

Albert Wu Cheng, PhD

Contact Information

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Academic Appointments

Assistant Professor, The Jackson Laboratory for Genomic Medicine, Farmington, CT	2015-present
JAX Scholar, The Jackson Laboratory, Bar Harbor, ME	2014-2015

Education

Massachusetts Institute of Technology (MIT) – Cambridge, MA

PhD in Computational and Systems Biology 2007-2014

- Supervisors: Prof. Chris Burge, Prof. Rudolf Jaenisch
- Concentrations: Gene Regulation: Epigenetics, Transcriptional, mRNA processing, Bioinformatics, Cancer and Metastasis, Stem Cell and Development, Somatic Cell Reprogramming, Synthetic Biology, Genome Engineering
- Thesis: Epigenetic and post-transcriptional regulation of gene expression in pluripotent stem cells, differentiation and metastasis

Hong Kong University of Science and Technology (HKUST) – Hong Kong

MPhil in Biology 2005-2007

- Supervisor: Prof. King L. Chow
- Concentrations: Developmental Genetics, RNAi screen
- Thesis: Characterization of *irx-1* in *C. elegans* sensory ray development

BSc in Biochemistry 2002-2005

- First Class Honors with Academic Achievement Medal
- Supervisors: Prof. Nancy Ip, Prof. Hong Xue, Prof. Robert Ko
- Final Year Project Thesis: SLAM-associated protein (SAP) as a potential negative regulator in Trk signaling. Second Year Research Project: Computational design of primers for genotyping

Research Topics

Cheng Lab, The Jackson Laboratory for Genomic Medicine, Farmington, CT 2015-present

- Development of novel and improved CRISPR/Cas-based enzymes for genome and epigenome editing
- Development of CRISPR/Cas-based DNA probes to study 3D structure of genome
- Development of approaches for therapeutic delivery of CRISPR/Cas

JAX Scholar, The Jackson Laboratory – Bar Harbor, ME 2014-2015

- Parameters affecting CRISPR/Cas-mediated genome editing efficiency
- Novel nucleases for genome editing with improved specificity
- Epigenetic editing of enhancers

PhD, Massachusetts Institute of Technology (MIT) – Cambridge, MA 2007-2014

- Conducted research through computational analysis and experimental biology
- Constructed CRISPR-on, an RNA-programmable transcriptional activator based on CRISPR/Cas, that allows multiplexed activation of endogenous genes. See <http://crispr-on.org>
- Provided computational support to TALEN and CRISPR/Cas-based genome editing efforts mainly in off-target prediction algorithm design.
- Dissected the RNA transcriptome of epithelial-mesenchymal transition and cancer cell lines leading to the identification of a panel of splicing markers for metastatic cancers. Patent application submitted outlining the detection of metastatic cancer using splicing molecular signature.
- Contributed to pioneering studies of pluripotency states in mouse and human embryonic stem cells
- Studied enhancer epigenetics leading to the discovery of H3K27ac as an histone mark for active enhancers
- Research published in 26 papers in peer-reviewed journals.
- Collaborators: Prof Frank Gertler, Prof Harvey Lodish, Prof Richard Young, Prof Phil Sharp, Prof Alexander van Oudenaarden, Prof Laurie Boyer

MPhil, Hong Kong University of Science and Technology (HKUST) – Hong Kong 2002-2007

- Involved in a genome-wide RNAi screen for genes required for proper specification and morphogenesis of *C. elegans* male sensory rays.
- Developed an integrative computational and experimental approach to study gene functions in *C. elegans* sensory ray formation. Dissected the functions of *irx-1* (*Iroquois*) gene.
- Involved in a study of a regulator of receptor tyrosine kinase Trk-mediated signaling
- Developed a software kit for the design of primers for genotyping (Finalist in President's Cup competition)

Publications

(*These authors contributed equally)

