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](https://immunogenomics.hms.harvard.edu/)) 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](https://people.math.umass.edu/~flaherty/) (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](https://genomemedicine.biomedcentral.com/articles/10.1186/s13073-021-00881-3). ***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](https://www.biorxiv.org/content/10.1101/2020.11.18.389189v2). 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](https://www.biorxiv.org/content/10.1101/2021.05.14.443150v1). 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](https://www.nature.com/articles/s12276-020-0422-0). ***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](https://www.nejm.org/doi/full/10.1056/NEJMoa2004114). ***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](https://www.nature.com/articles/s41590-019-0378-1). ***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](https://link.springer.com/chapter/10.1007/978-3-030-15310-6_7). 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](https://www.nature.com/articles/s41592-019-0619-0). ***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](https://stm.sciencemag.org/content/11/491/eaau8587?rss=1&intcmp=trendmd-stm&utm_source=TrendMD&utm_medium=cpc&utm_campaign=TrendMD_1). ***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](https://www.nature.com/articles/s41590-019-0398-x). ***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](https://link.springer.com/article/10.1186/s12859-016-1451-5). ***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](https://academic.oup.com/bioinformatics/article/31/17/2785/183308). ***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](https://pubmed.ncbi.nlm.nih.gov/24894030/). ***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](https://ieeexplore.ieee.org/abstract/document/6346539). 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](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0021750). ***PloS one****, 6*(7), e21750, 2011

**Software/Toolkit**

1. [**Toolkit**](https://github.com/immunogenomics/amp_phase1_ra)(R): An integrative pipeline to in integrate single-cell RNA-seq, bulk RNA-seq, and mass cytometry data (Zhang, *et al*. 2019)
2. [**GOP**](https://github.com/fzhangcode/global_optimization) (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**](https://github.com/fzhangcode/rvd2-variational)(Python): A variational Bayesian model to identify rare variants in heterogeneous NGS clinical samples (Zhang, *et al*. 2017)
4. [**RA**](https://immunogenomics.io/ampra/)**/**[**SLE websites**](https://immunogenomics.io/ampsle/)(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

1. 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

1. 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

1. AMP RA/SLE – Systems Biology Group (NIH NIAMS)

Key Personnel (PI: Dr. Soumya Raychaudhuri) 2017

1. 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*