



Peter Parham

Professor of Structural Biology and of Microbiology and Immunology

Bio

ACADEMIC APPOINTMENTS

- Professor, Structural Biology
- Professor, Microbiology & Immunology
- Member, Bio-X
- Member, Stanford Cancer Institute

LINKS

- The Parham Laboratory: <http://www.stanford.edu/group/parhamlab/>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

The Parham laboratory investigates the biology, genetics, and evolution of Major Histocompatibility Complex (MHC) class I molecules, natural killer (NK) cell receptors, and other immune system molecules. Classical MHC class I molecules are peptide-binding glycoproteins expressed on the surface of most vertebrate cells where they interact with the receptors of cytolytic CD8⁺ T lymphocytes and NK cells of the immune system. Both these types of killer lymphocytes are important for defence against viruses - generalised NK cell response at the beginning of infection, and specific T cell response further on if the pathogen is not eliminated by innate immunity. The rapid evolution of viruses selects for diversity of MHC class I molecules within populations of humans and other vertebrates. One consequence of this diversity is that MHC class I difference is a major immunological barrier to tissue transplants between unrelated donors and patients. A second consequence is that MHC class I molecules of different taxonomic species are very different, for example, there is no true orthologue between the classical class I genes of humans and mice. Whereas once considered homogeneous, NK cells are now shown to have both clonal diversity arising from differential expression of NK cell receptors within an individual, and population diversity in haplotype content and gene polymorphism. Clinical consequences analogous to those for MHC class I are expected due to NK cell receptor diversity. In humans, NK cell receptors consist of both immunoglobulin-like molecules and lectin-like molecules, however, only the lectin-like receptors are functional homologues in mice. As with their MHC class I ligands, NK cell receptors have also undergone rapid evolution.

One goal of our research is to understand how the continual battle between vertebrates and viruses has driven the diversification and divergence of MHC class I molecules and NK cell receptors. In human, we examine the polymorphism of NK receptor genes in different populations which are shaped by different histories of pathogen encounters. We also examine the coevolution of MHC class I and NK receptor genes in two close cousins of human, the chimpanzee and the orangutan.

A second goal is to understand the molecular and biochemical interactions between NK cell receptors and their MHC class I ligands. We perform mutagenesis studies to fine map interactions between NK cell receptors and MHC class I molecules. We also examine essential residues that determine the expression or retention of NK cell receptor alleles.

A third goal is to understand how MHC class I and NK cell receptor differences influence the outcomes of clinical transplantation. We follow the recovery of NK cell populations in leukemia and lymphoma patients after bone-marrow transplants and correlate the reconstitution of NK cell with the donor's and patient's genotypes, therapies and clinical consequences.

Teaching

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Michelle Drews

Postdoctoral Faculty Sponsor

Fuguo Liu, Jason Pugh, Katherine Walwyn-Brown

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Immunology (Phd Program)
- Microbiology and Immunology (Phd Program)
- Structural Biology (Phd Program)

Publications

PUBLICATIONS

- **Genetic diversity affects the nanoscale membrane organization and signaling of natural killer cell receptors.** *Science signaling*
Kennedy, P. R., Barthen, C., Williamson, D. J., Pitkeathly, W. T., Hazime, K. S., Cumming, J., Stacey, K. B., Hilton, H. G., Carrington, M., Parham, P., Davis, D. M.
2019; 12 (612)
- **Diversity of Killer Cell Ig-Like Receptor, HLA Class I, and Their Interactions in Seven Populations of Sub-Saharan Africans.** *Journal of immunology (Baltimore, Md. : 1950)*
Nemat-Gorgani, N., Guethlein, L. A., Henn, B. M., Norberg, S. J., Chiaroni, J., Sikora, M., Quintana-Murci, L., Mountain, J. L., Norman, P. J., Parham, P.
2019
- **Papa-B (MHC) diversity of wild bonobos (*Pan paniscus*) east and west of the Lomami River suggest different patterns of immunity**
Wroblewski, E. E., Anderson, A. G., Guethlein, L. A., Li, Y., Avitto, A. N., Bertolani, P., Hart, J. A., Hart, T. B., Hahn, B. H., Parham, P.
WILEY.2019: 274
- **Genetics of Natural Killer Cells in Human Health, Disease, and Survival.** *Annual review of immunology*
Parham, P., Guethlein, L. A.
2018; 36: 519–48
- **Molecular definition of the transplantation antigens.** *The FEBS journal*
Parham, P.
2018
- **Different Selected Mechanisms Attenuated the Inhibitory Interaction of KIR2DL1 with C2(+) HLA-C in Two Indigenous Human Populations in Southern Africa** *JOURNAL OF IMMUNOLOGY*
Nemat-Gorgani, N., Hilton, H. G., Henn, B. M., Lin, M., Gignoux, C. R., Myrick, J. W., Werely, C. J., Granka, J. M., Moeller, M., Hoa, E. G., Yawata, M., Yawata, N., Boelen, et al
2018; 200 (8): 2640–55

