Stanford

Peter Parham

Professor of Structural Biology and, by courtesy, of Microbiology and Immunology

Bio

ACADEMIC APPOINTMENTS

- Professor, Structural Biology
- Professor (By courtesy), Microbiology & Immunology
- Member, Bio-X
- Member, Stanford Cancer Institute

LINKS

- The Parham Laboratory: https://web.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

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

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

Publications

PUBLICATIONS

- **Following Transplantation for Acute Myelogenous Leukemia, Donor KIR Cen B02 Better Protects against Relapse than KIR Cen B01.** *Journal of immunology (Baltimore, Md. : 1950)*
  Guethlein, L. A., Beyzaie, N., Nemat-Gorgani, N., Wang, T., Ramesh, V., Marin, W. M., Hollenbach, J. A., Schetelig, J., Spellman, S. R., Marsh, S. G., Cooley, S., Weisdorf, D. J., Norman, et al
  2021

- **Meta-analysis of the CD56-negative NK cell subset indicates altered functional responses and unique KIR regulation**
  Cocker, A., Parham, P.
  AMER ASSOC IMMUNOLOGISTS.2021

- **Genetically Determined Strength of Natural Killer Cells is Enhanced by Adaptive Admixture of HLA class I Allotypes in East <a>Asians**
  Harrison, G. F., Deng, Z., Zhen, J., Zhang, G., Chen, R., Sun, G., Yu, Q., Nemat-Gorgani, N., Guethlein, L., He, L., Tang, M., Gao, X., Cai, et al
  AMER ASSOC IMMUNOLOGISTS.2021

- **Adaptive Admixture of HLA class I Allotypes Enhanced Genetically Determined Strength of Natural Killer Cells in East Asians.** *Molecular biology and evolution*
  Deng, Z., Zhen, J., Harrison, G. F., Zhang, G., Chen, R., Sun, G., Yu, Q., Nemat-Gorgani, N., Guethlein, L. A., He, L., Tang, M., Gao, X., Cai, et al
  2021

- **High-Resolution Characterization of KIR Genes in a Large North American Cohort Reveals Novel Details of Structural and Sequence Diversity.** *Frontiers in immunology*
  Amorim, L. M., Augusto, D. G., Nemat-Gorgani, N., Montero-Martin, G., Marin, W. M., Shams, H., Dandekar, R., Caillier, S., Parham, P., Fernandez-Vina, M. A., Oksenberg, J. R., Norman, P. J., Hollenbach, et al
  2021; 12: 674778

- **Abundant CpG-sequences in human genomes inhibit KIR3DL2-expressing NK cells.** *PeerJ*
  Pugh, J., Guethlein, L., Parham, P.
  2021; 9: e12258

- **In Memoriam: Peter Hartmann (1946-2020), publisher, colleague and friend.** *Traffic (Copenhagen, Denmark)*
  Brodsky, F. M., Parham, P. n.
  2020

- **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
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- **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
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- **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 Memoriam: Peter Hartmann (1946-2020), publisher, colleague and friend** *HLA*
  Brodsky, F. M., Parham, P.
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- **Killer Cell Immunoglobulin-like Receptor Variants Are Associated with Protection from Symptoms Associated with More Severe Course in Parkinson Disease.** *Journal of immunology (Baltimore, Md. : 1950)*
  Anderson, K. M., Augusto, D. G., Dandekar, R., Shams, H., Zhao, C., Yusufali, T., Montero-Martin, G., Marin, W. M., Nemat-Gorgani, N., Creary, L. E., Caillier, S., Mofrad, M. R., Parham, et al
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- **Dimorphism in the TCRgamma-chain repertoire defines 2 types of human immunity to Epstein-Barr virus.** *Blood advances*
  Djaoud, Z., Parham, P.
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- **Distinctive phenotypes and functions of innate lymphoid cells in human decidua during early pregnancy.** *Nature communications*
  Huhn, O., Ivarsson, M. A., Gardner, L., Hollinshead, M., Stinchcombe, J. C., Chen, P., Shreeve, N., Chazara, O., Farrell, L. E., Theorell, J., Ghadially, H., Parham, P., Griffiths, et al
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- **KIR Variation in Iranians Combines High Haplotype and Allotype Diversity With an Abundance of Functional Inhibitory Receptors.** *Frontiers in immunology*
  Alicata, C., Ashouri, E., Nemat-Gorgani, N., Guethlein, L. A., Marin, W. M., Tao, S., Moretta, L., Hollenbach, J. A., Trowsdale, J., Traherne, J. A., Ghaderi, A., Parham, P., Norman, et al
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- **HLAs, TCRs, and KIRs, a Triumvirate of Human Cell-Mediated Immunity** *ANNUAL REVIEW OF BIOCHEMISTRY, VOL 89*
  Djaoud, Z., Parham, P., Kornberg, R. D.
  2020; 89: 717–39

- **HLAs, TCRs, and KIRs, a Triumvirate of Human Cell-Mediated Immunity.** *Annual review of biochemistry*
  Djaoud, Z. n., Parham, P. n.
  2020; 89: 717–39

- **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*
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- **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.
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- **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
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- **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*
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  2019; 25 (5): 949–54

- **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*
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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
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  Wroblewski, E. E., Parham, P., Guethlein, L. A.
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- **Casting a wider net: Immunosurveillance by nonclassical MHC molecules** *PLOS PATHOGENS*
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  2019; 15 (2)

- **Casting a wider net: Immunosurveillance by nonclassical MHC molecules.** *PLoS pathogens*
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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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- **Nomenclature report for killer-cell immunoglobulin-like receptors (KIR) in macaque species: new genes/alleles, renaming recombinant entities and IPD-NHKIR updates.** *Immunogenetics*

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- **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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