Fan Zhang, PhD

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Employment

Harvard Medical School/ Brigham and Women's Hospital (BWH)	US
Research Scientist (Dr. Soumya Raychaudhuri, Immunogenomics Lab)	2017 – Present
Broad Institute of MIT and Harvard	
Associate Scientist	2017 – Present
BWH Single Cell Genomics Core	
Computational Biologist	2018 – Present
Chinese Academy of Sciences	China
Research Associate	2012 – 2013

Education

Ph.D. Biomedical Engineering and Bioinformatics, Worcester Polytechnic Institute (WPI), MA, US
Dissertation: Statistical methods for characterizing genomic heterogeneity in mixed samples
Advisor: Dr. Patrick Flaherty, Statistical Genomics Lab (now in Statistics Dep. UMass Amherst) 2013 – 2017

M.S. Bioinformatics (Full Fellowship), Jilin University, China 2009 – 2012
B.S. Computer Science (Ranking Top 1%), Jilin University, China 2005 – 2009

Selected Publications

1. **Zhang, F.**, Mears, J.R., Shakib, L., Beynor, J.I., Shanaj, S., Korsunsky, I., Nathan, A., the Accelerating Medicines Partnership (AMP) RA/SLE, Donlin, L.T.*, Raychaudhuri, S*. IFN-γ and TNF-α drive a CXCL10+ CCL2+ macrophage phenotype expanded in severe COVID-19 lungs and inflammatory diseases with tissue inflammation. ***Genome Medicine*** 13(1):64, 2021
2. Jonsson, A.H.*, **Zhang, F.***, Gomez-Rivas, E., Watts, G., Faust, H., Rupani, K., Mears, J.R., Rao, D.A., Keras, G., Coblyn, J., Massarotti, E., Todd, D., Weinblatt, M., the AMP RA/SLE, Wei, K., Raychaudhuri, S.*, Brenner, M.B.*. Granzyme K+ CD8 T cells (TteK) form the core population of inflamed human tissue-associated CD8 T cells, In Review, 2021
3. Kang, J.B., Nathan, A., **Zhang, F.**, Millard, N., Rumker, L., Moody, D.B., Korsunsky, I., Raychaudhuri, S. Efficient and precise single-cell reference atlas mapping with Symphony. In Review, 2021
4. Meednu, N., Rangel-Moreno, J., **Zhang, F.**, Escaiera-Rivera, K., Corsiero, E., …, McDavid, A., Anolik, J.H. Single cell analysis of RA synovial B cells reveals a dynamic spectrum of ectopic lymphoid B cell activation and hypermutation characterized by NR4A nuclear receptor expression. In Review, 2021
5. Guan, S., Mehta, B., Slater, D., Thompson, J., DiCarlo, E., Pannellini, T., Pearce-Fisher, D., **Zhang, F.** Raychaudhuri, S., Hale, C., Jiang, C.S., Goodman, S., Orange, D. Rheumatoid arthritis synovial inflammation quantification using computer vision. In Review, 2021
6. Fan, J., Slowikowski, K, **Zhang, F**. Single-cell transcriptomics in cancer: computational challenges and opportunities. ***Nature Experimental & Molecular Medicine***, pp.1-14., 2020
7. Orange, D., Yao, V., Sawicka, K., Jak, J., Frank, M.O., Parveen, S., Blachere, N.E., Hale, C., **Zhang, F.**, Raychaudhuri, S., Troyanskya, O.G., Darnell, R.B. RNA identification of PRIME cells predicting rheumatoid arthritis flares. ***New England Journal of Medicine (NEJM)***, *383*(3), pp.218-228, 2020
8. **Zhang, F.***, Wei, K.*, Slowikowski, K.*, Fonseka, C.Y.*, Rao, D.A.*, Kelly, S., Goodman, S.M., Tabechian, D., Hughes, L.B., Salomon-Escoto, K., Watts, G.F.M., Jonsson, A.H., Rangel-Moreno, J., Pellett, N.M., Rozo, C., Aprezzese, W., Eisenhaure, T.M., Lieb, D., Boyle, D.L., Mandelin A.M., the AMP RA/SLE, Boyce, B.F., DiCarlo, E., Gravallese, E.M., Gregersen, P.K., Moreland, L., Firestein, G.S., Hacohen, N., Nusbaum, C., Lederer, J.A., Perlman, H., Pitzalis, C., Filer, A., Holers, M.V., Bykerk, V.P., Donlin, L.T.*, Anolik, J.H.*, Brenner, M.B.*, Raychaudhuri, S*. Defining inflammatory cell states in rheumatoid arthritis joint synovial tissues by integrating single-cell transcriptomics and mass cytometry. ***Nature Immunology***, *20*(7), pp.928-942, 2019

