


Stanford



Edgar Engleman

Professor of Pathology and of Medicine (Immunology and Rheumatology)

 NIH Biosketch available Online

 Curriculum Vitae available Online

CONTACT INFORMATION

• Administrative Contact

Donna Jones - Administrative Associate

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Bio

ACADEMIC APPOINTMENTS

- Professor, Pathology
- Professor, Medicine - Immunology & Rheumatology
- Member, Bio-X
- Member, Maternal & Child Health Research Institute (MCHRI)
- Member, Stanford Cancer Institute
- Member, Wu Tsai Neurosciences Institute

ADMINISTRATIVE APPOINTMENTS

- Co-Director, Tumor Immunology and Immunotherapy, Stanford Cancer Institute, (2008- present)
- Medical Director, Stanford Blood Center, (1980- present)
- Member, Stanford Diabetes Research Center, Stanford, (2018- present)

LINKS

- Engleman lab website: <http://med.stanford.edu/englemanlab.html>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

We study the biology of immune cells and their roles in the pathogenesis of cancers and other life-threatening diseases. By applying new and more precise analytical tools for assessing this system in mice and humans, we have been successful at identifying disease-promoting immune abnormalities. By targeting the cells responsible for or affected by these abnormalities, we have succeeded in reversing the abnormalities and ameliorating the diseases they cause. We make extensive use of mouse models for in depth mechanistic studies, but we also use human tissues to confirm the clinical relevance of our findings. To pursue this work, we have been using newer multiplex imaging technologies and deep gene sequencing.

We have been particularly interested in myeloid immune cells, including dendritic cells (DCs) and macrophages, that can either induce or suppress immunity. Our first generation methods for isolating and arming human myeloid cells with tumor antigens provided the basis for the first FDA-approved cell-based immunotherapy --- i.e., Sipuleucel-T (Provenge) that was approved in 2010 for the treatment of advanced prostate cancer. Subsequently, we developed a treatment that reprograms immunosuppressive myeloid cells in tumors into immunostimulatory cells that present tumor antigens to host T cells, resulting in potent anti-tumor immunity. This strategy entered clinical trials in late 2020 for the treatment of multiple cancers. Most recently, we discovered that tumor cells colonizing lymph nodes alter their gene expression to enable interactions with immune cells in the involved nodes, resulting in tumor-specific immune tolerance that, in turn, enables distant metastasis. This discovery formed the basis for an ongoing multi-laboratory effort to decipher the cellular and molecular mechanisms underlying tumor metastasis.

In addition to cancer, we have been studying the role of immune cells in neurodegenerative disease, metabolic diseases, and organ transplant rejection. We helped to develop a therapy that utilizes radiation to lymphoid organs to induce immune tolerance, enabling patients who receive organ transplants to retain those organs life-long without the need for immunosuppressive drugs. This therapy is now in advanced clinical trials in kidney transplant patients. The key to the success of this therapy appears to be the selective activation of tolerogenic myeloid immune cells. Our evidence suggests that the same cells function normally to prevent autoimmunity in healthy individuals but are hijacked by cancers to enable their escape from the host immune system. Once we fully understand this mechanism, which is independent of known checkpoint mechanisms, we believe there is the potential to manipulate it for the treatment of many diseases, including cancers and autoimmune disorders.

Teaching

COURSES

2020-21

- Tumor Immunology: CBIO 275, IMMUNOL 275 (Spr)

2019-20

- Cellular and Clinical Aspects of Cancer: CBIO 242 (Spr)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Anthony Cordova, Alea Delmastro, Haotian Du, Katie Freitas, Joseph González, Noah Greenwald, R. Andres Parra Sperberg, Amanda Rabe, David Seong

Postdoctoral Faculty Sponsor

Sreya Bagchi, David Kung-Chun Chiu, Kazukuni Hayashi, Hyungjoo Kim, Ian Linde, Guotao Yu

Doctoral Dissertation Advisor (AC)

