



## Justin P. Annes M.D., Ph.D.

Associate Professor of Medicine (Endocrinology)

Medicine - Endocrinology, Gerontology, & Metabolism

### CLINICAL OFFICE (PRIMARY)

- **Division of Endocrinology**

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### Bio

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#### BIO

Dr. Justin Annes specializes in the treatment of hereditary endocrine disorders with particular focus on neuroendocrine-related conditions.

He developed the Stanford Endocrine Genetics Clinic in 2012 which is part of the interdisciplinary Stanford Hypertension Center and Stanford Neuroendocrine Tumor Program.

He has medical practice has focused on hereditary endocrine disease since 2008.

#### CLINICAL FOCUS

- Pheochromocytoma and Paraganglioma
- Multiple Endocrine Neoplasia
- Hereditary Endocrine Disorders
- Endocrinology
- Diabetes and Metabolism

#### ACADEMIC APPOINTMENTS

- Associate Professor, Medicine - Endocrinology, Gerontology, & Metabolism
- Member, Bio-X
- Member, Cardiovascular Institute
- Member, Maternal & Child Health Research Institute (MCHRI)
- Faculty Fellow, Sarafan ChEM-H
- Member, Stanford Cancer Institute

#### HONORS AND AWARDS

- Stanford Cancer Center Innovation Award, Stanford University (2018)
- Stanford Diabetes Research Center, Training Outreach Program (PI), Stanford University (2017-)
- Translation Research Innovation Award, The Friedenrich BII Diabetes Fund (2016-2017)

- R01: The Role of Adenosine Kinase in Controlling Beta-Cell Regeneration, NIH NIDDK (2015-20)
- The Best of Basic Research, Endocrine Society (2014)
- Cellome Award for "Best High-Content Screening Publication in 2012", Thermo Fisher Scientific (2013)
- Hoopes Mentorship Award, Harvard University (2012)
- Mentored Clinical Scientist Research Career Development Award, NIH (2009-2014)
- AOA, Delta Chapter, NYU Medical School (2004)
- Medical Scientist Training Award, NIH (1996-2002)

## **BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS**

- Medical Advisory Board Member, Pheo Para Alliance (2018 - present)
- Admissions Committee, Stanford MSTP (2013 - present)

## **PROFESSIONAL EDUCATION**

- Medical Education: New York University School of Medicine (2004) NY
- Board Certification: Internal Medicine, American Board of Internal Medicine (2024)
- Residency: Childrens Hospital Harvard Medical School Medical Genetics Residency (2009) MA
- Residency: Brigham and Women's Hospital Internal Medicine Residency (2009) MA
- Internship: Brigham and Women's Hospital Internal Medicine Residency (2005) MA
- Fellowship, Brigham and Women's Hospital / Harvard Medical School , Clinical Genetics (2009)
- Residency, Brigham and Women's Hospital , Internal Medicine (2009)
- M.D., Ph.D., NYU School of Medicine , Cell Biology (2004)
- BS, Haverford College , Molecular Biology (1996)

## **LINKS**

- Annes Laboratory: <http://med.stanford.edu/annes-lab.html>

## **Research & Scholarship**

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### **CURRENT RESEARCH AND SCHOLARLY INTERESTS**

The ANNES LABORATORY of Molecular Endocrinology: Leveraging Chemical Biology to Treat Endocrine Disorders

#### **DIABETES**

The prevalence of diabetes is increasing at a staggering rate. By the year 2050 an astounding 25% of Americans will be diabetic. The goal of my research is to uncover therapeutic strategies to stymie the ensuing diabetes epidemic. To achieve this goal we have developed a variety of innovative experimental approaches to uncover novel approaches to curing diabetes.

(1) Beta-Cell Regeneration: Diabetes results from either an absolute or relative deficiency in insulin production. Our therapeutic strategy is to stimulate the regeneration of insulin-producing beta-cells to enhance an individual's insulin secretion capacity. We have developed a unique high-throughput chemical screening platform which we use to identify small molecules that promote beta-cell growth. This work has led to the identification of key molecular pathways (therapeutic targets) and candidate drugs that promote the growth and regeneration of islet beta-cells. Our goal is to utilize these discoveries to treat and prevent diabetes.

(2) The Metabolic Syndrome: A major cause of the diabetes epidemic is the rise in obesity which leads to a cluster of diabetes- and cardiovascular disease-related metabolic abnormalities that shorten life expectancy. These physiologic aberrations are collectively termed the Metabolic Syndrome (MS). My laboratory has developed an original in vivo screening platform to identify novel hormones that influence the behaviors (excess caloric consumption, deficient exercise and disrupted sleep-wake cycles) and the metabolic abnormalities caused by obesity. We aim to manipulate these hormone levels to prevent the development and detrimental consequences of the MS.

