Fan Zhang, PhD

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**Employment**

**Harvard Medical School (HMS)** US

Research Scientist (Immunogenomics Lab, Dr. Soumya Raychaudhuri) 2017 – Present

**Broad Institute of MIT and Harvard**

Associate Scientist 2017 – Present

**Brigham and Women's Hospital (BWH) Single Cell Genomics Core**

Computational Biologist 2019 – 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 (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 RA/SLE, Donlin, L.T.\*, Raychaudhuri, S\*. [IFN-γ and TNF-α drive a CXCL10+ CCL2+ macrophage phenotype expanded in severe COVID-19 and other diseases with tissue inflammation](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7418716/). *bioRxiv*, 2020
2. Fan, J., Slowikowski, K, **Zhang, F**. Single-cell transcriptomics in cancer: computational challenges and opportunities. ***Nature Experimental & Molecular Medicine***, In press, 2020
3. 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
4. **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 Accelerating Medicines Partnership Rheumatoid Arthritis and Systemic Lupus Erythematosus (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
5. **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
6. 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
7. 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
8. 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, Browne, E.P., Noma, A., Sutherby, D., Steelman, S., Smilek, D.E., Tosta, P., Apruzzese, W., Massarotti, E., Dall, Era, M., Park, M., Kamen, D.L., Furie, R.A., Payan- Schober, F., Pendergraft WF 3rd, Mclnnis E.A., Buyon, J.P., Petri, M.A., Putterman, C., Kalunian, L.C., Woodle, E.S., Lederer, J.A., Hildeman, D.A., Nusbaum, C., Raychaudhuri S., Kretzler, M., Anolik, J.H., Brenner, M.B., Wofsy D., Hacohen, N.\*, Diamond, B.\*, the AMP RA/SLE Consortium. [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
9. **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
10. 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
11. **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
12. 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
13. 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
14. Wang, J., **Zhang, F**., Wang, Y., Fu, Y., Xu, D., and Liang, Y. Identification of Salt Tolerance Genes in Rice from Microarray Data using SVM-RFE. *The 3rd International Conference on Bioinformatics and Computational Biology (****BICoB****)*, New Orleans, pp. 30-35, 2011

**In Review Articles**

1. Mysore, V., Cullere, X., Mears, J., Rosetti, F., Okubo, K., Liew, P.X., **Zhang, F.**, Madera-Salcedo, I., Rosenbauer, F., Stone, R.M., Aster, J.A., Andrian, U.V., Lichtman, A., Raychaudhuri, S., Mayadas. T.N. FcγR engagement reprograms neutrophils into antigen cross-presenting cells that elicit acquired immunity, In Review, 2020

**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**

1. **Invited Talk. Research Methods Workshop,** Center for Skeletal Research at **Massachusetts General Hospital**, Boston, MA,May, 2020

Integration of single-cell transcriptomic and proteomic data to study autoimmune diseases

1. **Invited Talk.** ***American College of Rheumatology (ACR)****,* Atlanta, GA, Nov. 2019

System-level multi-modality data integration for single-cell transcriptomics

1. **Oral Talk.** ***American College of Rheumatology (ACR)****,* Atlanta, GA, Nov. 2019

Integration of single cells from inflammatory disease tissues reveals common and unique pathogenic cell states

1. **Oral Talk. The AMP RA/SLE Face to Face,** Washington DC, Sep. 2019

Integration of single cells from inflammatory disease tissues reveals common and unique pathogenic cell states

1. **Oral Talk. Single Cell Biology Keystone Symposia,** Breckenridge, CA, Jan. 2019

Integrating single-cell transcriptomics and mass cytometry to define cell states in rheumatoid arthritis

1. **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. Oct. 2018

Functional genetics and genomics to define rheumatoid arthritis

1. **Invited Talk**. ***Federation of Clinical Immunology Societies (FOCIS)***, San Francisco, CA. June 2018.

Defining inflammatory cell states in rheumatoid arthritis joint synovia tissues by single-cell technology

1. **Invited Talk**. ***American College of Rheumatology (ACR)****,* San Diego, CA. Nov. 2017.

Technology in precision medicine: data analysis and integration of high dimensional data from rheumatoid arthritis joint tissue

1. **Oral Talk**. ***Immunogenomics***, HudsonAlpha Institute for Biotechnology, Huntsville, AL. Oct. 2017.

A novel computational method to resolve cellular heterogeneity in disease tissues

1. **Oral Talk**. Accelerating Medicines Partnership (AMP) RA/SLE Face-to-Face, Houston, TX, Feb. 2017.

Disease relevant signatures identification in rheumatoid arthritis (RA)

1. **Oral Talk**. Computational Biomedicine, **Boston University** and **Dana-Farber Cancer Institute**, 2016

From data to the clinic: statistical methods for characterizing genomic heterogeneity in mixed samples

**Selected Posters** 

*Immunology or Rheumatology Conferences*

1. 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
2. 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
3. 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)****, 2020*
4. 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 Accelerating Medicine Partnership (AMP)-RA network. ***American College of Rheumatology (ACR)****,*Washington, DC,2019
5. **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).*** Boston, MA, 2019

*Computational Biology Conferences*

1. **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, CA, Jan. 2019
2. **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
3. 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
4. **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, 2016
5. **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
6. **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, 2014

**Grant Applications** 

1. Integrating single-cell genomics and proteomics to define pathogenic cell states shared between RA and RA-ILD Grant K99 (NIH NIAMS, In Review)

PI: Dr. Fan Zhang 2020

1. Differentiation of immune cells and fibroblasts in inflamed tissue in RA and SLE – Computational systems immunology core (NIH NIAID, In Review)

Key Personnel (PI: Dr. Soumya Raychaudhuri) 2019

1. A genome-wide survey of point mutations modulating methotrexate

PhRMA Foundation Informatics Grant 2013080079

Key Personnel (PI: Dr. Patrick Flaherty) 2015

**Professional Skill**

**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 HMS

“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

**Awards & Honor****s**

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

**Professional Affiliations** 

**Member,** American College of Rheumatology (ACR) Sep. 2017 – Present

**Member**, International Society for Computational Biology (ISCB) 2014 – 2015

**Member**, American Association for the Advancement of Science (AAAS) Sep. 2013 – Present

**Peer Review **

Ad Hoc Reviewer (*General Journal*) 2017 – 2020

*Nature, Nature Communication, Cell Reports, 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*