Markus Diehl, Alex Muselman

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

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

Publications

PUBLICATIONS

- **Lymph node colonization induces tumor-immune tolerance to promote distant metastasis.** *Cell*
Reticker-Flynn, N. E., Zhang, W., Belk, J. A., Basto, P. A., Escalante, N. K., Pilarowski, G. O., Bejnood, A., Martins, M. M., Kenkel, J. A., Linde, I. L., Bagchi, S., Yuan, R., Chang, et al
2022
- **Immune-stimulating antibody conjugates elicit robust myeloid activation and durable antitumor immunity.** *Nature cancer*

- Ackerman, S. E., Pearson, C. I., Gregorio, J. D., Gonzalez, J. C., Kenkel, J. A., Hartmann, F. J., Luo, A., Ho, P. Y., LeBlanc, H., Blum, L. K., Kimmey, S. C., Luo, A., Nguyen, et al
2021; 2 (1): 18-33
- **Structure of the IFN gamma receptor complex guides design of biased agonists** *NATURE*
Mendoza, J. L., Escalante, N. K., Jude, K. M., Bellon, J., Su, L., Horton, T. M., Tsutsumi, N., Berardinelli, S. J., Haltiwanger, R. S., Pichler, J., Engleman, E. G., Garcia, K.
2019; 567 (7746): 56-+
 - **An Immunosuppressive Dendritic Cell Subset Accumulates at Secondary Sites and Promotes Metastasis in Pancreatic Cancer.** *Cancer research*
Kenkel, J. A., Tseng, W. W., Davidson, M. G., Tolentino, L. L., Choi, O., Bhattacharya, N., Seeley, E. S., Winer, D. A., Reticker-Flynn, N. E., Engleman, E. G.
2017; 77 (15): 4158-4170
 - **Systemic Immunity Is Required for Effective Cancer Immunotherapy.** *Cell*
Spitzer, M. H., Carmi, Y., Reticker-Flynn, N. E., Kwek, S. S., Madhiredy, D., Martins, M. M., Gherardini, P. F., Prestwood, T. R., Chabon, J., Bendall, S. C., Fong, L., Nolan, G. P., Engleman, et al
2017; 168 (3): 487-502 e15
 - **Role of innate and adaptive immunity in obesity-associated metabolic disease** *JOURNAL OF CLINICAL INVESTIGATION*
McLaughlin, T., Ackerman, S. E., Shen, L., Engleman, E.
2017; 127 (1): 5-13
 - **Normalizing Microbiota-Induced Retinoic Acid Deficiency Stimulates Protective CD8(+) T Cell-Mediated Immunity in Colorectal Cancer.** *Immunity*
Bhattacharya, N., Yuan, R., Prestwood, T. R., Penny, H. L., DiMaio, M. A., Reticker-Flynn, N. E., Krois, C. R., Kenkel, J. A., Pham, T. D., Carmi, Y., Tolentino, L., Choi, O., Hulett, et al
2016; 45 (3): 641-655