#### HEREDITARY PARAGANGLIOMA SYNDROME

The Hereditary Paraganglioma Syndrome (hPGL) is a rare genetic cancer syndrome that is most commonly caused by a defect in mitochondrial metabolism. Our goal is to understand how altered cellular metabolism leads to the development of cancer. Although hPGL is uncommon, it serves as an excellent model for the abnormal metabolic behavior displayed by nearly all cancers. Our goal is to develop novel therapeutic strategies that target the abnormal behavior of cancer cells. In the laboratory we have developed hPGL mouse models and use high throughput chemical screening to identify the therapeutic susceptibilities that result from the abnormal metabolic behavior of cancer cells.

As a physician scientist trained in clinical genetics I have developed expertise in hereditary endocrine disorders and devoted my efforts to treating families affected by the hPGL syndrome. By leveraging our laboratory expertise in the hPGL syndrome, our care for individuals who have inherited the hPGL syndrome is at the forefront of medicine. Our goal is to translate our laboratory discoveries to the treatment of affected families.

## Teaching

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### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)
- Endocrinology (Fellowship Program)

## Publications

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### PUBLICATIONS

- **Succinate Dehydrogenase-Deficient Cancer Cells Have Increased Susceptibility to Ym155-Induced DNA Damage.** *Endocrine-related cancer*  
Guo, Q., Lee, S., Armstrong, N., Lim, B., Schugar, R. C., Tomz, D., Xu, H., Zhen, A., Needleman, L., Kebebew, E., Annes, J. P.  
2026
- **Pseudopheochromocytoma With Catecholamine Excess and End-organ Damage: A 30-year Course Treated With Escitalopram.** *JCEM case reports*  
Anvaripour, A. S., Needleman, L., Brady, B., Annes, J. P.  
2026; 4 (2): luaf321
- **Functional Characterization of SDHB Variants Clarifies Hereditary Pheochromocytoma and Paraganglioma Risk and Genotype-Phenotype Relationships.** *The Journal of clinical investigation*  
Lee, S., Needleman, L., Park, J., Schugar, R. C., Guo, Q., Ford, J. M., Annes, J. P.  
2025
- **Pharmacologic stimulation of insulin granule acidification increases  $\beta$ -cell zinc content and augments  $\beta$ -cell-targeted drug delivery.** *The Journal of biological chemistry*  
Lee, S., Fraser, H. P., Schugar, R. C., Xu, H., Horton, T. M., Thomson, E. A., Park, J., Zhang, X., Annes, J. P.  
2025: 110645
- **A Wireless Implantable Closed-Loop Electrochemical Drug Delivery System** *IEEE TRANSACTIONS ON BIOMEDICAL CIRCUITS AND SYSTEMS*  
Wang, M. L., Yeon, P., Mofidfar, M., Chamberlayne, C., Xu, H., Annes, J. P., Zare, R. N., Arbabian, A.  
2025; 19 (4): 777-790

