

# Stanford

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## Yueh-hsiu Chien

Professor of Microbiology & Immunology

### Bio

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#### ACADEMIC APPOINTMENTS

- Professor, Microbiology & Immunology
- Member, Stanford Cancer Institute

### Research & Scholarship

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#### CURRENT RESEARCH AND SCHOLARLY INTERESTS

One of our main research focuses is to define  $\gamma\delta$  T cell function so that we can better understand host immune defense.  $\gamma\delta$  T cells, together with B cells and  $\alpha\beta$  T cells, are the only cells that use somatic V, D, J gene rearrangement to generate diverse antigen receptors. All three types of cells are present together in all but the most primitive vertebrates, suggesting that each population contributes to host immune competence uniquely and that all three are necessary for maintaining immune competence. Functional analysis indicates that in infections,  $\gamma\delta$  T cells respond earlier than  $\alpha\beta$  T cells do; and also emerge late after pathogen numbers start to decline. Thus, these cells may be involved in both establishing and resolving the inflammatory response. Our past studies indicate that  $\gamma\delta$  T cells and  $\alpha\beta$  T cells are clearly distinct in their antigen recognition and activation requirements and also in antigen-specific repertoire and effector-function development. These aspects allow  $\gamma\delta$  T cells to occupy unique temporal and functional niches in host immune defense. We are following up on these studies to determine how  $\gamma\delta$  T cell function affect the development and the termination of the inflammatory response and to study  $\gamma\delta$  T cells function in infections and autoimmune diseases. These include a mouse model of *Toxoplasma gondii* infection (in collaboration with Dr. John Boothroyd) and celiac patients in response to gluten challenge (in collaboration with Dr. Mark Davis). We will expand the analysis to TB patients.

### Teaching

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#### COURSES

##### 2018-19

- Advanced Immunology I: IMMUNOL 201 (Win)

##### 2017-18

- Advanced Immunology I: IMMUNOL 201 (Win)

#### STANFORD ADVISEES

##### Doctoral Dissertation Reader (AC)

Jared Honeycutt

##### Postdoctoral Faculty Sponsor

Megha Dubey, Jing Guo

**Postdoctoral Research Mentor**

Megha Dubey, Jing Guo

**GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS**

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

**Publications**

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**PUBLICATIONS**

- **Casting a wider net: Immunosurveillance by nonclassical MHC molecules.** *PLoS pathogens*  
D'Souza, M. P., Adams, E., Altman, J. D., Birnbaum, M. E., Boggiano, C., Casorati, G., Chien, Y., Conley, A., Eckle, S. B., Fruh, K., Gondre-Lewis, T., Hassan, N., Huang, et al  
2019; 15 (2): e1007567
- **Author Correction: A multi-cohort study of the immune factors associated with M. tuberculosis infection outcomes.** *Nature*  
Roy Chowdhury, R., Vallania, F., Yang, Q., Lopez Angel, C. J., Darboe, F., Penn-Nicholson, A., Rozot, V., Nemes, E., Malherbe, S. T., Ronacher, K., Walzl, G., Hanekom, W., Davis, et al  
2018
- **A multi-cohort study of the immune factors associated with M. tuberculosis infection outcomes.** *Nature*  
Roy Chowdhury, R., Vallania, F., Yang, Q., Lopez Angel, C. J., Darboe, F., Penn-Nicholson, A., Rozot, V., Nemes, E., Malherbe, S. T., Ronacher, K., Walzl, G., Hanekom, W., Davis, et al  
2018
- **Does selecting ligand shape gamma delta-TCR repertoire?** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Chien, Y.  
2018; 115 (16): E3606
- **From T Cell Receptor to Antigen, Systems Approach to Discovering T Cell Antigen(s) in Multiple Sclerosis and Experimental Autoimmune Encephalomyelitis**  
Saligrama, N., Zhao, F., Fernandes, R. A., Serratelli, W. S., Louis, D. M., Chien, Y., Garcia, C. K., Oksenberg, J., Davis, M. M.  
SAGE PUBLICATIONS LTD.2018: 5
- **A Macrophage Colony-Stimulating-Factor-Producing ## T Cell Subset Prevents Malarial Parasitemic Recurrence.** *Immunity*  
Mamedov, M. R., Scholzen, A., Nair, R. V., Cumnock, K., Kenkel, J. A., Oliveira, J. H., Trujillo, D. L., Saligrama, N., Zhang, Y., Rubelt, F., Schneider, D. S., Chien, Y. H., Sauerwein, et al  
2018; 48 (2): 350–63.e7
- **Concerted T cell response in experimental autoimmune encephalomyelitis and multiple sclerosis**  
Saligrama, N., Zhao, F., Fernandes, R., Serratelli, W. S., Louis, D. M., Chien, Y. C., Garcia, C. K., Oksenberg, J., Davis, M. M.  
SAGE PUBLICATIONS LTD.2017: 201
- **Microbiota-activated CD103(+) DCs stemming from microbiota adaptation specifically drive gamma delta T17 proliferation and activation** *MICROBIOME*  
Fleming, C., Cai, Y., Sun, X., Jala, V. R., Xue, F., Morrissey, S., Wei, Y., Chien, Y., Zhang, H., Haribabu, B., Huang, J., Yan, J.  
2017; 5
- **Defective Signaling in the JAK-STAT Pathway Tracks with Chronic Inflammation and Cardiovascular Risk in Aging Humans.** *Cell systems*  
Shen-Orr, S. S., Furman, D., Kidd, B. A., Hadad, F., Lovelace, P., Huang, Y., Rosenberg-Hasson, Y., Mackey, S., Grisar, F. A., Pickman, Y., Maecker, H. T., Chien, Y., Dekker, et al  
2016; 3 (4): 374-384 e4
- **Detection, phenotyping, and quantification of antigen-specific T cells using a peptide-MHC dodecamer** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*