 - **Normalizing microbiota-induced retinoic acid deficiency stimulates protective CD8+ T-cell-mediated immunity in colorectal cancer** *Immunity*
Bhattacharya, N., Yuan, R., Prestwood, T., Penny, H., DiMaio, M., Reticker-Flynn, N., Krois, C., Kenkel, J., Pham, T., Carmi, Y., Tolentino, L., Choi, O., Hulett, et al
2016; 45: 641-55
 - **IMMUNOLOGY. An interactive reference framework for modeling a dynamic immune system.** *Science*
Spitzer, M. H., Gherardini, P. F., Fragiadakis, G. K., Bhattacharya, N., Yuan, R. T., Hotson, A. N., Finck, R., Carmi, Y., Zunder, E. R., Fantl, W. J., Bendall, S. C., Engleman, E. G., Nolan, et al
2015; 349 (6244)
 - **Allogeneic IgG combined with dendritic cell stimuli induce antitumour T-cell immunity.** *Nature*
Carmi, Y., Spitzer, M. H., Linde, I. L., Burt, B. M., Prestwood, T. R., Perlman, N., Davidson, M. G., Kenkel, J. A., Segal, E., Pusapati, G. V., Bhattacharya, N., Engleman, E. G.
2015; 521 (7550): 99-104
 - **Allogeneic IgG combined with dendritic cell stimuli induce antitumour T-cell immunity** *NATURE*
Carmi, Y., Spitzer, M. H., Linde, I. L., Burt, B. M., Prestwood, T. R., Perlman, N., Davidson, M. G., Kenkel, J. A., Segal, E., Pusapati, G. V., Bhattacharya, N., Engleman, E. G.
2015; 521 (7550): 99-U254
 - **B-1a lymphocytes attenuate insulin resistance.** *Diabetes*
Shen, L., Chng, M. H., Alonso, M. N., Yuan, R., Winer, D. A., Engleman, E. G.
2015; 64 (2): 593-603
 - **B cells promote insulin resistance through modulation of T cells and production of pathogenic IgG antibodies** *NATURE MEDICINE*
Winer, D. A., Winer, S., Shen, L., Wadia, P. P., Yantha, J., Paltser, G., Tsui, H., Wu, P., Davidson, M. G., Alonso, M. N., Leong, H. X., Glassford, A., Caimol, et al
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 - **Using signaling pathways to overcome immune tolerance to tumors.** *Science's STKE : signal transduction knowledge environment*
Engleman, E. G., Brody, J., Soares, L.
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 - **Depletion of host Langerhans cells before transplantation of donor alloreactive T cells prevents skin graft-versus-host disease** *NATURE MEDICINE*
Merad, M., Hoffmann, P., Ranheim, E., Slaymaker, S., Manz, M. G., Lira, S. A., Charo, I., Cook, D. N., Weissman, I. L., Strober, S., Engleman, E. G.

