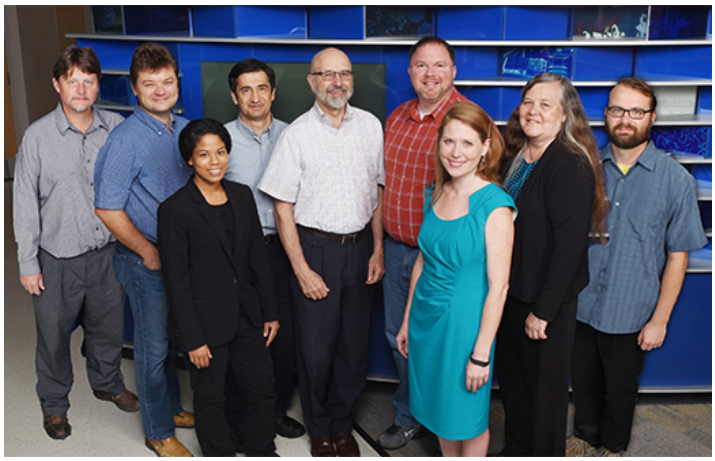
Cincinnati Children's

2015 Research Annual Report

Center for Autoimmune Genomics and Etiology

RESEARCH AND TRAINING DETAILS



Click to view members

Faculty	11
Joint Appointment Faculty	3
Research Fellows	8
Research Students	12
Support Personnel	31
Direct Annual Grant Support	$2,346,350
Direct Annual Industry Support	$196,802
Peer Reviewed Publications	57

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Significant Publications

Lu X, Zoller EE, **Weirauch MT**, Wu Z, **Namjou B**, Williams AH, Ziegler JT, Comeau ME, Marion MC, Glenn SB, Adler A, Shen N, Nath SK, Stevens AM, Freedman BI, Tsao BP, Jacob CO, Kamen DL, Brown EE, Gilkeson GS, Alarcon GS, Reveille JD, Anaya JM, James JA, Sivils KL, Criswell LA, Vila LM, Alarcon-Riquelme ME, Petri M, Scofield RH, Kimberly RP, Ramsey-Goldman R, Joo YB, Choi J, Bae SC, Boackle SA, Graham DC, Vyse TJ, Guthridge JM, Gaffney PM, Langefeld CD, Kelly JA, Greis KD, **Kaufman KM**, **Harley JB**, **Kottyan LC**. Lupus Risk Variant Increases pSTAT1 Binding

and Decreases Ets1 Expression. *Am J Hum Genet*. 2015 May 7;96(5):731-9.

There are 11,000 known genetic associations for 900 diseases, but only for a few of these is it known why the piece of particular DNA sequence is associated with the disease. Lu and colleagues have shown that the association with systemic lupus erythematosus may be related to a particular single small change in the DNA and that this change influences the binding of a factor important in the inflammatory response that is only a few molecules away from the risk variant. This is one of the many steps needed to carry genetic work from association with a piece of DNA to the genetic mechanisms predisposing to disease, which when known will be the basis of improved therapeutics and management.

Pan W, Zhu S, Dai D, Liu Z, Li D, Li B, Gagliani N, Zheng Y, Tang Y, **Weirauch MT**, Chen X, Zhu W, Wang Y, Chen B, Qian Y, Chen Y, Fang J, Herbst R, Richman L, Jallal B, **Harley JB**, Flavell RA, Yao Y, Shen N. Mir-125A Targets Effector Programs to Stabilize Treg-Mediated Immune Homeostasis.*Nat Commun*. 2015 May 12;6:7096.

Micro-RNAs are small RNAs that decrease the expression of genes. Their existence has only been known for a few years, but it is clear that they are very important in careful decisions that are made when a gene is expressed or suppressed. This study shows that micro-RNA 125A is important in whether to respond by suppressing or enhancing inflammation in the Treg type of T lymphocyte. In two different animal models genetic manipulation inactivates micro-RNA 125A results, respectively, in more severe gastrointestinal and brain inflammation. Knowing how manipulations of these micro-RNAs influence the course and progression of inflammatory and autoimmune disease will place us in a position to design new therapies that are more specific and more effective than the therapies now in use.

Rydyznski C, Daniels KA, Karmele EP, Brooks TR, Mahl SE, Moran MT, Li C, Sutiwisesak R, Welsh RM, **Waggoner SN**. Generation of Cellular Immune Memory and B-Cell Immunity Is Impaired by Natural Killer Cells. *Nat Commun*. 2015 Feb;276:6375.

Cells called Natural Killer Cells are an important defense in the immune system for cancer and infection, particularly by viruses, intracellular bacteria, and some parasites. The group working at Cincinnati Children's under Steven Waggoner has shown that these Natural Killer Cells also down regulate the normal immune response. This paper shows that Natural Killer Cells act to diminish established immune responses of B lymphocytes, the cells that make immunoglobulin antibodies. Controlling how Natural Killer Cells do this could be used to improve illnesses caused by chronic infections and generate circumstances where some vaccines are more efficacious.