- **Functional Suppression of a Prolactinoma by a Dopamine-Secreting Paraganglioma.** *JCEM case reports*  
Fox, T., Needleman, L., Bharani, K. L., Mihm, F., Annes, J. P., Chang, J. J.  
2025; 3 (6): luaf080
- **American Association of Clinical Endocrinology Consensus Statement on Management of Multiple Endocrine Neoplasia Type 1.** *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*  
Del Rivero, J., Gangi, A., Annes, J. P., Jasim, S., Keller, J., Lundholm, M. D., Silverstein, J. M., Vaghaiwalla, T. M., Wermers, R. A.  
2025
- **Intermittent Low-Magnitude Pressure Applied Across Macroencapsulation Devices Enables Physiological Insulin Delivery Dynamics.** *Diabetes*  
Thomson, E. A., Lee, S., Xu, H., Moeller, H., Sands, J., Lal, R. A., Annes, J. P., Poon, A. S.  
2025
- **CDC73 c.1155-3A>G is a pathogenic variant that causes aberrant splicing, disrupted parafibromin expression, and hyperparathyroidism-jaw tumor syndrome.** *JBMR plus*  
Needleman, L., Chun, N., Sitaraman, S., Tan, M., Sellmeyer, D. E., Kebebew, E., Annes, J. P.  
2025; 9 (1): ziae149
- **Itaconate drives mtRNA-mediated type I interferon production through inhibition of succinate dehydrogenase (vol 6, pg 2060, 2024)** *NATURE METABOLISM*  
O'Carroll, S. M., Peace, C. G., Toller-Kawahisa, J. E., Min, Y., Hooftman, A., Charki, S., Kehoe, L., O'Sullivan, M. J., Zoller, A., Mcgettrick, A. F., Zotta, A., Day, E. A., Simarro, et al  
2024
- **Itaconate drives mtRNA-mediated type I interferon production through inhibition of succinate dehydrogenase** *NATURE METABOLISM*  
O'Carroll, S. M., Peace, C. G., Toller-Kawahisa, J. E., Min, Y., Hooftman, A., Charki, S., Kehoe, L., O'Sullivan, M. J., Zoller, A., Mcgettrick, A. F., Day, E. A., Simarro, M., Armstrong, et al  
2024
- **Overcoming Limitations Of Identifying Proliferating  $\beta$ -cells In Dispersed Primary Islets Culture For Drug Discovery**  
Xu, H., Rebecca, S., Lee, S., Annes, J. P.  
ENDOCRINE SOC.2024: A456
- **Sol-moiety: Discovery of a water-soluble prodrug technology for enhanced oral bioavailability of insoluble therapeutics.** *Nature communications*  
Karbasi, A. B., Barfuss, J. D., Morgan, T. C., Collins, D., Costenbader, D. A., Dennis, D. G., Hinman, A., Ko, K., Messina, C., Nguyen, K. C., Schugar, R. C., Stein, K. A., Williams, et al  
2024; 15 (1): 8487
- **An shRNA screen in primary human beta cells identifies the serotonin 1F receptor as a negative regulator of survival during transplant.** *bioRxiv : the preprint server for biology*  
Lee, R. A., Chopra, D. G., Nguyen, V., Huang, X., Zhang, Y., Shariati, K., Yiv, N., Schugar, R., Annes, J., Roth, B., Ku, G. M.  
2024
- **Vascular Ensheatment Reflects Characteristic Migratory Behavior of Paragangliomas.** *JCEM case reports*  
Needleman, L., Holsinger, F. C., Annes, J. P.  
2024; 2 (4): luae064
- **Caution on the Use of 68Ga-DOTATATE for the Diagnosis of Pheochromocytoma: A Report of 2 Cases.** *JCEM case reports*  
Needleman, L., Enamandram, S., Annes, J. P.  
2023; 1 (6): luad149
- **Rare Presentation of Paroxysmal High B-Pee.** *Hypertension (Dallas, Tex. : 1979)*  
Bradshaw, C., Abounasr, A., Brunsing, R. L., Kao, C. S., Reejhsinghani, R., Annes, J. P., Chung, B. I., Mihm, F., Bhalla, V.  
2023
- **On-demand electrochemically controlled compound release from an ultrasonically powered implant.** *RSC advances*  
Wang, M. L., Chamberlayne, C. F., Xu, H., Mofidfar, M., Baltasvias, S., Annes, J. P., Zare, R. N., Arbabian, A.  
2022; 12 (36): 23337-23345