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- **Vaccination of patients with B-cell lymphoma using autologous antigen-pulsed dendritic cells** *NATURE MEDICINE*
Hsu, F. J., Benike, C., Fagnoni, F., Liles, T. M., Czerwinski, D., Taidi, B., Engleman, E. G., Levy, R.
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- **PREVENTION OF AIDS TRANSMISSION THROUGH SCREENING OF THE BLOOD-SUPPLY** *ANNUAL REVIEW OF IMMUNOLOGY*
Galel, S. A., Lifson, J. D., Engleman, E. G.
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- **GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR PROMOTES DIFFERENTIATION AND SURVIVAL OF HUMAN PERIPHERAL-BLOOD DENDRITIC CELLS-INVITRO** *JOURNAL OF CLINICAL INVESTIGATION*
Markowicz, S., Engleman, E. G.
1990; 85 (3): 955-961
- **PH-INDEPENDENT HIV ENTRY INTO CD4-POSITIVE T-CELLS VIA VIRUS ENVELOPE FUSION TO THE PLASMA-MEMBRANE** *CELL*
Stein, B. S., GOWDA, S. D., Lifson, J. D., Penhallow, R. C., Bensch, K. G., Engleman, E. G.
1987; 49 (5): 659-668
- **INDUCTION OF CD4-DEPENDENT CELL-FUSION BY THE HTLV-III/LAV ENVELOPE GLYCOPROTEIN** *NATURE*
Lifson, J. D., Feinberg, M. B., Reyes, G. R., Rabin, L., Banapour, B., Chakrabarti, S., Moss, B., WONGSTAAL, F., Steimer, K. S., Engleman, E. G.
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- **AIDS RETROVIRUS INDUCED CYTOPATHOLOGY - GIANT-CELL FORMATION AND INVOLVEMENT OF CD4 ANTIGEN** *SCIENCE*
Lifson, J. D., Reyes, G. R., McGrath, M. S., Stein, B. S., Engleman, E. G.
1986; 232 (4754): 1123-1127
- **Identification of cell types in multiplexed in situ images by combining protein expression and spatial information using CELESTA.** *Nature methods*
Zhang, W., Li, I., Reticker-Flynn, N. E., Good, Z., Chang, S., Samusik, N., Saumyaa, S., Li, Y., Zhou, X., Liang, R., Kong, C. S., Le, Q., Gentles, et al
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- **Abdominopelvic FLASH Irradiation Improves PD-1 Immune Checkpoint Inhibition in Preclinical Models of Ovarian Cancer.** *Molecular cancer therapeutics*
Eggold, J. T., Chow, S., Melemenidis, S., Wang, J., Natarajan, S., Loo, P. E., Manjappa, R., Viswanathan, V., Kidd, E. A., Engleman, E., Dorigo, O., Loo, B. W., Rankin, et al
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- **DECTIN-2, A NOVEL TARGET FOR TUMOR MACROPHAGE REPROGRAMMING IN CANCER IMMUNOTHERAPY**
Kenkel, J., Ho, P., Kongara, S., Henning, K., Kreder, C., Nolin, J., Chapin, S., Kowanzet, M., Alonso, M., Ackerman, S., Engleman, E., Dornan, D.
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- **Brain profiling in murine colitis and human epilepsy reveals neutrophils and TNFalpha as mediators of neuronal hyperexcitability.** *Journal of neuroinflammation*
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- **Development of immunosuppressive myeloid cells to induce tolerance in solid organ and hematopoietic cell transplant recipients.** *Blood advances*
Jensen, K. P., Hongo, D., Ji, X., Zheng, P., Pawar, R. D., Wu, H., Busque, S., Scandling, J. D., Shizuru, J. A., Lowsky, R., Shori, A., Dutt, S., Waters, et al
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- **Targeting Glycolysis in Macrophages Confers Protection Against Pancreatic Ductal Adenocarcinoma** *INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES*
Penny, H., Sieow, J., Gun, S., Lau, M., Lee, B., Tan, J., Phua, C., Toh, F., Nga, Y., Yeap, W., Janela, B., Kumar, D., Chen, et al
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- **Antitumor effects of iPSC-based cancer vaccine in pancreatic cancer.** *Stem cell reports*
Ouyang, X., Liu, Y., Zhou, Y., Guo, J., Wei, T., Liu, C., Lee, B., Chen, B., Zhang, A., Casey, K. M., Wang, L., Kooreman, N. G., Habtezion, et al