9. **Zhang, F.**, Wang, C., Trapp, A., and Flaherty, P. A Global Optimization Algorithm for Sparse Mixed Membership Matrix Factorization. In ***Contemporary Biostatistics with Biopharmaceutical Applications*** (pp. 129-156), ICSA Book Series in Statistics. Springer, Cham, 2019
10. Korsunsky, I., Millard, N., Fan, J., Slowikowski, K., **Zhang, F.**, Wei, K., ..., Raychaudhuri, S. Fast, sensitive and accurate integration of single-cell data with Harmony. ***Nature Methods***, pp.1-8, 2019
11. Kuo, D.*, Ding J.*, Cohn, I., **Zhang, F.**, Wei, K., Rao, D., Rozo. C., Sokhi U.K., Shanaj, S., Oliver, D., Echeverria, A.P., DiCarlo E.F., Brenner, M.B., Bykerk, V.P., Goodman, S.M., Raychaudhuri, S., Ratsch, G., Ivashkiv, L.B., Donlin, L.T. HBEGF+ macrophages in rheumatoid arthritis induce fibroblast invasiveness. ***Science Translational Medicine***, *11*(491), 2019
12. Arazi, A.*, Rao, D.A.*, Berthier, C.C.*, Davidson, A., Liu, Y., Hoover, P.J., Chicoine, A., Eisenhaure, T.M., Jonsson, A.H., Li, S., Lieb, D.J., **Zhang, F.**, Slowikovski K, …, Raychaudhuri S., Kretzler, M., Anolik, J.H., Brenner, M.B., Wofsy D., Hacohen, N.*, Diamond, B.*, the AMP RA/SLE. The immune cell landscape in kidneys of patients with lupus nephritis. ***Nature Immunology***, *20*(7), pp.902-914, 2019
13. **Zhang, F.** and Flaherty, P. Variational inference for rare variant detection in deep, heterogeneous next-generation sequencing data. ***BMC Bioinformatics***, *18*(1), 45**,** 2017
14. He, Y., **Zhang, F.**, and Flaherty, P. RVD2: an ultra-sensitive variant detection model for low-depth heterogeneous next-generation sequencing data. ***Bioinformatics***, *31*(17), 2785-2793, 2015
15. **Zhang, F.**, Chen, S., Zhang, H., Zhang, X., and Li, G. Bioelectric signal detrending using smoothness prior approach. ***Medical Engineering & Physics***, *36*(8), 1007-1013, 2014
16. Geng, Y., **Zhang, F.**, Yang, L., Zhang, Y., and Li, G. Reduction of the effect of arm position variation on real-time performance of motion classification. In *Engineering in Medicine and Biology Society (**EMBC**), 2012 Annual International Conference of the IEEE* (pp. 2772-2775), 2012
17. Liang, Y., **Zhang, F.**, Wang, J., Joshi, T., Wang, Y., and Xu, D. Prediction of drought-resistant genes in Arabidopsis thaliana using SVM-RFE. ***PloS one***, *6*(7), e21750, 2011

Software/Toolkit

1. **Toolkit** (R): An integrative pipeline to in integrate single-cell RNA-seq, bulk RNA-seq, and mass cytometry data (Zhang, *et al*. 2019)
2. **GOP** (Python): A global optimization model to identify global optimum for a parse mixed membership matrix factorization for heterogeneous gene expression samples (Zhang, *et al*. 2019)
3. **RVD/RVD2** (Python): A variational Bayesian model to identify rare variants in heterogeneous NGS clinical samples (Zhang, *et al*. 2017)
4. **RA/SLE websites** (R): single-cell data visualization (Zhang, *et al*. 2019; Arazi, *et al*, 2019)

Invited Talks

2021 **Oral Talk**. ***Federation of Clinical Immunology Societies (FOCIS)***, 2021 virtual
IFN-γ and TNF-α drive a CXCL10+ CCL2+ macrophage phenotype expanded in severe COVID-19 lungs and inflammatory diseases with tissue inflammation

2020 **Invited Talk.** Center for Skeletal Research at **Massachusetts General Hospital**, Boston, MA, May
Integration of single-cell transcriptomic and proteomic data to study autoimmune diseases

2019 **Invited Talk. *American College of Rheumatology (ACR)***, Atlanta, GA
System-level multi-modality data integration for single-cell transcriptomics