Division Publications

1. Alexander ES, Martin LJ, Collins MH, Kottyan LC, Sucharew H, He H, Mukkada VA, Succop PA, Abonia JP, Foote H, Eby MD, Grotjan TM, Greenler AJ, Dellon ES, Demain JG, Furuta GT, Gurian LE, Harley JB, Hopp RJ, Kagalwalla A, Kaul A, Nadeau KC, Noel RJ, Putnam PE, von Tiehl KF, Rothenberg ME. **Twin and family studies reveal strong environmental and weaker genetic cues explaining heritability of eosinophilic esophagitis**. *J Allergy Clin Immunol*. 2014; 134:1084-1092 e1.

2. Ballester B, Medina-Rivera A, Schmidt D, Gonzalez-Porta M, Carlucci M, Chen X, Chessman K, Faure AJ, Funnell AP, Goncalves A, Kutter C, Lukk M, Menon S, McLaren WM, Stefflova K, Watt S, Weirauch MT, Crossley M, Marioni JC, Odom DT, Flicek P, Wilson MD. **Multi-species, multi-transcription factor binding highlights conserved control of tissue-specific biological pathways**. *Elife*. 2014; 3:e02626.

3. Botta Gordon-Smith S, Ursu S, Eaton S, Moncrieffe H, Wedderburn LR. **Correlation of low CD73 expression on synovial lymphocytes with reduced adenosine generation and higher disease severity in juvenile idiopathic arthritis**. *Arthritis Rheumatol*. 2015; 67:545-54.

4. Brungs L, A. L, K. K, Levy B, Moncrieffe H. **Genetics basis of the rheumatic diseases or the importance of teh GWAS studies in pediatric rheumatology**. *Ann Paediatr Rheum*. 2014; 3:105-115.

5. Cook KD, Waggoner SN, Whitmire JK. **NK cells and their ability to modulate T cells during virus infections**. *Crit Rev Immunol*. 2014; 34:359-88.

6. Cranert S, Heyse S, Linger BR, Lescasse R, Price C. **Tetrahymena Pot2 is a developmentally regulated paralog of Pot1 that localizes to chromosome breakage sites but not to telomeres**. *Eukaryot Cell*. 2014; 13:1519-29.

7. Crosslin DR, Carrell DS, Burt A, Kim DS, Underwood JG, Hanna DS, Comstock BA, Baldwin E, de Andrade M, Kullo IJ, Tromp G, Kuivaniemi H, Borthwick KM, McCarty CA, Peissig PL, Doheny KF, Pugh E, Kho A, Pacheco J, Hayes MG, Ritchie MD, Verma SS, Armstrong G, Stallings S, Denny JC, Carroll RJ, Crawford DC, Crane PK, Mukherjee S, Bottinger E, Li R, Keating B, Mirel DB, Carlson CS, Harley JB, Larson EB, Jarvik GP. **Genetic variation in the HLA region is associated with susceptibility to herpes zoster**. *Genes Immun*. 2015; 16:1-7.

8. Cutler DJ, Zwick ME, Okou DT, Prahalad S, Walters T, Guthery SL, Dubinsky M, Baldassano R, Crandall WV, Rosh J, Markowitz J, Stephens M, Kellermayer R, Pfefferkorn M, Heyman MB, LeLeiko N, Mack D, Moulton D, Kappelman MD, Kumar A, Prince J, Bose P, Mondal K, Ramachandran D, Bohnsack JF, Griffiths AM, Haberman Y, Essers J, Thompson SD, Aronow B, Keljo DJ, Hyams JS, Denson LA, Group P-KR, Kugathasan S. **Dissecting Allele Architecture of Early Onset IBD Using High-Density Genotyping**. *PLoS One*. 2015; 10:e0128074.

9. de Bruin C, Mericq V, Andrew SF, van Duyvenvoorde HA, Verkaik NS, Losekoot M, Porollo A, Garcia H, Kuang Y, Hanson D, Clayton P, van Gent DC, Wit JM, Hwa V, Dauber A. **An XRCC4 splice mutation associated with severe short stature, gonadal failure, and early-onset metabolic syndrome**. *J Clin Endocrinol Metab*. 2015; 100:E789-98.

10. Ding L, Kurowski BG, He H, Alexander ES, Mersha TB, Fardo DW, Zhang X, Pilipenko VV, Kottyan L, Martin LJ. **Modeling of multivariate longitudinal phenotypes in family genetic studies with Bayesian multiplicity adjustment**. *BMC Proc*. 2014; 8:S69.

11. Ellis JA, Scurrah KJ, Li YR, Ponsonby AL, Chavez RA, Pezic A, Dwyer T, Akikusa JD, Allen RC, Becker ML, Thompson SD, Lie BA, Flato B, Forre O, Punaro M, Wise C, Finkel TH, Hakonarson H, Munro JE. **Epistasis amongst PTPN2 and genes of the vitamin D pathway contributes to risk of juvenile idiopathic arthritis**. *J Steroid Biochem Mol Biol*. 2015; 145:113-20.