2021

- **Mechanical Stiffness Controls Dendritic Cell Metabolism and Function.** *Cell reports*
Chakraborty, M., Chu, K., Shrestha, A., Revelo, X. S., Zhang, X., Gold, M. J., Khan, S., Lee, M., Huang, C., Akbari, M., Barrow, F., Chan, Y. T., Lei, et al
2021; 34 (2): 108609
- **Immune-stimulating antibody conjugates elicit robust myeloid activation and durable antitumor immunity** *NATURE CANCER*
Ackerman, S. E., Pearson, C. I., Gregorio, J. D., Gonzalez, J. C., Kenkel, J. A., Hartmann, F. J., Luo, A., Ho, P. Y., LeBlanc, H., Blum, L. K., Kimmey, S. C., Luo, A., Nguyen, et al
2021; 2 (1): 18+
- **Identification of Two Subsets of Murine DC1 Dendritic Cells That Differ by Surface Phenotype, Gene Expression, and Function.** *Frontiers in immunology*
Hongo, D., Zheng, P., Dutt, S., Pawar, R. D., Meyer, E., Engleman, E. G., Strober, S.
2021; 12: 746469
- **Immune Checkpoint Inhibitors for the Treatment of Cancer: Clinical Impact and Mechanisms of Response and Resistance.** *Annual review of pathology*
Bagchi, S., Yuan, R., Engleman, E. G.
2020
- **COVALENT ATTACHMENT OF A TLR7/8 AGONIST TO TUMOR-TARGETING ANTIBODIES DRIVES POTENT ANTI-TUMOR EFFICACY BY SYNERGISTICALLY ACTIVATING FCGR- AND TLR- SIGNALING AND ENABLES SAFE SYSTEMIC ADMINISTRATION**
Ackerman, S., Hartmann, F., Pearson, C., Gonzalez, J., Ho, P., Kimmey, S., Luo, A., Ackerman, B., Lee, A., Laura, R., Paik, J., Henning, K., Jackson, et al
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- **A versatile system to record cell-cell interactions.** *eLife*
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- **Human Regulatory Dendritic Cells Develop From Monocytes in Response to Signals From Regulatory and Helper T Cells.** *Frontiers in immunology*
Zhang, X., Zheng, P., Prestwood, T. R., Zhang, H., Carmi, Y., Tolentino, L. L., Wu, N., Choi, O., Winer, D. A., Strober, S., Kang, E. S., Alonso, M. N., Engleman, et al
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- **ImmunoGlobe: enabling systems immunology with a manually curated intercellular immune interaction network.** *BMC bioinformatics*
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- **Lymph node colonization promotes distant tumor metastasis through the induction of tumor-specific immunosuppression**
Reticker-Flynn, N. E., Basto, P. A., Zhang, W., Martins, M. M., Chang, S., Gentles, A. J., Sunwoo, J. B., Plevritis, S. K., Engleman, E. G.
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- **Cancer systems immunology.** *eLife*
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- **Lymph node colonization promotes distant tumor metastasis through the induction of tumor-specific immunosuppression.**
Reticker-Flynn, N. E., Basto, P. A., Zhang, W., Bejnood, A., Kenkel, J. A., Martins, M. M., Chang, S., Gentles, A. J., Sunwoo, J. B., Plevritis, S. K., Engleman, E. G.
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- **Mixed chimerism and acceptance of kidney transplants after immunosuppressive drug withdrawal.** *Science translational medicine*
Busque, S. n., Scandling, J. D., Lowsky, R. n., Shizuru, J. n., Jensen, K. n., Waters, J. n., Wu, H. H., Sheehan, K. n., Shori, A. n., Choi, O. n., Pham, T. n., Fernandez Vina, M. A., Hoppe, et al
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- **Enteric Glia Play a Critical Role in Promoting the Development of Colorectal Cancer** *Frontiers in Oncology*
Yuan, R., Bhattacharya, N., Kenkel, J. A., Shen, J., DiMaio, M. A., Bagchi, S., Prestwood, T. R., Habtezion, A., Engleman, E. G.
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- **Human regulatory dendritic cells develop from monocytes in response to signals from regulatory and helper T cells** *Frontiers In Immunology*
Zhang, X., Zheng, P., Prestwood, T., Zhang, H., Cami, Y., Tolentino, L., Wu, N., Choi, O., Winer, D., Strober, S., Kang, E., Alonso, M., Engleman, et al