- **On-demand electrochemically controlled compound release from an ultrasonically powered implant** *RSC ADVANCES*  
Wang, M. L., Chamberlayne, C. F., Xu, H., Mofidfar, M., Baltasvias, S., Annes, J. P., Zare, R. N., Arbabian, A.  
2022; 12 (36): 23337-23345
- **beta-Cell Succinate Dehydrogenase Deficiency Triggers Metabolic Dysfunction and Insulinopenic Diabetes.** *Diabetes*  
Lee, S., Xu, H., Van Vleck, A., Mawla, A. M., Li, A. M., Ye, J., Huising, M. O., Annes, J. P.  
2022
- **SDHB knockout and succinate accumulation are insufficient for tumorigenesis but dual SDHB/NF1 loss yields SDHx-like pheochromocytomas.** *Cell reports*  
Armstrong, N., Storey, C. M., Noll, S. E., Margulis, K., Soe, M. H., Xu, H., Yeh, B., Fishbein, L., Kebebew, E., Howitt, B. E., Zare, R. N., Sage, J., Annes, et al  
2022; 38 (9): 110453
- **Novel Pathogenic de novo INS p.T97P Variant Presenting with Severe Neonatal DKA.** *Endocrinology*  
Lal, R. A., Moeller, H. P., Thomson, E. A., Horton, T. M., Lee, S., Freeman, R., Prahalad, P., Poon, A. S., Annes, J. P.  
2021
- **Protocol for determining zinc-dependent beta cell-selective small-molecule delivery in mouse pancreas.** *STAR protocols*  
Horton, T. M., Kraemer, B. R., Annes, J. P.  
2021; 2 (1): 100263
- **Metastatic Paraganglioma of the Spine With SDHB Mutation: Case Report and Review of the Literature** *INTERNATIONAL JOURNAL OF SPINE SURGERY*  
Jabarkheel, R., Pendharkar, A., Lavezo, J. L., Annes, J., Desai, K., Vogel, H., Desai, A. M.  
2021; 14: S37–S45
- **Metastatic Paraganglioma of the Spine With SDHB Mutation: Case Report and Review of the Literature.** *International journal of spine surgery*  
Jabarkheel, R., Pendharkar, A. V., Lavezo, J. L., Annes, J., Desai, K., Vogel, H., Desai, A. M.  
2021; 14 (s4): S37-S45
- **A Wireless Implantable Potentiostat for Programmable Electrochemical Drug Delivery** *IEEE Biomedical Circuits and Systems (BIOCAS)*  
Wang, M. L., Yeon, P., Chamberlayne, C. F., Mofidfar, M., Xu, H., Annes, J. P., Zare, R. N., Arbabian, A.  
2021
- **Intracardiac paragangliomas: surgical approach and perioperative management.** *General thoracic and cardiovascular surgery*  
Guenthart, B. A., Trope, W., Keeyapaj, W., Weiel, J. J., Edmonson, A., MacArthur, J. W., Annes, J. P., Woo, Y. J., Lui, N. S.  
2020
- **Probability of positive genetic testing in patients diagnosed with pheochromocytoma and paraganglioma: Criteria beyond a family history.** *Surgery*  
Alobuia, W. M., Ammar, S., Tyagi, M., Ghosh, C., Gunda, V., Annes, J. P., Kebebew, E.  
2020
- **Genetic testing in endocrine surgery: Opportunities for precision surgery.** *Surgery*  
Alobuia, W., Annes, J., Kebebew, E.  
2020
- **PAM staining intensity of primary neuroendocrine neoplasms is a potential prognostic biomarker.** *Scientific reports*  
Horton, T. M., Sundaram, V. n., Lee, C. H., Hornbacker, K. n., Van Vleck, A. n., Benjamin, K. N., Zemek, A. n., Longacre, T. A., Kunz, P. L., Annes, J. P.  
2020; 10 (1): 10943
- **Generation of highly potent DYRK1A-dependent inducers of human beta-Cell replication via Multi-Dimensional compound optimization.** *Bioorganic & medicinal chemistry*  
Allegretti, P. A., Horton, T. M., Abdolazimi, Y., Moeller, H. P., Yeh, B., Caffet, M., Michel, G., Smith, M., Annes, J. P.  
2019: 115193
- **On-demand drug release from polypyrrole nanoparticulate films**  
Chamberlayne, C., Baltasvias, S., Xu, H., Arbabian, A., Annes, J., Zare, R.