12. Fang J, Barker B, Bolanos L, Liu X, Jerez A, Makishima H, Christie S, Chen X, Rao DS, Grimes HL, Komurov K, Weirauch MT, Cancelas JA, Maciejewski JP, Starczynowski DT. **Myeloid malignancies with chromosome 5q deletions acquire a dependency on an intrachromosomal NF-kappaB gene network**. *Cell Rep*. 2014; 8:1328-38.

13. Fardo DW, Zhang X, Ding L, He H, Kurowski B, Alexander ES, Mersha TB, Pilipenko V, Kottyan L, Nandakumar K, Martin L. **On family-based genome-wide association studies with large pedigrees: observations and recommendations**. *BMC Proc*. 2014; 8:S26.

14. Fechter K, Porollo A. **MutaCYP: Classification of missense mutations in human cytochromes P450**. *BMC Med Genomics*. 2014; 7:47.

15. Fowler T, Garruss AS, Ghosh A, De S, Becker KG, Wood WH, Weirauch MT, Smale ST, Aronow B, Sen R, Roy AL. **Divergence of transcriptional landscape occurs early in B cell activation**. *Epigenetics Chromatin*. 2015; 8:20.

16. Garman L, Vineyard AJ, Crowe SR, Harley JB, Spooner CE, Collins LC, Nelson MR, Engler RJ, James JA. **Humoral responses to independent vaccinations are correlated in healthy boosted adults**. *Vaccine*. 2014; 32:5624-31.

17. Harley JB, Moura JM. **Dispersion curve recovery with orthogonal matching pursuit**. *J Acoust Soc Am*. 2015;

137:EL1-7.

18. Harley JB, Zoller EE. **Editorial: What caused all these troubles, anyway? Epstein-Barr virus in Sjogren's syndrome reevaluated**. *Arthritis Rheumatol*. 2014; 66:2328-30.

19. Kariuki SN, Ghodke-Puranik Y, Dorschner JM, Chrabot BS, Kelly JA, Tsao BP, Kimberly RP, Alarcon-Riquelme ME, Jacob CO, Criswell LA, Sivils KL, Langefeld CD, Harley JB, Skol AD, Niewold TB. **Genetic analysis of the pathogenic molecular sub-phenotype interferon-alpha identifies multiple novel loci involved in systemic lupus erythematosus**. *Genes Immun*. 2015; 16:15-23.

20. Kaufman KM, Linghu B, Szustakowski JD, Husami A, Yang F, Zhang K, Filipovich AH, Fall N, Harley JB, Nirmala NR, Grom AA. **Whole-exome sequencing reveals overlap between macrophage activation syndrome in systemic juvenile idiopathic arthritis and familial hemophagocytic lymphohistiocytosis**. *Arthritis Rheumatol*. 2014; 66:3486-95.

21. Kottyan LC, Davis BP, Sherrill JD, Liu K, Rochman M, Kaufman K, Weirauch MT, Vaughn S, Lazaro S, Rupert AM, Kohram M, Stucke EM, Kemme KA, Magnusen A, He H, Dexheimer P, Chehade M, Wood RA, Pesek RD, Vickery BP, Fleischer DM, Lindbad R, Sampson HA, Mukkada VA, Putnam PE, Abonia JP, Martin LJ, Harley JB, Rothenberg ME. **Genome-wide association analysis of eosinophilic esophagitis provides insight into the tissue specificity of this allergic disease**. *Nat Genet*. 2014; 46:895-900.

22. Kottyan LC, Weirauch MT, Rothenberg ME. **Making it big in allergy**. *J Allergy Clin Immunol*. 2015; 135:43-5.

23. Kottyan LC, Zoller EE, Bene J, Lu X, Kelly JA, Rupert AM, Lessard CJ, Vaughn SE, Marion M, Weirauch MT, Namjou B, Adler A, Rasmussen A, Glenn S, Montgomery CG, Hirschfield GM, Xie G, Coltescu C, Amos C, Li H, Ice JA, Nath SK, Mariette X, Bowman S, Registry UKPSsS, Rischmueller M, Lester S, Brun JG, Goransson LG, Harboe E, Omdal R, Cunninghame-Graham DS, Vyse T, Miceli-Richard C, Brennan MT, Lessard JA, Wahren-Herlenius M, Kvarnstrom M, Illei GG, Witte T, Jonsson R, Eriksson P, Nordmark G, Ng WF, Registry UKPSsS, Anaya JM, Rhodus NL, Segal BM, Merrill JT, James JA, Guthridge JM, Scofield RH, Alarcon-Riquelme M, Bae SC, Boackle SA, Criswell LA, Gilkeson G, Kamen DL, Jacob CO, Kimberly R, Brown E, Edberg J, Alarcon GS, Reveille JD, Vila LM, Petri M, Ramsey-Goldman R, Freedman BI, Niewold T, Stevens AM, Tsao BP, Ying J, Mayes MD, Gorlova OY, Wakeland W, Radstake T, Martin E, Martin J, Siminovitch K, Moser Sivils KL, Gaffney PM, Langefeld CD, Harley JB, Kaufman KM. **The IRF5-TNPO3 association with systemic lupus erythematosus has two components that other autoimmune disorders variably share**. *Hum Mol Genet*. 2015; 24:582-96.