- **Elevated HLA-A expression impairs HIV control through inhibition of NKG2A-expressing cells** *SCIENCE*
Ramsuran, V., Naranbhai, V., Horowitz, A., Qi, Y., Martin, M. P., Yuki, Y., Gao, X., Walker-Sperling, V., Del Prete, G. Q., Schneider, D. K., Lifson, J. D., Fellay, J., Deeks, et al
2018; 359 (6371): 86–90
- **Two alternate strategies for innate immunity to Epstein-Barr virus: One using NK cells and the other NK cells and ?d T cells.** *journal of experimental medicine*
Djaoud, Z., Guethlein, L. A., Horowitz, A., Azzi, T., Nemat-Gorgani, N., Olive, D., Nadal, D., Norman, P. J., Münz, C., Parham, P.
2017; 214 (6): 1827-1841
- **. Genome research**
Norman, P. J., Norberg, S. J., Guethlein, L. A., Nemat-Gorgani, N., Royce, T., Wroblewski, E. E., Dunn, T., Mann, T., Alicata, C., Hollenbach, J. A., Chang, W., Shults Won, M., Gunderson, et al
2017; 27 (5): 813-823
- **Bonobos Maintain Immune System Diversity with Three Functional Types of MHC-B** *JOURNAL OF IMMUNOLOGY*
Wroblewski, E. E., Guethlein, L. A., Norman, P. J., Li, Y., Shaw, C. M., Han, A. S., Ndjango, J. N., Ahuka-Mundeke, S., Georgiev, A. V., Peeters, M., Hahn, B. H., Parham, P.
2017; 198 (9): 3480-3493
- **Sequences of 95 human MHC haplotypes reveal extreme coding variation in genes other than highly polymorphic HLA class I and II** *GENOME RESEARCH*
Norman, P. J., Norberg, S. J., Guethlein, L. A., Nemat-Gorgani, N., Royce, T., Wroblewski, E. E., Dunn, T., Mann, T., Alicata, C., Hollenbach, J. A., Chang, W., Won, M. S., Gunderson, et al
2017; 27 (5): 813-823
- **Resurrecting KIR2DP1: A Key Intermediate in the Evolution of Human Inhibitory NK Cell Receptors That Recognize HLA-C.** *Journal of immunology*
Hilton, H. G., Blokhuis, J. H., Guethlein, L. A., Norman, P. J., Parham, P.
2017; 198 (5): 1961-1973
- **Class I HLA haplotypes form two schools that educate NK cells in different ways.** *Science immunology*
Horowitz, A., Djaoud, Z., Nemat-Gorgani, N., Blokhuis, J., Hilton, H. G., Béziat, V., Malmberg, K., Norman, P. J., Guethlein, L. A., Parham, P.
2016; 1 (3)
- **Co-evolution of MHC class I and variable NK cell receptors in placental mammals** *IMMUNOLOGICAL REVIEWS*
Guethlein, L. A., Norman, P. J., Hilton, H. H., Parham, P.
2015; 267 (1): 259-282
- **Loss and Gain of Natural Killer Cell Receptor Function in an African Hunter-Gatherer Population.** *PLoS genetics*
Hilton, H. G., Norman, P. J., Nemat-Gorgani, N., Goyos, A., Hollenbach, J. A., Henn, B. M., Gignoux, C. R., Guethlein, L. A., Parham, P.
2015; 11 (8)
- **Genetic and environmental determinants of human NK cell diversity revealed by mass cytometry.** *Science translational medicine*
Horowitz, A., Strauss-Albee, D. M., Leipold, M., Kubo, J., Nemat-Gorgani, N., Dogan, O. C., Dekker, C. L., Mackey, S., Maecker, H., Swan, G. E., Davis, M. M., Norman, P. J., Guethlein, et al
2013; 5 (208): 208ra145-?
- **Co-evolution of Human Leukocyte Antigen (HLA) Class I Ligands with Killer-Cell Immunoglobulin-Like Receptors (KIR) in a Genetically Diverse Population of Sub-Saharan Africans.** *PLoS genetics*
Norman, P. J., Hollenbach, J. A., Nemat-Gorgani, N., Guethlein, L. A., Hilton, H. G., Pando, M. J., Koram, K. A., Riley, E. M., Abi-Rached, L., Parham, P.
2013; 9 (10)
- **In vitro education of human natural killer cells by KIR3DL1.** *Life science alliance*
Pugh, J., Nemat-Gorgani, N., Djaoud, Z., Guethlein, L. A., Norman, P. J., Parham, P.
2019; 2 (6)
- **Nomenclature report 2019: major histocompatibility complex genes and alleles of Great and Small Ape and Old and New World monkey species.** *Immunogenetics*
de Groot, N. G., Otting, N., Maccari, G., Robinson, J., Hammond, J. A., Blancher, A., Lafont, B. A., Guethlein, L. A., Wroblewski, E. E., Marsh, S. G., Shiina, T., Walter, L., Vigilant, et al
2019