2020

- **Hyaluronan synthesis inhibition impairs antigen presentation and delays transplantation rejection.** *Matrix biology : journal of the International Society for Matrix Biology*
Marshall, P. L., Nagy, N. n., Kaber, G. n., Barlow, G. L., Ramesh, A. n., Xie, B. J., Linde, M. H., Haddock, N. L., Lester, C. A., Tran, Q. L., de Vries, C. n., Hargil, A. n., Malkovskiy, et al
2020
- **HER2-targeting TLR7/8 immune-stimulating antibody conjugates elicit robust myeloid activation and anti-tumor immune responses in a TLR- and FcR-dependent manner**
Gonzalez, J., Pearson, C., Ackerman, S., Kenkel, J., Ho, P., Luo, A., Nguyen, M., Paik, J., Lee, A., Laura, R., Li, H., Kreder, C., Henning, et al
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- **Tumor-binding antibodies induce potent dendritic cell-mediated tumor immunity** *ONCOIMMUNOLOGY*
Carmi, Y., Prestwood, T., Engleman, E. G.
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- **A Novel Type of Blood Biomarker: Distinct Changes of Cytokine-Induced STAT Phosphorylation in Blood T Cells Between Colorectal Cancer Patients and Healthy Individuals.** *Cancers*
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- **Lymph node colonization promotes distant tumor metastasis through the induction of systemic immune tolerance**
Reticker-Flynn, N. E., Martins, M. M., Basto, P. A., Zhang, W., Bejnood, A., Gentles, A. J., Sunwoo, J. B., Plevritis, S. K., Engleman, E. G.
AMER ASSOC CANCER RESEARCH.2019
- **Tumor-binding antibodies induce potent dendritic cell-mediated tumor immunity.** *Oncoimmunology*
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- **Structure of the IFN γ receptor complex guides design of biased agonists.** *Nature*
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2019
- **A gut punch fights cancer and infection** *NATURE*
Reticker-Flynn, N. E., Engleman, E. G.
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- **Myeloid sphingosine-1-phosphate receptor 1 is important for CNS autoimmunity and neuroinflammation.** *Journal of autoimmunity*
Tsai, H. C., Nguyen, K. n., Hashemi, E. n., Engleman, E. n., Hla, T. n., Han, M. H.
2019
- **Insulin Receptor-Mediated Stimulation Boosts T Cell Immunity during Inflammation and Infection** *CELL METABOLISM*
Tsai, S., Clemente-Casares, X., Zhou, A. C., Lei, H., Ahn, J. J., Chan, Y., Choi, O., Luck, H., Woo, M., Dunn, S. E., Engleman, E. G., Watts, T. H., Winer, et al
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- **Leveraging heterogeneity across multiple datasets increases cell-mixture deconvolution accuracy and reduces biological and technical biases.** *Nature communications*
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- **Use of Flow Cytometry for Diagnosis of Epilepsy Associated With Homozygous PIGW Variants.** *Pediatric neurology*
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- **The Interface of Pancreatic Cancer With Diabetes, Obesity, and Inflammation: Research Gaps and Opportunities: Summary of a National Institute of Diabetes and Digestive and Kidney Diseases Workshop** *PANCREAS*
Abbruzzese, J. L., Andersen, D. K., Borrebaeck, C. K., Chari, S. T., Costello, E., Cruz-Monserrate, Z., Eibl, G., Engleman, E. G., Fisher, W. E., Habtezion, A., Kim, S. K., Korc, M., Logsdon, et al
2018; 47 (5): 516–25

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Santana-Magal, N., Rasoulouniriana, D., Saperia, C., Gutwillig, A., Rider, P., Engleman, E. G., Carmi, Y.
2018
- **Macrochimerism and clinical transplant tolerance.** *Human immunology*
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2018
- **In vitro and in vivo metabolite identification of a novel benzimidazole compound ZLN005 by LC-MS/MS.** *Rapid communications in mass spectrometry : RCM*
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2017; 2 (10)
- **Tolerogenic interactions between CD8(+) dendritic cells and NKT cells prevent rejection of bone marrow and organ grafts** *BLOOD*
Hongo, D., Tang, X., Zhang, X., Engleman, E. G., Strober, S.
2017; 129 (12): 1718-1728
- **A distinct subset of plasmacytoid dendritic cells induces activation and differentiation of B and T lymphocytes.** *Proceedings of the National Academy of Sciences of the United States of America*
Zhang, H., Gregorio, J. D., Iwahori, T., Zhang, X., Choi, O., Tolentino, L. L., Prestwood, T., Carmi, Y., Engleman, E. G.
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- **Tolerogenic interactions between CD8+ dendritic cells and NKT cells prevent rejection of bone marrow and organ grafts.** *Blood*
Hongo, D., Tang, X., Zhang, X., Engleman, E. G., Strober, S.
2017
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Liu, L. F., Craig, C. M., Tolentino, L. L., Choi, O., Morton, J., Rivas, H., Cushman, S. W., Engleman, E. G., McLaughlin, T.
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