24. Kurtulus S, Sholl A, Toe J, Tripathi P, Raynor J, Li KP, Pellegrini M, Hildeman DA. **Bim controls IL-15 availability and limits engagement of multiple BH3-only proteins**. *Cell Death Differ*. 2015; 22:174-84.

25. Li Q, Wang HY, Chepelev I, Zhu Q, Wei G, Zhao K, Wang RF. **Stage-dependent and locus-specific role of histone demethylase Jumonji D3 (JMJD3) in the embryonic stages of lung development**. *PLoS Genet*. 2014; 10:e1004524.

26. Li Q, Zou J, Wang M, Ding X, Chepelev I, Zhou X, Zhao W, Wei G, Cui J, Zhao K, Wang HY, Wang RF. **Critical role of histone demethylase Jmjd3 in the regulation of CD4+ T-cell differentiation**. *Nat Commun*. 2014; 5:5780.

27. Liu C, Harley JB, Berges M, Greve DW, Oppenheim IJ. **Robust ultrasonic damage detection under complex environmental conditions using singular value decomposition**. *Ultrasonics*. 2015; 58:75-86.

28. Lu X, Zoller EE, Weirauch MT, Wu Z, Namjou B, Williams AH, Ziegler JT, Comeau ME, Marion MC, Glenn SB, Adler A, Shen N, Nath SK, Stevens AM, Freedman BI, Tsao BP, Jacob CO, Kamen DL, Brown EE, Gilkeson GS, Alarcon GS, Reveille JD, Anaya JM, James JA, Sivils KL, Criswell LA, Vila LM, Alarcon-Riquelme ME, Petri M, Scofield RH,

Kimberly RP, Ramsey-Goldman R, Joo YB, Choi J, Bae SC, Boackle SA, Graham DC, Vyse TJ, Guthridge JM, Gaffney PM, Langefeld CD, Kelly JA, Greis KD, Kaufman KM, Harley JB, Kottyan LC. **Lupus Risk Variant Increases pSTAT1 Binding and Decreases ETS1 Expression**. *Am J Hum Genet*. 2015; 96:731-9.

29. Lu-Fritts PY, Kottyan LC, James JA, Xie C, Buckholz JM, Pinney SM, Harley JB. **Association of systemic lupus erythematosus with uranium exposure in a community living near a uranium-processing plant: a nested case-control study**. *Arthritis Rheumatol*. 2014; 66:3105-12.

30. Makashir SB, Kottyan LC, Weirauch MT. **Meta-analysis of differential gene co-expression: application to lupus**. *Pac Symp Biocomput*. 2015; :443-54.

31. Martin LJ, Pilipenko V, Kaufman KM, Cripe L, Kottyan LC, Keddache M, Dexheimer P, Weirauch MT, Benson DW. **Whole exome sequencing for familial bicuspid aortic valve identifies putative variants**. *Circ Cardiovasc Genet*. 2014; 7:677-83.

32. Martins M, Williams AH, Comeau M, Marion M, Ziegler JT, Freedman BI, Merrill JT, Glenn SB, Kelly JA, Sivils KM, James JA, Guthridge JM, Alarcon-Riquelme ME, Bae SC, Kim JH, Kim D, Anaya JM, Boackle SA, Criswell LA, Kimberly RP, Alarcon GS, Brown EE, Vila LM, Petri MA, Ramsey-Goldman R, Niewold TB, Tsao BP, Gilkeson GS, Kamen DL, Jacob CO, Stevens AM, Gaffney PM, Harley JB, Langefeld CD, Fesel C. **Genetic association of CD247 (CD3zeta) with SLE in a large-scale multiethnic study**. *Genes Immun*. 2015; 16:142-50.

33. Mersha TB, Ding L, He H, Alexander ES, Zhang X, Kurowski BG, Pilipenko V, Kottyan L, Martin LJ, Fardo DW. **Impact of Population Stratification on Family-Based Association in an Admixed Population**. *Int J Genomics*. 2015; 2015:501617.

34. Moncrieffe H, Prahalad S, Thompson SD. **Genetics of juvenile idiopathic arthritis: new tools bring new approaches**. *Curr Opin Rheumatol*. 2014; 26:579-84.

35. Moncrieffe H, Tillery D, Harris RM. **Addressing Healthcare Disparities in Autoimmune Disease: A Focus on Systemic Lupus Erythematosus in the USA**. *J Pan African Studies*. 2015; 7:64-71.