- **KIR3DL1/S1 Allotypes Contribute Differentially to the Development of Behcet Disease.** *Journal of immunology (Baltimore, Md. : 1950)*
Petrushkin, H., Norman, P. J., Lougee, E., Parham, P., Wallace, G. R., Stanford, M. R., Fortune, F.
2019
- **Diversity of KIR, HLA Class I, and Their Interactions in Seven Populations of Sub-Saharan Africans** *JOURNAL OF IMMUNOLOGY*
Nemat-Gorgani, N., Guethlein, L. A., Henn, B. M., Norberg, S. J., Chiaroni, J., Sikora, M., Quintana-Murci, L., Mountain, J. L., Norman, P. J., Parham, P.
2019; 202 (9): 2636–47
- **DEEP ANALYSIS OF KIR2DL1 AND KIR3DL1S1 BY NEXT GENERATION SEQUENCING IN 3,695 INDIVIDUALS IDENTIFIES NOVEL VARIANTS WITH POSSIBLE FUNCTIONAL RELEVANCE**
Augusto, D. G., Nemat-Gorgani, N., Montero-Martin, G., Marin, W., Dendekar, R., Parham, P., Fernandez-Vina, M. A., Oksenberg, J. R., Norman, P. J., Hollenbach, J. A.
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- **ALLELIC POLYMORPHISM IN KIR3DL1S1 MEDIATES RISK IN MULTIPLE SCLEROSIS AND IS ASSOCIATED WITH INCREASED RELAPSE RATE AND BRAIN LESION BURDEN**
Anderson, K., Marin, W., Dandekar, R., Augusto, D., Nemat-Gorgani, N., Parham, P., Fernandez-Vina, M., Oksenberg, J., Norman, P. J., Hollenbach, J.
WILEY.2019: 284–85
- **CONSERVATION, EXTENSIVE HETEROZYGOSITY, AND CONVERGENCE OF SIGNALING POTENTIAL ALL INDICATE A CRITICAL ROLE FOR KIR3DL3 IN HIGHER PRIMATES**
Leaton, L., Shortt, J., Kichula, K. M., Tao, S., Nemat-Gorgani, N., Mentzer, A., Oppenheimer, S. J., Deng, Z., Hollenbach, J. A., Gignoux, C. R., Guethlein, L. A., Parham, P., Carrington, et al
WILEY.2019: 391
- **Donor Killer Cell Immunoglobulin-Like Receptor Genotype Does Not Improve Graft-versus-Leukemia Responses in Chronic Lymphocytic Leukemia after Unrelated Donor Transplant: A Center for International Blood and Marrow Transplant Research Analysis** *BIOLOGY OF BLOOD AND MARROW TRANSPLANTATION*
Bachanova, V., Weisdorf, D. J., Wang, T., Marsh, S. E., Cereb, N., Haagenson, M. D., Spellman, S. R., Lee, S. J., Guethlein, L. A., Parham, P., Miller, J. S., Cooley, S. A.
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- **A specific amino acid motif of HLA-DRB1 mediates risk and interacts with smoking history in Parkinson's disease** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Hollenbach, J. A., Norman, P. J., Creary, L. E., Damotte, V., Montero-Martin, G., Caillier, S., Anderson, K. M., Misra, M. K., Nemat-Gorgani, N., Osoegawa, K., Santaniello, A., Renschen, A., Marin, et al
2019; 116 (15): 7419–24
- **A specific amino acid motif of HLA-DRB1 mediates risk and interacts with smoking history in Parkinson's disease.** *Proceedings of the National Academy of Sciences of the United States of America*
Hollenbach, J. A., Norman, P. J., Creary, L. E., Damotte, V., Montero-Martin, G., Caillier, S., Anderson, K. M., Misra, M. K., Nemat-Gorgani, N., Osoegawa, K., Santaniello, A., Renschen, A., Marin, et al
2019
- **Two to Tango: Co-evolution of Hominid Natural Killer Cell Receptors and MHC** *FRONTIERS IN IMMUNOLOGY*
Wroblewski, E. E., Parham, P., Guethlein, L. A.
2019; 10
- **Casting a wider net: Immunosurveillance by nonclassical MHC molecules** *PLOS PATHOGENS*
D'Souza, M., Adams, E., Altman, J. D., Birnbaum, M. E., Boggiano, C., Casorati, G., Chien, Y., Conley, A., Eckle, S., Fruh, K., Gondre-Lewis, T., Hassan, N., Huang, et al
2019; 15 (2)
- **Casting a wider net: Immunosurveillance by nonclassical MHC molecules.** *PLoS pathogens*
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2019; 15 (2): e1007567
- **Conservation, Extensive Heterozygosity, and Convergence of Signaling Potential All Indicate a Critical Role for KIR3DL3 in Higher Primates** *FRONTIERS IN IMMUNOLOGY*
Leaton, L. A., Shortt, J., Kichula, K. M., Tao, S., Nemat-Gorgani, N., Mentzer, A. J., Oppenheimer, S. J., Deng, Z., Hollenbach, J. A., Gignoux, C. R., Guethlein, L. A., Parham, P., Carrington, et al