- Huang, J., Zeng, X., Sigal, N., Lund, P. J., Su, L. F., Huang, H., Chien, Y., Davis, M. M.  
2016; 113 (13): E1890-E1897
- **A highly focused antigen receptor repertoire characterizes gamma delta T cells that are poised to make IL-17 rapidly in naive animals** *FRONTIERS IN IMMUNOLOGY*  
Wei, Y., Han, A., Glanville, J., Fang, F., Zuniga, L. A., Lee, J. S., Cue, D. J., Chien, Y.  
2015; 6: 1-6
  - **The Split Virus Influenza Vaccine rapidly activates immune cells through Fc gamma receptors** *VACCINE*  
O'Gorman, W. E., Huang, H., Wei, Y., Davis, K. L., Leipold, M. D., Bendall, S. C., Kidd, B. A., Dekker, C. L., Maecker, H. T., Chien, Y., Davis, M. M.  
2014; 32 (45): 5989-5997
  - **Gamma delta T cells recognize haptens and mount a hapten-specific response** *ELIFE*  
Zeng, X., Meyer, C., Huang, J., Newell, E. W., Kidd, B. A., Wei, Y., Chien, Y.  
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  - **## T cells: first line of defense and beyond** *Annu Rev Immunol*  
Chien, Y., Meyer, C., Bonneville, M.  
2014
  - **Gamma delta T cells recognize haptens and mount a hapten-specific response.** *eLife*  
Zeng, X., Meyer, C., Huang, J., Newell, E. W., Kidd, B. A., Wei, Y., Chien, Y.  
2014; 3
  - **gamma delta T Cells: First Line of Defense and Beyond** *ANNUAL REVIEW OF IMMUNOLOGY, VOL 32*  
Chien, Y., Meyer, C., Bonneville, M.  
2014; 32: 121-155
  - **A Single Peptide-Major Histocompatibility Complex Ligand Triggers Digital Cytokine Secretion in CD4(+) T Cells.** *Immunity*  
Huang, J., Brameshuber, M., Zeng, X., Xie, J., Li, Q., Chien, Y., Valitutti, S., Davis, M. M.  
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  - **Dietary gluten triggers concomitant activation of CD4(+) and CD8(+) alpha beta T cells and gamma delta T cells in celiac disease** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Han, A., Newell, E. W., Glanville, J., Fernandez-Becker, N., Khosla, C., Chien, Y., Davis, M. M.  
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  - **Dietary gluten triggers concomitant activation of CD4+ and CD8+ αβ T cells and γδ T cells in celiac disease.** *Proceedings of the National Academy of Sciences of the United States of America*  
Han, A., Newell, E. W., Glanville, J., Fernandez-Becker, N., Khosla, C., Chien, Y., Davis, M. M.  
2013; 110 (32): 13073-13078
  - **Correlation of Gene Expression and Genome Mutation in Single B-Cells** *PLOS ONE*  
Weinstein, J. A., Zeng, X., Chien, Y., Quake, S. R.  
2013; 8 (6)
  - **The natural and the inducible: interleukin (IL)-17-producing γδ T cells.** *Trends in immunology*  
Chien, Y., Zeng, X., Prinz, I.  
2013; 34 (4): 151-154
  - **Correlation of gene expression and genome mutation in single B-cells.** *PloS one*  
Weinstein, J. A., Zeng, X., Chien, Y., Quake, S. R.  
2013; 8 (6)
  - **gamma delta T Cells Recognize a Microbial Encoded B Cell Antigen to Initiate a Rapid Antigen-Specific Interleukin-17 Response** *IMMUNITY*  
Zeng, X., Wei, Y., Huang, J., Newell, E. W., Yu, H., Kidd, B. A., Kuhns, M. S., Waters, R. W., Davis, M. M., Weaver, C. T., Chien, Y.  
2012; 37 (3): 524-534
  - **Toxoplasma Polymorphic Effectors Determine Macrophage Polarization and Intestinal Inflammation** *CELL HOST & MICROBE*  
Jensen, K. D., Wang, Y., Wojno, E. D., Shastri, A. J., Hu, K., Cornel, L., Boedec, E., Ong, Y., Chien, Y., Hunter, C. A., Boothroyd, J. C., Saeij, J. P.  
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- **Ligand recognition during thymic development and gamma delta T cell function specification** *SEMINARS IN IMMUNOLOGY*  
Meyer, C., Zeng, X., Chien, Y.  
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- **Evidence for a functional sidedness to the alpha beta TCR** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Kuhns, M. S., Girvin, A. T., Klein, L. O., Chen, R., Jensen, K. D., Newell, E. W., Huppa, J. B., Lillemeier, B. F., Huse, M., Chien, Y., Garcia, K. C., Davis, M. M.  
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- **The Salmonella SPI2 Effector SseI Mediates Long-Term Systemic Infection by Modulating Host Cell Migration** *PLOS PATHOGENS*  
McLaughlin, L. M., Govoni, G. R., Gerke, C., Gopinath, S., Peng, K., Laidlaw, G., Chien, Y., Jeong, H., Li, Z., Brown, M. D., Sacks, D. B., Monack, D.  