36. Najafabadi HS, Mnaimneh S, Schmitges FW, Garton M, Lam KN, Yang A, Albu M, Weirauch MT, Radovani E, Kim PM, Greenblatt J, Frey BJ, Hughes TR. **C2H2 zinc finger proteins greatly expand the human regulatory lexicon**. *Nat Biotechnol*. 2015; 33:555-62.

37. Namjou B, Marsolo K, Caroll RJ, Denny JC, Ritchie MD, Verma SS, Lingren T, Porollo A, Cobb BL, Perry C, Kottyan LC, Rothenberg ME, Thompson SD, Holm IA, Kohane IS, Harley JB. **Phenome-wide association study (PheWAS) in EMR-linked pediatric cohorts, genetically links PLCL1 to speech language development and IL5-IL13 to Eosinophilic Esophagitis**. *Front Genet*. 2014; 5:401.

38. Namjou B, Ni Y, Harley IT, Chepelev I, Cobb B, Kottyan LC, Gaffney PM, Guthridge JM, Kaufman K, Harley JB. **The effect of inversion at 8p23 on BLK association with lupus in Caucasian population**. *PLoS One*. 2014; 9:e115614.

39. Narasimhan K, Lambert SA, Yang AW, Riddell J, Mnaimneh S, Zheng H, Albu M, Najafabadi HS, Reece-Hoyes JS, Bass JI, Walhout AJ, Weirauch MT, Hughes TR. **Mapping and analysis of Caenorhabditis elegans transcription factor sequence specificities**. *Elife*. 2015; 4.

40. Pan W, Zhu S, Dai D, Liu Z, Li D, Li B, Gagliani N, Zheng Y, Tang Y, Weirauch MT, Chen X, Zhu W, Wang Y, Chen B, Qian Y, Chen Y, Fang J, Herbst R, Richman L, Jallal B, Harley JB, Flavell RA, Yao Y, Shen N. **MiR-125a targets effector programs to stabilize Treg-mediated immune homeostasis**. *Nat Commun*. 2015; 6:7096.

41. Pestle WJ, Crowley BE, Weirauch MT. **Quantifying inter-laboratory variability in stable isotope analysis of ancient**

skeletal remains. *PLoS One*. 2014; 9:e102844.

42. Pilipenko VV, He H, Kurowski BG, Alexander ES, Zhang X, Ding L, Mersha TB, Kottyan L, Fardo DW, Martin LJ. **Using Mendelian inheritance errors as quality control criteria in whole genome sequencing data set**. *BMC Proc*. 2014; 8:S21.

43. Porollo A. **EC2KEGG: a command line tool for comparison of metabolic pathways**. *Source Code Biol Med*. 2014; 9:19.

44. Porollo A, Sesterhenn TM, Collins MS, Welge JA, Cushion MT. **Comparative genomics of pneumocystis species suggests the absence of genes for myo-inositol synthesis and reliance on inositol transport and metabolism**. *MBio*. 2014; 5:e01834.

45. Premkumar VL, Cranert S, Linger BR, Morin GB, Minium S, Price C. **The 3' overhangs at Tetrahymena thermophila telomeres are packaged by four proteins, Pot1a, Tpt1, Pat1, and Pat2**. *Eukaryot Cell*. 2014; 13:240-5.

46. Qu B, Shen N. **miRNAs in the Pathogenesis of Systemic Lupus Erythematosus**. *Int J Mol Sci*. 2015; 16:9557-72.

47. Rydyznski C, Daniels KA, Karmele EP, Brooks TR, Mahl SE, Moran MT, Li C, Sutiwisesak R, Welsh RM, Waggoner SN. **Generation of cellular immune memory and B-cell immunity is impaired by natural killer cells**. *Nat Commun*. 2015; 6:6375.

48. Sadhasivam S, Zhang X, Prows CA, Kaufman KM, Martin LJ. **Challenges and cautions with small and retrospective postoperative pain genome-wide association studies with TAOK3**. *Pain*. 2014; 155:2434-5.

49. Sullivan AM, Arsovski AA, Lempe J, Bubb KL, Weirauch MT, Sabo PJ, Sandstrom R, Thurman RE, Neph S, Reynolds AP, Stergachis AB, Vernot B, Johnson AK, Haugen E, Sullivan ST, Thompson A, Neri FV, 3rd, Weaver M, Diegel M, Mnaimneh S, Yang A, Hughes TR, Nemhauser JL, Queitsch C, Stamatoyannopoulos JA. **Mapping and dynamics of regulatory DNA and transcription factor networks in A. thaliana**. *Cell Rep*. 2014; 8:2015-30.

50. Taft DH, Ambalavanan N, Schibler KR, Yu Z, Newburg DS, Deshmukh H, Ward DV, Morrow AL. **Center Variation in Intestinal Microbiota Prior to Late-Onset Sepsis in Preterm Infants**. *PLoS One*. 2015; 10:e0130604.

51. Taft DH, Ambalavanan N, Schibler KR, Yu Z, Newburg DS, Ward DV, Morrow AL. **Intestinal microbiota of preterm infants differ over time and between hospitals**. *Microbiome*. 2014; 2:36.