2019 **Oral Talk. *American College of Rheumatology (ACR)***, Atlanta, GA
Integration of single cells from inflammatory disease tissues reveals common pathogenic cell states

2019 **Oral Talk. The Accelerating Medicines Partnership (AMP) RA/SLE Face to Face,** Washington, DC
Integration of single cells from inflammatory disease tissues reveals common pathogenic cell states

2019 **Oral Talk. Single Cell Biology Keystone Symposia,** Breckenridge, CO
Integrating single-cell transcriptomics and mass cytometry to define cell states in rheumatoid arthritis

2018 **Keynote Speak**. ***IV European Conference "Genomics of Complex Diseases: New Challenges***".
Pfizer-University of Granada-Junta de Andalucia Center for Genomics and Oncological Research (GEYNO), Granada, Spain
Functional genetics and genomics to define rheumatoid arthritis

2018 **Invited Talk**. ***Federation of Clinical Immunology Societies (FOCIS)***, San Francisco, CA
Defining inflammatory cell states in rheumatoid arthritis joint synovia tissues by single-cell technology

2017 **Invited Talk**. ***American College of Rheumatology (ACR)****,* San Diego, CA
Technology in precision medicine: data analysis and integration of high dimensional data from rheumatoid arthritis joint tissue

2017 **Oral Talk**. ***Immunogenomics***, HudsonAlpha Institute for Biotechnology, Huntsville, AL
A novel computational method to resolve cellular heterogeneity in disease tissues

2017 **Oral Talk**. **The AMP RA/SLE Face to Face**, Houston, TX
Disease relevant signatures identification in rheumatoid arthritis (RA)

2016 **Oral Talk**. Computational Biomedicine, **Boston University** and **Dana-Farber Cancer Institute**
From data to the clinic: statistical methods for characterizing genomic heterogeneity in mixed samples

Selected Posters

Immunology or Rheumatology Conferences

2021 Kang, J.B., Nathan, A., **Zhang, F.**, …, Korsunsky, I., Raychaudhuri, S.. Efficient and precise single-cell reference atlas mapping with Symphony. **Single Cell Biology Keystone Symposia**

2020 Jonsson, A.H.*, Wei, K.*, **Zhang, F.***, Nathan, A., Mears, J., Watts, G.F.M., …, Accelerating Medicines Partnership RA/SLE Network, Anolik, J., Raychaudhuri, S., Brenner, M. A high-throughput single cell multiomics pipeline to obtain multiple types of single-cell data from synovial biopsies: experience from Phase 2 of the Accelerating Medicines Partnership (AMP) RA/SLE network. ***American College of Rheumatology (ACR)***

2020 Jonsson, A.H., **Zhang, F.**, Watts, G., Wei, K., Rao, D., Raychaudhuri, S., Brenner, M. An expanded granzyme K+ CD8 T cell population induces inflammatory responses in rheumatoid arthritis synovium. ***American College of Rheumatology (ACR)***

2020 Meednu, N., **Zhang, F.**, Escalera-Rivera, K., Corsiero, E., Prediletto, E., Bombardieri, M., Dicarlo, E., Orange, E., Goodman, S., Donlin, L., Raychauduri, S., Pitzalis, S., McDavid, A., Anolik, J.H. Role of NR4A nuclear receptor family in RA synovial ectopic lymphoid neogenesis revealed by single cell profiling. ***American College of Rheumatology (ACR)***

2019 Wei, K.*, Jonsson, A.H.*, **Zhang, F.***, Nathan, A., Mears, J., Watts, G., Zhu, Z., Korsunsky, I., Donlin, L.T., Rao, D., Filer, A., Boyce, B., Gravallese, E., Holers, V.M., Moreland, L., Gregersen, P., Bykerk, V., Anolik, J., Raychaudhuri, S., Brenner, M. Towards a single cell portrait of rheumatoid arthritis-development of a single cell multiomics pipeline for phase 2 of the AMP RA/SLE network. ***American College of Rheumatology (ACR)***

2019 **Zhang, F.**, Mears, J., ..., Raychaudhuri, S. Integration of single cells from inflamed tissue in RA and SLE reveals shared immune and stromal cell population. ***Federation of Clinical Immunology Societies (FOCIS)***

Computational Biology Conferences

2019 **Zhang, F.**, Wei, K., Slowikowski, K., Fonseka, C.Y., Rao, D.A., …, Raychaudhuri, S. Multi-model single-cell transcriptomics and mass cytometry integration to define cell states in rheumatoid arthritis. **Single Cell Biology Keystone Symposia,** Breckenridge, CO

