Improved Specificity for Precise Genome Engineering. PLOS One, 10 (7), e0133373.
19. **TJ Cradick**, P Qiu, CM Lee, EJ Fine and G Bao. (2014) COSMID: A Web-based Tool for Identifying and Validating CRISPR/Cas Off-target Sites. Molecular Therapy – Nucleic Acids, 3(12): e214
18. C Abarrategui-Pontes, A Créneguy, R Thinard, EJ Fine, V Thepenier, L Fournier, **TJ Cradick**, G Bao, L Tesson, G Podevin, I Anegon, TH Nguyen. (2014) Codon swapping of zinc finger nucleases confers expression in primary cells and in vivo from a single lentiviral vector. Current Gene Therapy,14(5): 365-376.
17. C Mussolino, J Alzubi, EJ Fine, R Morbitzer, **TJ Cradick**, T Lahaye, G Bao, and T Cathomen.(2014) TALENs facilitate targeted genome editing in human cells with high specificity and low cytotoxicity. Nucleic Acids Research 42(10): 6762-6773.
16. L Ye, J Wang, AI Beyer, F Teque, **TJ Cradick**, Z Qi, JC Chang, G Bao, MO Muench, J Yu, JA Levy, and YW Kan. (2014) Seamless modification of wild-type induced pluripotent stem cells to the natural CCR5Δ32 mutation confers resistance to HIV infection. Proc Natl Acad Sci U S A. 111(26): 9591-6.
15. Y Lin, **TJ Cradick**, MT Brown, H Deshmukh, P Ranjan, N Sarode, BM Wile, PM Vertino, FJ Stewart, and G Bao. (2014) CRISPR/Cas9 systems have off-target activity with insertions or deletions between target DNA and guide RNA sequences. Nucleic Acids Research, 42(11): 7473-85.
14. S Tong, EJ Fine, Y Lin, **TJ Cradick**, and G Bao. (2014) Nanomedicine: tiny particles and machines give huge gains. Annual of Biomed Eng. 42(2): 243-59 55, 843-861.
13. **TJ Cradick**, CJ Antico and G Bao. (2014) High-throughput cellular screening of engineered nuclease activity using the single-strand annealing assay and luciferase reporter. Methods in Molecular Biology, 1114, 339-52.

12. EJ Fine, **TJ Cradick** and G Bao. (2014) Identification of Off-Target Cleavage Sites of Zinc Finger Nucleases and TAL Effector Nucleases Using Predictive Models. Methods in Molecular Biology, 1114, 371-383.
11. Y Lin, **TJ Cradick** and G Bao. (2014) Designing and Testing the Activities of TAL Effector Nucleases. Methods in Molecular Biology, 1114, 203-219.
10. Y Lin, EJ Fine, Z Zheng, CJ Antico, RA Voit, MH Porteus, **TJ Cradick*** and G Bao*. (2014) SAPTA: a new design tool for improving TALE nuclease activity. Nucleic Acids Research, 42 (6): e47. *Co-corresponding authors.
9. EJ Fine, **TJ Cradick**, CL Zhao, Y Lin and G Bao. (2014) An online bioinformatics tool predicts zinc finger and TALE nuclease off-target cleavage. Nucleic Acids Research, 42 (6): e42.
8. **TJ Cradick,** EJ Fine, CJ Antico and G Bao. (2013) CRISPR/Cas9 systems targeting β-globin and CCR5 genes have substantial off-target activity. Nucleic Acids Research, 41: 9584-9592.
7. PD Hsu, DA Scott, JA Weinstein, FA Ran, S Konermann, V Agarwala, Y Li, EJ Fine, W Wu, O Shalem, **TJ Cradick**, LA Marraffini, G Bao and F Zhang. (2013) DNA targeting specificity of RNA guided Cas9 nucleases. Nature Biotechnology, 31 (9): 827-832.
6. S Tong, **TJ Cradick**, Y Ma, Z Dai, and G Bao. (2012) Engineering imaging probes and molecular machines for nanomedicine. Science China, Life Science, 55: 843-861.
5. CL Ramirez, MT Certo, C Mussolino, MJ Goodwin, **TJ Cradick**, AP McCaffrey, T Cathomen, AM Scharenberg, and JK Joung. (2012) Engineered zinc finger nickases induce homology-directed repair with reduced mutagenic effects. Nucleic Acids Research, 40: 5560-5568.
4. **TJ Cradick**, G Ambrosini, C Iseli, P Bucher and AP McCaffrey. (2011) ZFN-Site searches genomes for zinc finger nuclease target sites and off-target sites. BMC Bioinformatics, 12: 152.
3. **TJ Cradick**, K Keck, S Bradshaw, AC Jamieson, and AP McCaffrey. (2010) Zinc-finger nucleases as a novel therapeutic strategy for targeting hepatitis B virus DNAs. Mol. Therapy, 18: 947-954.
2. AC Jamieson, B Guan, **TJ Cradick**, H Xiao, M Holmes, PD Gregory and PM Carroll. (2006) Controlling gene expression in Drosophila using engineered zinc finger protein transcription factors. Biochemical and Biophysical Research Communication, 348: 873-879.
1. CL Jellis, **TJ Cradick**, PD Rennert, P Salinas, J Boyd, J., T Amirault, and GS Gray. (1993) Defining critical residues in the epitope for a HIV-neutralizing monoclonal antibody using phage display and peptide array technologies. Gene, 137: 63-68.

EDITORIAL & REVIEWER ACTIVITIES

Nucleic Acids Research, Molecular Therapy, Molecular Therapy - Nucleic Acids, Bioinformatics, Briefings in Bioinformatics, Cancer Gene Therapy, Nature Publishing Group, & CRISPR Journal.