52. Verma SS, de Andrade M, Tromp G, Kuivaniemi H, Pugh E, Namjou-Khales B, Mukherjee S, Jarvik GP, Kottyan LC, Burt A, Bradford Y, Armstrong GD, Derr K, Crawford DC, Haines JL, Li R, Crosslin D, Ritchie MD. **Imputation and quality control steps for combining multiple genome-wide datasets**. *Front Genet*. 2014; 5:370.

53. Waggoner SN. **Specialization in Adaptive Immunity** . In: LM McManus, RN Mitchell, eds. *Pathobiology of Human Disease: A Dynamic Encyclopedia of Disease Mechanisms*. San Diego: Elsevier; 2014:5-19.

54. Weirauch MT, Yang A, Albu M, Cote AG, Montenegro-Montero A, Drewe P, Najafabadi HS, Lambert SA, Mann I, Cook K, Zheng H, Goity A, van Bakel H, Lozano JC, Galli M, Lewsey MG, Huang E, Mukherjee T, Chen X, Reece-Hoyes JS, Govindarajan S, Shaulsky G, Walhout AJ, Bouget FY, Ratsch G, Larrondo LF, Ecker JR, Hughes TR. **Determination and inference of eukaryotic transcription factor sequence specificity**. *Cell*. 2014; 158:1431-43.

55. Wu Y, Zhang F, Ma J, Zhang X, Wu L, Qu B, Xia S, Chen S, Tang Y, Shen N. **Association of large intergenic noncoding RNA expression with disease activity and organ damage in systemic lupus erythematosus**. *Arthritis Res Ther*. 2015; 17:131.

56. Zhang X, Ulm A, Somineni HK, Oh S, Weirauch MT, Zhang HX, Chen X, Lehn MA, Janssen EM, Ji H. **DNA**

methylation dynamics during ex vivo differentiation and maturation of human dendritic cells. *Epigenetics Chromatin*. 2014; 7:21.

57. Zhao J, Giles BM, Taylor RL, Yette GA, Lough KM, Ng HL, Abraham LJ, Wu H, Kelly JA, Glenn SB, Adler AJ, Williams AH, Comeau ME, Ziegler JT, Marion M, Alarcon-Riquelme ME, Biolupus, Networks G, Alarcon GS, Anaya JM, Bae SC, Kim D, Lee HS, Criswell LA, Freedman BI, Gilkeson GS, Guthridge JM, Jacob CO, James JA, Kamen DL, Merrill JT, Sivils KM, Niewold TB, Petri MA, Ramsey-Goldman R, Reveille JD, Scofield RH, Stevens AM, Vila LM, Vyse TJ, Kaufman KM, Harley JB, Langefeld CD, Gaffney PM, Brown EE, Edberg JC, Kimberly RP, Ulgiati D, Tsao BP, Boackle SA. **Preferential association of a functional variant in complement receptor 2 with antibodies to double-stranded DNA**. *Ann Rheum Dis*. 2014; .

Faculty, Staff, and Trainees

Faculty Members

John B. Harley, MD, PhD, Professor
Leadership Division Director; Co-Chair, Center for Pediatric Genomics; Director, Cincinnati Biobank

Iouri Chepelev, PhD, Assistant Professor

Kenneth Kaufman, PhD, Professor

Halima Moncrieffe, PhD, Instructor

Alexey Porollo, PhD, Assistant Professor

Nan Shen, MD, Professor

Susan Thompson, PhD, Professor

Stephen Waggoner, PhD, Assistant Professor

Matthew Weirauch, PhD, Assistant Professor

Bahram Namjou, MD, Assistant Professor

Leah Kottyan, PhD, Assistant Professor

Trainees

- **Ke Liu, BS**, 2003, Nanchang University
- **Samuel Vaughn, BS**, 2004, Brigham Young University
- **Jiadi Xu, BS**, 2010, China Agricultural University
- **Erin Zoller, PhD**, 2011, University of Cincinnati
- **Dong Liang, PhD**, 2010, Université Paris Descartes
- **Mariana Saint Just Ribeiro, PhD**, 2009, Karolinska Institute, Sweden
- **Carolyn Rydyznski, BS**, 2012, University of Cincinnati
- **Xiaoming Lu, BS**, 2011, Sun Yat-sen University

- **Laura Brungs, BS**, 2012, Thomas Moore College
- **Xiaoting Chen, PhD**, 2015, University of Cincinnati
- **Diana Taft, PhD**, 2014, University of Cincinnati
- **Jeremy Cox, BS**, 2001, University of Cincinnati
- **Michael Moran, BS**, 2014, University of Dayton
- **Zubin Patel, BS**, 2009, Worcester Polytechnic Institute
- **Pulak Tripathi, PhD**, 1993, Jadavpur University
- **Stacey Cranert, PhD**, 2014, University of Cincinnati
- **Mario Pujato, PhD**, 2014, Albert Einstein College of Medicine
- **Jonathan McNally, PhD**, 2015, University of Cincinnati
- **Seth Reighard, BS**, 2010, University of Pittsburgh
- **Michael Sirignano, MS**, 2015, University of Cincinnati

Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct

Chepelev, I

Identification of Lupus Causal Variants at BLK Locus by Mapping 3D Genome

Lupus Research Institute

	1/1/2015-12/31/2017	$100,000

Kaufman, K

Genetic Susceptibility for Occupational Asthma

National Institutes of Health (University of Cincinnati)

R01 OH008795	9/1/2013-8/31/2015	$18,103

Porollo, A

GM-CSF-Induced Metal Sequestration and Histoplasma

National Institutes of Health (University of Cincinnati)

R01 AI106269	5/15/2013-04/30/2015	$19,556

Directed Culturing of Pneumocystis Using Metatranscriptomics

National Institutes of Health (University of Cincinnati)

R01 HL119190	5/22/2013-2/29/2016	$64,046

Suppression of IgE-Mediated Disease by Polyclonal Rapid Desensitization

National Institute of Health (University of Cincinnati)

R01 AI113162	07/15/2014-06/30/2018	$55,878

Rydyznski, C

Bio-Techne Travel Grant

Bio-Techne

	5/8/2015-5/7/2016	$1,000

A Follicular Regulatory Subset of Natural Killer Cells

National Institutes of Health

F32 AI118179	5/3/2015-5/2/2018	$35,580

Thompson, S

Gene Expression In Pediatric Arthritis

National Institutes of Health

P01 AR048929		9/1/2011-8/31/2016	$972,588
	Thompson, S	Administrative Core	$227,892
	Thompson, S	Core A	$195,158
	Wagner, M	Core B	$184,820
	Harley, J	Project 1	$56,139
	Lovell, D	Project 2	$37,827
	Thompson, S	Project 3	$184,624
	Grom, A	Project 4	$86,128

Cincinnati Rheumatic Disease Core Center

National Institutes of Health

P30 AR047363		8/25/2011-6/30/2016	$386,908
	Thompson, S	Administrative Core	$104,047
	Thompson, S	Core 1	$57,275

Flick, M	Animal Core	$46,471
Thornton, S	Flow Core	$56,567
Wagner, M	Bioinformatics Core	$62,548
Thompson, S	PF1 Project	$30,000
Thompson, S	PF2 Project	$30,000

Waggoner, S

Anatomic Redistribution of Natural Killer Cells within Secondary Organs during Virus Infection

American Association of Immunologists

5/1/2015-4/30/2016 $500

Effect of Aging on Natural Killer Cell Regulation of T Cells in Viral Pathogenesis

Ellison Medical Foundation

7/1/2013-6/30/2016 $92,593

A Revolutionary Approach to an Efficacious HIV Vaccine

National Institutes of Health

DP1 DA038017 6/1/2014-5/31/2019 $492,500

Weirauch, M

Effect of Disease-Associated Genetic Variants on Viral Protein DNA Binding

National Institutes of Health

R21 HG008186 12/15/2014-11/30/2017 $100,000

Data Coordination and Integration Center for LINCS-BD2K

National Institutes of Health (Icahn School of Medicine at Mt Sinai)

U54 HL127624 9/29/2014-4/30/2019 $7,098

Current Year Direct **$2,346,350**

Service Collaborations

Shen, N

MedImmune, LLC $183,630

Thompson, S

Duke University		$9,833
UAB		$3,339
	Current Year Direct	**$196,802**
	Total	**$2,543,152**

Novel Mapping Approach for DNA Sequence Binding Motifs Sharply Expands Library of Genetic Knowledge

Matthew Weirauch, PhD

RESEARCH AND TRAINING DETAILS

Faculty	11
Joint Appointment Faculty	3
Research Fellows	8
Research Students	12
Support Personnel	31
Direct Annual Grant Support	$2.3M
Direct Annual Industry Support	$196,802
Peer Reviewed Publications	57

Weirauch MT, Yang A, Albu M, Cote AG, Montenegro-Montero A, Drewe P, Najafabadi HS, Lambert SA, Mann I, Cook K, Zheng H, Goity A, van Bakel H, Lozano JC, Galli M, Lewsey MG, Huang E, Mukherjee T, Chen X, Reece-Hoyes JS, Govindarajan S, Shaulsky G, Walhout AJ, Bouget FY, Ratsch G, Larrondo LF, Ecker JR, Hughes TR. Determination and inference of eukaryotic transcription factor sequence specificity. *Cell*. 2014;158(6):1431-1443.