2016 **Zhang, F.,** Wang, C., Trapp, A.C., Flaherty, P. A global optimization algorithm for sparse mixed membership matrix factorization. ***Conference of Reproducibility in Personalized Medicine Research***. Department of Biostatistics at the Harvard TH Chan School of Public Health, Boston, MA

2016 Saddiki, H., **Zhang, F.**, Trapp, A.C., Flaherty, P. A Deterministic Global Optimization Method for Variational Inference. ***Workshop at Neural Information Processing Systems (NIPS)***, Barcelona, Spain

2016 **Zhang, F.,** and Flaherty, P. Variational inference for rare variant detection in deep, heterogeneous next-generation sequencing data. ***New England Statistics Symposium (NESS)***, Yale, CT

2014 **Zhang, F.,** and Flaherty, P. Variant detection model with improved robustness and accuracy for low-depth targeted next-generation sequencing data. The 22th Annual International Conference on ***Intelligent Systems for Molecular Biology (ISMB)***, Boston, MA

2014 **Zhang, F.,** and Flaherty, P. An ultra-sensitive variant detection model for low-depth heterogeneous next-generation sequence. The 18th Annual International Conference on ***Research in Computational Molecular Biology (RECOMB).*** Pittsburgh, PA

Awards and Honors

Full Fellowship for Graduate Student, Jilin University	2009 – 2012
Outstanding Graduate Student, Jilin University (Top 1%)	2011
Graduate Student Entrance Scholarship, Jilin University	2009
“Outstanding Star” of Software Engineering for Undergraduate, IBM	2007

Grant Applications

1. Integrating single-cell genomics and proteomics to identify pro-inflammatory monocytes that drive tissue inflammation in RA and RA-ILD (NIH NIAMS K99/R00, Score: 32)
   PI: Dr. Fan Zhang 2020

2. Identification of novel molecular targets for the development and progression of rheumatoid arthritis-associated lung disease (RA-ILD) (R03)
   Key Personnel (PI: Dr. Tracy J. Doyle) 2019

3. Differentiation of immune cells and fibroblasts in inflamed tissue in RA and SLE – Computational Systems Immunology Core (NIH NIAID PPG)
   Key Personnel (PI: Dr. Soumya Raychaudhuri) 2019

4. AMP RA/SLE – Systems Biology Group (NIH NIAMS)
   Key Personnel (PI: Dr. Soumya Raychaudhuri) 2017

5. A genome-wide survey of point mutations modulating methotrexate
   PhRMA Foundation Informatics Grant
   Key Personnel (PI: Dr. Patrick Flaherty) 2015

Professional Skills

Computation/Statistics: Bayesian statistics, mixture modeling, convex and global optimization, deep learning

Genomic data analysis:
- Multi-omics: single-cell RNA-seq, single-cell ATAC-seq, and single-cell CITE-seq data integration
- Rare variant detection: time-series next-generation sequencing (NGS) DNA-seq data

Programming: Proficient in R and Python, and shell scripting in Linux

Teaching Experience

Teaching Assistant, Biomedical Data Analysis and Programming, WPI	2015, 2016
Teaching Assistant, Biomedical Engineering Design, WPI	2015
Teaching Assistant, Introduction of Biomedical Engineering, WPI	2014

Mentorship

Kathryn Weinand, PhD student at Bioinformatics and Integrative Genomics Program at Harvard
“Method development for integrating single-cell ATAC-seq with single-cell RNA-seq” 2019 – Present

Joseph Mears, Bioinformatics Analyst II at BWH
“Characterization of macrophage heterogeneity using single-cell transcriptomics” 2018 – Present

Gaurav Luthria, PhD student at Bioinformatics and Integrative Genomics Program at Harvard
“Text mining methods for single-cell RNA-seq data annotation” Summer 2017

Yifan Zhao and Tete Zhang, Master student at WPI
“NGS data analysis in mixed tumor samples” 2015 – 2016

Peer Review

Review Editor: *Frontiers in Medicine* 2021 – Present

Ad Hoc Reviewer (*General Journal*): 2017 – 2020
Nature, Nature Communication, Cell Reports Medicine, iScience, Scientific Reports

Ad Hoc Reviewer (*Computational Biology Journal)*: 2017 – 2020
Genomics, Proteomics & Bioinformatics, *Journal of Computational Statistics,*
NESS (New England Statistics Symposium)

Ad Hoc Reviewer (*Rheumatology/Immunology Journal)*: 2018 – 2019
Arthritis Research & Therapy, Cancer Letters