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- **Nomenclature report for killer-cell immunoglobulin-like receptors (KIR) in macaque species: new genes/alleles, renaming recombinant entities and IPD-NHKIR updates.** *Immunogenetics*
Bruijnesteijn, J., de Groot, N. G., Otting, N., Maccari, G., Guethlein, L. A., Robinson, J., Marsh, S. G., Walter, L., O'Connor, D. H., Hammond, J. A., Parham, P., Bontrop, R. E.
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- **Correction to: Nomenclature report 2019: major histocompatibility complex genes and alleles of great and small ape and old and new world monkey species.** *Immunogenetics*
de Groot, N. G., Otting, N., Maccari, G., Robinson, J., Hammond, J. A., Blancher, A., Lafont, B. A., Guethlein, L. A., Wroblewski, E. E., Marsh, S. G., Shiina, T., Walter, L., Vigilant, et al
2019
- **KIR Donor Selection: Feasibility in Identifying better Donors.** *Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation*
Weisdorf, D., Cooley, S., Wang, T., Trachtenberg, E., Haagenson, M. D., Vierra-Green, C., Spellman, S., Spahn, A., Vogel, J., Kobusingye, H., Fehninger, T., Woolfrey, A., Devine, et al
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- **Conservation, Extensive Heterozygosity, and Convergence of Signaling Potential All Indicate a Critical Role for KIR3DL3 in Higher Primates.** *Frontiers in immunology*
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2019; 10: 24
- **Two to Tango: Co-evolution of Hominid Natural Killer Cell Receptors and MHC.** *Frontiers in immunology*
Wroblewski, E. E., Parham, P., Guethlein, L. A.
2019; 10: 177
- **A natural killer cell receptor takes sharp aim at the world of bacteria.** *Proceedings of the National Academy of Sciences of the United States of America*
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2019
- **Genetic diversity of CHC22 clathrin impacts its function in glucose metabolism.** *eLife*
Fumagalli, M., Camus, S. M., Diekmann, Y., Burke, A., Camus, M. D., Norman, P. J., Joseph, A., Abi-Rached, L., Benazzo, A., Rasteiro, R., Mathieson, I., Topf, M., Parham, et al
2019; 8
- **Donor killer-cell immunoglobulin-like receptor (KIR) genotype does not improve graft-versus-leukemia responses in chronic lymphocytic leukemia (CLL) after unrelated donor transplant: a CIBMTR analysis.** *Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation*
Bachanova, V., Weisdorf, D. J., Wang, T., Marsh, S. G., Cereb, N., Haagenson, M. D., Spellman, S. R., Lee, S. J., Guethlein, L. A., Parham, P., Miller, J. S., Cooley, S. A.
2018
- **HLA-B57 micropolymorphism defines the sequence and conformational breadth of the immunopeptidome.** *Nature communications*
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- **HLA-B57 micropolymorphism defines the sequence and conformational breadth of the immunopeptidome** *NATURE COMMUNICATIONS*
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2018; 9
- **High-Resolution Genetic and Phenotypic Analysis of KIR2DL1 Alleles and Their Association with Pre-Eclampsia** *JOURNAL OF IMMUNOLOGY*
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- **Nomenclature for the KIR of non-human species** *IMMUNOGENETICS*
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2018; 70 (9): 571–83
- **Characterization of MHC-DRB immuno-genetic diversity in the wild chimpanzees (*Pan troglodytes schweinfurthii*) of Gombe National Park, Tanzania**