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Cell

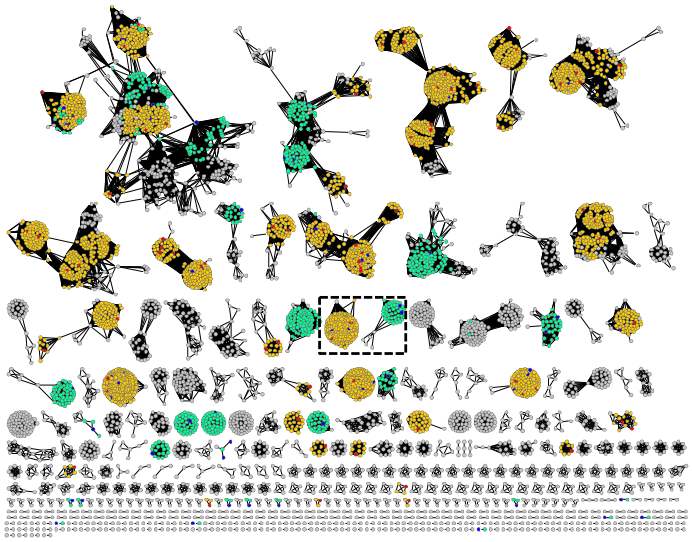
In a study with wide-ranging impact, researchers effectively increased the DNA sequence binding motifs that are known for eukaryotic transcription factors over 10-fold, including doubling knowledge for human transcription factors.

This new insight significantly improves predicting capacity for gene expression mechanisms for many disease-mechanism problems, and essentially all of eukaryotic biology.

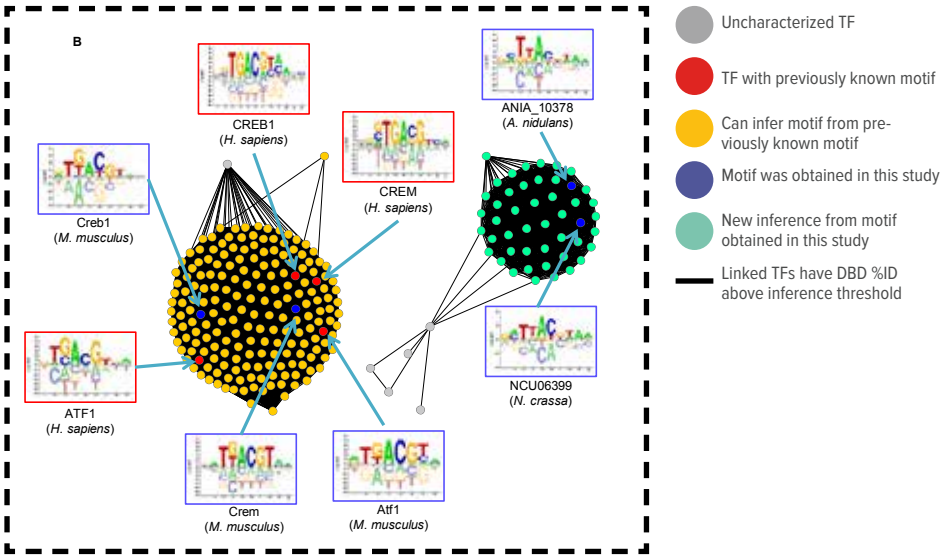
The study, led by Matthew Weirauch, PhD, a computational biologist in the Center for Autoimmune Genomics and Etiology, was published Sept. 11, 2014, in the journal *Cell*. The findings have enabled researchers who study any organism to begin to understand how genes are regulated on a global scale. For human disease, the study increases researchers' ability to understand the function of disease-associated genetic variants that fall in non-coding regions. It is estimated that approximately 90 percent of disease-associated variants are non-coding. In genomics, noncoding DNA sequences are components of an organism's DNA that do not encode protein sequences. "Doubling our knowledge of human DNA sequence binding motifs essentially doubles our chance of figuring out which proteins these variants might affect the binding of," Weirauch says.

The center's primary focus is the genesis of lupus and other immunological diseases, and to explore the mechanisms of disease through the complex interactions of genetics, the immune system and environmental factors such as stress, exercise and diet.

Two findings of the study surprised researchers. "First, that our scheme for mapping DNA sequence binding motifs across organisms based on protein similarity works for most protein families," says Weirauch. "Second, the fact that we increased knowledge of these motifs so substantially across all of eukaryotic life, from less than one percent to almost 40 percent of all proteins."



In a pictorial overview of transcription factors (TF) choosing strategy and motif inferences, this figure shows the network schematic depicting TFs (nodes), their related TFs (edges with nodes), and their motif status (node color.) This figure depicts all 3,715 TFs across 246 species that contain a single bZIP domain.



This figure is a close-up of the boxed region in the first figure. Here, motifs are shown for characterized TFs. Researchers noticed that motifs from the left group strongly resemble one another, as do motifs within the right group (as predicted by their DBD AA %ID). However, the motifs from the left and right groups are not related, as predicted by the fact that the DBD %ID of their TF members fall below the inference threshold for bZIPs. That is, there are no links between the two groups. Motifs with blue outlines were determined using PBMs; red outlined motifs are from the Transfac database. The findings illustrated here improve the understanding of gene expression mechanisms connected to disease.