Key papers

1. **Cheng, A.W.***, Shi, J.*, Wong P.*, Luo, K.L., Trepman, P., Wang, E.T., Choi, H., Burge, C.B., Lodish, H.F. (2014) Muscleblind-like 1 (Mbnl1) regulates pre-mRNA alternative splicing during terminal erythropoiesis. **Blood** doi: 10.1182/blood-2013-12-542209 PMID: 24869935
2. **Cheng, A.W.***, Wang, H.*, Yang, H, Shi, L., Katz, Y., Theunissen, T.W., Rangarajan, S., Shivalila, C.S., Dadon, D.B., Jaenisch, R. (2013) Multiplexed activation of endogenous genes by CRISPR-on, an RNA-guided transcriptional activator system. **Cell Res.** 23(10):1163-71 PMID: 23979020
3. Shapiro, I.M. *, **Cheng, A.W. ***, Flytzanis, N.C., Balsamo, M., Condeelis, J.S., Oktay, M.H., Burge, C.B., Gertler, F.B. (2011) An EMT-driven alternative splicing program occurs in human breast cancer and modulates cellular phenotype. **PLoS Genet.** 7(8):e1002218 PMID: 21876675
4. Creighton, M.P.* , **Cheng A.W.***, Welstead, G.G., Kooistra, T., Carey, B.W., Steine, E.J., Hanna, J., Lodato, M.A., Frampton, G.M., Sharp, P.A., Boyer, L.A., Young, R.A., Jaenisch, R. (2010) Histone H3K27ac separates active from poised enhancers and predicts developmental state. **Proc. Natl. Acad. Sci. U.S.A.** 107(50):21931-6 PMID: 21106759

Others

5. Wiles, M.V., Qin, W., Cheng, A.W., Wang, H. (2015) CRISPR-Cas9-mediated genome editing and guide RNA design. **Mammalian Genome** DOI 10.1007/s00335-015-9565-z
6. Qin, W., Dion, S.L., Kutny, P.M., Zhang, Y., **Cheng, A.W.**, Jillette, N.L., Malhotra, A., Geurts, A.M., Chen, Y.-G., Wang, H. (2015) Efficient CRISPR/Cas9-mediated genome editing in mice by zygote electroporation of nuclease. **Genetics** 115.176594
7. Han, Y., Slivano, O.J., Christie, C.K., **Cheng, A.W.**, Miano, J.M. (2014) CRISPR-Cas9 Genome Editing of a Single Regulatory Element Nearly Abolishes Target Gene Expression in Mice. **Arterioscler Thromb Vasc Biol.** pii: ATVB.AHA.114.305017. PMID: 25538209
8. Katz, Y., Li, F., Lambert, N.J., Sokol, E.S., Tam, W.L., Cheng, A.W., Airoidi, E.M., Lengner, C.J., Gupta, P.B., Yu, Z., Jaenisch, R., Burge, C.B. (2014) Musashi proteins are post-transcriptional regulators of the epithelial-luminal cell state. **Elife** doi: 10.7554/eLife.03915. PMID: 25380226
9. Wu, X., Scott, D.A., Kriz, A.J., Chiu, A.C., Hsu, P.D., Dadon, D.B., **Cheng, A.W.**, Trevino, A.E., Konermann, S., Chen, S., Jaenisch, R., Zhang, F., Sharp, P.A. (2014) Genome-wide binding of CRISPR endonuclease Cas9 in mammalian cells. **Nat. Biotechnol.** doi: 10.1038/nbt.2889 PMID: 24752079
10. Maetzel, D.* , Sarkar, S.* , Wang, H., Abi-Mosleh, L., Xu, P., **Cheng, A.W.**, Gao, Q., Mitalipova, M., Jaenisch, R. (2014) Genetic and Chemical Correction of Cholesterol Accumulation and Impaired Autophagy in Hepatic and Neural Cells Derived from Niemann-Pick Type C Patient-Specific iPS Cells. **Stem Cell Reports** doi: 10.1016/j.stemcr.2014.03.014