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- **Cutting Edge: gamma delta Intraepithelial Lymphocytes of the Small Intestine Are Not Biased toward Thymic Antigens** *JOURNAL OF IMMUNOLOGY*  
Jensen, K. D., Shin, S., Chien, Y.  
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- **An autonomous CDR3 delta is sufficient for recognition of the nonclassical MHC class I molecules T10 and T22 by gamma delta T cells** *NATURE IMMUNOLOGY*  
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- **Antigen recognition by gamma delta T cells** *IMMUNOLOGICAL REVIEWS*  
Chien, Y., Konigshofer, Y.  
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- **gamma delta T cells - innate immune lymphocytes?** *CURRENT OPINION IN IMMUNOLOGY*  
Konigshofer, Y., Chien, Y.  
2006; 18 (5): 527-533
- **Nonobese diabetic mice express aspects of both type 1 and type 2 diabetes** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Chaparro, R. J., Konigshofer, Y., Beilhack, G. F., Shizuru, J. A., McDevitt, H. O., Chien, Y.  
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- **The shaping of the gamma delta T cell receptor repertoire** *Annual Meeting of the American-Association-of-Immunologists*  
Jensen, K., Shin, S., Konigshofer, Y., Li, L., Chien, Y.  
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- **Structure of a gamma delta T cell receptor in complex with the nonclassical MHC T22** *SCIENCE*  
Adams, E. J., Chien, Y. H., Garcia, K. C.  
2005; 308 (5719): 227-231
- **Antigen recognition determinants of gamma delta T cell receptors** *SCIENCE*  
Shin, S., El-Diwany, R., Schaffert, S., Adams, E. J., Garcia, K. C., Pereira, P., Chien, Y. H.  
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- **The adaptor molecules LAT and SLP-76 are specifically targeted by Yersinia to inhibit T cell activation** *JOURNAL OF EXPERIMENTAL MEDICINE*  
Gerke, C., FALKOW, S., Chien, Y. H.  
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- **Differential roles of cytokine receptors in the development of epidermal gamma delta T cells** *JOURNAL OF IMMUNOLOGY*  
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Chien, Y. H., Hampl, J.  
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- **The specificity of a weak gamma delta TCR interaction can be modulated by the glycosylation of the ligand** *JOURNAL OF IMMUNOLOGY*  
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- **Visualizing lymphocyte recognition** *IMMUNOLOGY AND CELL BIOLOGY*  
Wulfing, C., Chien, Y. H., DAVIS, M. M.  
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- **Differential effect of B lymphocyte-induced maturation protein (Blimp-1) expression on cell fate during B cell development** *JOURNAL OF EXPERIMENTAL MEDICINE*  
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- Crowley, M. P., Reich, Z., Mavaddat, N., Altman, J. D., Chien, Y. H.  
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- **T cell receptor biochemistry, repertoire selection and general features of TCR and Ig structure** *Symposium on the Molecular Basis of Cellular Defence Mechanisms*  
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  - **Biological and chemical aspects of T-cell receptor-mediated recognition** *40th Symposium of the Alfred-Benzon-Foundation on HLA and Disease - the Molecular Basis*  
DAVIS, M. M., Lyons, D. S., Altman, J. D., Hampl, J., BONIFACE, J. J., Arden, B., Chien, Y.  
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  - **Ligand recognition by gamma delta T cells** *8th International Congress of Mucosal Immunology*  
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  - **FUNCTIONAL EXPRESSION AND RECOGNITION OF NONCLASSICAL MHC CLASS-I T10(B) IS NOT PEPTIDE-DEPENDENT** *JOURNAL OF IMMUNOLOGY*  
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  - **ISSUES CONCERNING THE NATURE OF ANTIGEN RECOGNITION BY ALPHA-BETA AND GAMMA-DELTA T-CELL RECEPTORS** *9th International Congress of Immunology*  
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  - **T-CELL RECEPTOR V-REGION USAGE AND ANTIGEN-SPECIFICITY - THE CYTOCHROME-C MODEL SYSTEM** *Conference on T-Cell Receptor Use in Human Autoimmune Diseases*  
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  - **The recognition of MHC molecules by gamma delta T cells.** *Behring Institute Mitteilungen*  
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