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- **Ecoimmunology of wild chimpanzees (*Pan troglodytes schweinfurthii*): Does MHC genotype or phenotype predict occurrence of respiratory infection?**
Phillips-Garcia, S., Thompson, M., Muller, M. N., Machanda, Z. P., Scully, E., Oтали, E., Goldberg, T. L., Wrangham, R. W., Parham, P., Wroblewski, E.
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- **Strategies to activate NK cells to prevent relapse and induce remission following hematopoietic stem cell transplantation** *BLOOD*
Cooley, S., Parham, P., Miller, J. S.
2018; 131 (10): 1053–62
- **Human NK Cells Downregulate Zap70 and Syk in Response to Prolonged Activation or DNA Damage** *JOURNAL OF IMMUNOLOGY*
Pugh, J. L., Nemat-Gorgani, N., Norman, P. J., Guethlein, L. A., Parham, P.
2018; 200 (3): 1146–58
- **Missing or altered self: human NK cell receptors that recognize HLA-C** *IMMUNOGENETICS*
Hilton, H. G., Parham, P.
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- **The Intergenic Recombinant HLA-B*46:01 Has a Distinctive Peptidome that Includes KIR2DL3 Ligands.** *Cell reports*
Hilton, H. G., McMurtrey, C. P., Han, A. S., Djaoud, Z., Guethlein, L. A., Blokhuis, J. H., Pugh, J. L., Goyos, A., Horowitz, A., Buchli, R., Jackson, K. W., Bardet, W., Bushnell, et al
2017; 19 (7): 1394-1405
- **Two Orangutan Species Have Evolved Different KIR Alleles and Haplotypes** *JOURNAL OF IMMUNOLOGY*
Guethlein, L. A., Norman, P. J., Heijmans, C. M., de Groot, N. G., Hilton, H. G., Babrzadeh, F., Abi-Rached, L., Bontrop, R. E., Parham, P.
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- **Alleles and Haplotypes.** *Journal of immunology*
Guethlein, L. A., Norman, P. J., Heijmans, C. M., de Groot, N. G., Hilton, H. G., Babrzadeh, F., Abi-Rached, L., Bontrop, R. E., Parham, P.
2017
- **Distinguishing functional polymorphism from random variation in the sequences of >10,000 HLA-A, -B and -C alleles.** *PLoS genetics*
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- **KIR2DS5 allotypes that recognize the C2 epitope of HLA-C are common among Africans and absent from Europeans.** *Immunity, inflammation and disease*
Blokhuis, J. H., Hilton, H. G., Guethlein, L. A., Norman, P. J., Nemat-Gorgani, N., Nakimuli, A., Chazara, O., Moffett, A., Parham, P.
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- **Clathrin light chains' role in selective endocytosis influences antibody isotype switching.** *Proceedings of the National Academy of Sciences of the United States of America*
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- **Defining KIR and HLA Class I Genotypes at Highest Resolution via High-Throughput Sequencing.** *American journal of human genetics*
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- **Hematopoietic stem cell transplantation: Improving alloreactive Bw4 donor selection by genotyping codon 86 of KIR3DL1/S1.** *European journal of immunology*
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- **Description of the novel KIR2DL4*035 allele identified using high-throughput sequencing.** *HLA : immune response genetics*
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Parham, P.
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- **Regulation of Adaptive NK Cells and CD8 T Cells by HLA-C Correlates with Allogeneic Hematopoietic Cell Transplantation and with Cytomegalovirus Reactivation** *JOURNAL OF IMMUNOLOGY*
Horowitz, A., Guethlein, L. A., Nemat-Gorgani, N., Norman, P. J., Cooley, S., Miller, J. S., Parham, P.
2015; 195 (9): 4524-4536
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