11. Dawlaty, M.M., Breiling, A., Le, T. Barrasa M.I., Raddatz, G., Gao, Q., Powell, B.E., **Cheng, A.W.**, Faull, K.F., Lyko, F., Jaenisch R. (2014) Loss of Tet enzymes compromises proper differentiation of embryonic stem cells. **Dev. Cell.** 29(1):102-11 PMID: 24735881
12. Li, Y., Wang, H., Muffat, J., **Cheng, A.W.**, Orlando, D.A., Loven, J., Kwok, S., Feldman, D.A., Bateup, H.S., Gao Q., Hockemeyer, D., Mitalipova, M., Lewis, C.A., Heiden, W.G.V., Sur, M., Young, R.A., Jaenisch, R. (2013) Global transcriptional and translational repression in human-embryonic-stem-cell-derived Rett Syndrome neurons. **Cell Stem Cell** 13(4):446-58 PMID: 24094325
13. Rudenko, A., Dawlaty, M.M., Seo, J., **Cheng, A.W.**, Meng, J., Le, T., Faull, K.F., Jaenisch, R., Tsai, L.H. (2013) Tet1 is critical for neuronal activity-regulated gene expression and memory extinction. **Neuron** 79(6):1109-22 PMID: 24050401
14. Yang, H.* , Wang, H.* , Shivalila, C.S.* , **Cheng, A.W.**, Shi, L., Jaenisch, R. (2013). One-step generation of mice carrying reporter and conditional alleles by CRISPR/Cas-mediated genome engineering. **Cell** 154(6):1370-9 PMID: 23992847
15. Faddah, D.A., Wang, H., **Cheng, A.W.**, Katz, Y., Buganim, Y., Jaenisch, R (2013). Single-cell analysis reveals that expression of nanog is biallelic and equally variable as that of other pluripotency factors in mouse ESCs. **Cell Stem Cell** 13(1):23-9 PMID: 23827708
16. Wang, H.* , Hu, Y.C.* , Markoulaki, S., Welstead, C.G., **Cheng, A.W.**, Shivalila, C.S., Pyntikova, T., Dadon, D.B., Voytas, D.F., Bogdanove, A.J., Page, D.C., Jaenisch, R (2013). TALEN-mediated editing of the mouse Y chromosome. **Nat. Biotechnol.** 31(6):530-2 PMID: 23666012
17. Wang, H.* , Yang, H.* , Shivalila, C.S.* , Dawlaty, M.M., **Cheng, A.W.**, Zhang, F., Jaenisch, R (2013). One-step generation of mice carrying mutations in multiple genes by CRISPR/Cas-mediated genome engineering. **Cell** 153(4):910-8 PMID: 23643243
18. Lodato, M.A., Ng, C.W.* , Wamstad, J.A.* , **Cheng, A.W.**, Thai, K.K., Faenkel, E., Jaenisch, R., Boyer, L.A. (2013) SOX2 Co-occupies Distal Enhancer Elements with Distinct POU Factors in ESCs and NPCs to Specify Cell State. **PLoS Genet.** 9(2):e1003288 PMID: 23437007
19. Dawlaty, M.M., Breiling, A., Le, T., Raddatz, G., Barrasa, M.I., **Cheng, A.W.**, Gao, Q., Powell, B.E., Li, Z., Xu, M., Faull, K.F., Lyko, F., Jaenisch R. (2013) Combined Deficiency of Tet1 and Tet2 Causes Epigenetic Abnormalities but Is Compatible with Postnatal Development. **Dev. Cell** 24(3):310-23 PMID: 23352810
20. Buganim, Y.* , Faddah D.A.* , **Cheng, A.W.**, Itskovich, E., Markoulaki, S., Gantz, K., Klemm S.L., van Oudenaarden A., Jaenisch, R. (2012) Single-Cell Expression Analyses during Cellular Reprogramming Reveal an Early Stochastic and a Late Hierarchic Phase. **Cell** 150(6):1209-22 PMID: 22980981
21. Buganim, Y., Itskovich, E., Hu, Y.-C., **Cheng, A.W.**, Ganz, K., Sarkar, S., Fu, D.D., Welstead, G., Page, D.C., Jaenisch, R. (2012) Direct Reprogramming of Fibroblasts into Embryonic Sertoli-like Cells by Defined Factors. **Cell Stem Cell** 11(3):373-86 PMID: 22958931
22. Welstead, G.G., Creighton, M.P., Bilodeau, S., **Cheng, A.W.**, Markoulaki, S., Young, R.A., Jaenisch R. X-linked H3K27me3 demethylase Utx is required for embryonic development in a sex-specific manner. **Proc. Natl. Acad. Sci. U.S.A.** 109(32):13004-9 PMID: 22826230

23. Kim, J., Su, S.C., Wang, H., **Cheng, A.W.**, Cassady, J.P., Lodato, M.A., Lengner, C.J., Chung, C.Y., Dawlaty, M.M., Tsai, L.H., Jaenisch R. (2011) Functional integration of dopaminergic neurons directly converted from mouse fibroblasts. *Cell Stem Cell* 9(5):413-9 PMID: 22019014
24. Wong, P., Hattangadi, S.M., **Cheng, A.W.**, Frampton, G.M., Young, R.A., Lodish, H.F. (2011) Gene induction and repression during terminal erythropoiesis are mediated by distinct epigenetic changes. *Blood* 118(16):e128-38 PMID: 21860024
25. Dawlaty, M.M., Ganz, K., Powell, B.E., Hu, Y.C., Markoulaki, S., **Cheng, A.W.**, Gao, Q., Kim, J., Choi, S.W., Page, D.C., Jaenisch, R. (2011) Tet1 is dispensable for maintaining pluripotency and its loss is compatible with embryonic and postnatal development. *Cell Stem Cell* 5;9(2):166-75 PMID: 21816367
26. Soldner, F., Laganière, J., **Cheng, A.W.**, Hockemeyer, D., Gao, Q., Alagappan, R., Khurana, V., Golbe, L.I., Myers, R.H., Lindquist, S., Zhang, L., Guschin, D., Fong, L.K., Vu, B.J., Meng, X., Urnov, F.D., Rebar, E.J., Gregory, P.D., Zhang, H.S., Jaenisch, R. (2011) Generation of isogenic pluripotent stem cells differing exclusively at two early onset Parkinson point mutations. *Cell* 146(2):318-31 PMID: 21757228
27. Lengner C.J., Erwin, J.A.*, Gimelbrant A.A.*, **Cheng A.W.**, Guenther M.G., Welstead G.G., Alagappan R., Frampton M.F., Xu P., Powers D., Barrett C.B., Young R.A., Lee J.T., Jaenisch R., Mitalipova, M. (2010) Derivation of pre-X inactivation human embryonic stem cells under physiological oxygen concentrations. *Cell* 141(5):872-83 PMID: 20471072
28. Hanna J., **Cheng, A.W.**, Saha K., Kim J.P., Lengner, C.J., Soldner, F., Cassady, J.P., Muffat, J., Carey, B.W., Jaenisch R. (2010) Human embryonic stem cells with biological and epigenetic characteristics similar to those of mouse ESCs. *Proc. Natl. Acad. Sci. U.S.A.* 107(20):9222-7 PMID: 20442331
29. Hanna, J.*, Markoulaki, S.*, Mitalipova, M., **Cheng, A.W.**, Cassady, J.P., Staerk, J., Carey, B.W., Lengner, C.J., Foreman, R., Love, J., Gao, Q., Kim, J., Jaenisch, R. (2009) Metastable Pluripotent States in NOD-Mouse-Derived ESCs. *Cell Stem Cell* 4(6):513-24 PMID: 19427283
30. Markoulaki, S.*, Hanna, J.*, Beard, C., Carey, B.W., **Cheng, A.W.**, Lengner, C.J., Dausman, J.A., Fu, D., Gao, Q., Wu, S., Cassady, J.P. and Jaenisch, R. (2008) Transgenic mice with defined combinations of drug-inducible reprogramming factors. *Nat Biotechnol* 27(2):169-71 PMID: 19151700
31. Lo, K.Y., Chin, W. H., Ng, Y. P., **Cheng, A. W.**, Cheung, Z. H and Ip, N. Y. (2005) SLAM-associated protein (SAP) as a potential negative regulator in Trk signaling. *J Biol Chem* 280(50):41744-52 PMID: 16223723

Patent Applications

- Alternatively Spliced mRNA Isoforms as Prognostic and Therapeutic Tools for Metastatic Breast Cancer and Other Invasive/Metastatic Cancers.
- Methods Of Mutating, Modifying Or Modulating Nucleic Acid In A Cell Or Nonhuman Mammal

References

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