AMER CHEMICAL SOC.2019

- **Zinc-Chelating Small Molecules Preferentially Accumulate and Function within Pancreatic beta Cells** *CELL CHEMICAL BIOLOGY*  
Horton, T. M., Allegretti, P. A., Lee, S., Moeller, H. P., Smith, M., Annes, J. P.  
2019; 26 (2): 213-+
- **CC-401 Promotes beta-Cell Replication via Pleiotropic Consequences of DYRK1A/B Inhibition** *ENDOCRINOLOGY*  
Abdolazimi, Y., Zhao, Z., Lee, S., Xu, H., Allegretti, P., Horton, T. M., Yeh, B., Moeller, H. P., Nichols, R. J., McCutcheon, D., Shalizi, A., Smith, M., Armstrong, et al  
2018; 159 (9): 3143-57
- **CC-401 Promotes  $\beta$ -Cell Replication via Pleiotropic Consequences of DYRK1A/B Inhibition.** *Endocrinology*  
Abdolazimi, Y. n., Lee, S. n., Xu, H. n., Allegretti, P. n., Horton, T. M., Yeh, B. n., Moeller, H. P., Nichols, R. J., McCutcheon, D. n., Shalizi, A. n., Smith, M. n., Armstrong, N. A., Annes, et al  
2018
- **Zinc-Chelating Small Molecules Preferentially Accumulate and Function within Pancreatic  $\beta$  Cells.** *Cell chemical biology*  
Horton, T. M., Allegretti, P. A., Lee, S. n., Moeller, H. P., Smith, M. n., Annes, J. P.  
2018
- **Genetic Disruption of Adenosine Kinase in Mouse Pancreatic  $\beta$ -Cells Protects Against High Fat Diet-Induced Glucose Intolerance.** *Diabetes*  
Navarro, G., Abdolazami, Y., Zhao, Z., Xu, H., Lee, S., Armstrong, N. A., Annes, J. P.  
2017
- **Electrically controlled release of insulin using polypyrrole nanoparticles** *NANOSCALE*  
Hosseini-Nassab, N., Samanta, D., Abdolazimi, Y., Annes, J. P., Zare, R. N.  
2017; 9 (1): 143-149
- **Hyaluronan content governs tissue stiffness in pancreatic islet inflammation.** *The Journal of biological chemistry*  
Nagy, N. n., de la Zerda, A. n., Kaber, G. n., Johnson, P. Y., Hu, K. H., Kratochvil, M. J., Yadava, K. n., Zhao, W. n., Cui, Y. n., Navarro, G. n., Annes, J. P., Wight, T. N., Heilshorn, et al  
2017
- **A High-content In Vitro Pancreatic Islet  $\beta$ -cell Replication Discovery Platform.** *Journal of visualized experiments : JoVE*  
Zhao, Z., Abdolazimi, Y., Armstrong, N. A., Annes, J. P.  
2016
- **Repurposing cAMP-Modulating Medications to Promote beta-Cell Replication** *MOLECULAR ENDOCRINOLOGY*  
Zhao, Z., Low, Y. S., Armstrong, N. A., Ryu, J. H., Sun, S. A., Arvanites, A. C., Hollister-Lock, J., Shah, N. H., Weir, G. C., Annes, J. P.  
2014; 28 (10): 1682-1697
- **Adult tissue sources for new beta cells** *TRANSLATIONAL RESEARCH*  
Nichols, R. J., New, C., Annes, J. P.  
2014; 163 (4): 418-431
- **A liver Hif-2a-Irs2 pathway sensitizes hepatic insulin signaling and is modulated by Vegf inhibition.** *Nature medicine*  
Wei, K., Pieciewicz, S. M., McGinnis, L. M., Taniguchi, C. M., Wiegand, S. J., Anderson, K., Chan, C. W., Mulligan, K. X., Kuo, D., Yuan, J., Vallon, M., Morton, L. C., Lefai, et al  
2013; 19 (10): 1331-1337
- **A liver Hif-2 alpha-Irs2 pathway sensitizes hepatic insulin signaling and is modulated by Vegf inhibition** *NATURE MEDICINE*  
Wei, K., Pieciewicz, S. M., McGinnis, L. M., Taniguchi, C. M., Wiegand, S. J., Anderson, K., Chan, C. W., Mulligan, K. X., Kuo, D., Yuan, J., Vallon, M., Morton, L. C., Lefai, et al  
2013; 19 (10): 1331-?
- **The influence of sodium- and calcium-regulatory hormone interventions on adipocytokines in obesity and diabetes.** *Metabolism*  
Vaidya, A., Underwood, P. C., Annes, J. P., Sun, B., Williams, G. H., Forman, J. P., Williams, J. S.  
2013; 62 (4): 539-547
- **In Vivo Screening for Secreted Proteins That Modulate Glucose Handling Identifies Interleukin-6 Family Members as Potent Hypoglycemic Agents** *PLOS ONE*

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- Chen, C. A., Carolan, P. C., Annes, J. P.  
2012; 7 (9)
- **Genetics of adrenocortical disease: an update** *CURRENT OPINION IN ENDOCRINOLOGY DIABETES AND OBESITY*  
Bar-Lev, A., Annes, J. P.  
2012; 19 (3): 159-167
  - **Adenosine kinase inhibition selectively promotes rodent and porcine islet beta-cell replication** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Annes, J. P., Ryu, J. H., Lam, K., Carolan, P. J., Utz, K., Hollister-Lock, J., Arvanites, A. C., Rubin, L. L., Weir, G., Melton, D. A.  
2012; 109 (10): 3915-3920
  - **Erdheim-Chester disease presenting with cutaneous involvement: a case report and literature review** *JOURNAL OF CUTANEOUS PATHOLOGY*  
Volpicelli, E. R., Doyle, L., Annes, J. P., Murray, M. F., Jacobsen, E., Murphy, G. F., Saavedra, A. P.  
2011; 38 (3): 280-285
  - **Risks of Presymptomatic Direct-to-Consumer Genetic Testing.** *NEW ENGLAND JOURNAL OF MEDICINE*  
Annes, J. P., Giovanni, M. A., Murray, M. F.  
2010; 363 (12): 1100-1101
  - **Integrin alpha(v)beta(6)-mediated activation of latent TGF-beta requires the latent TGF-beta binding protein-1** *JOURNAL OF CELL BIOLOGY*  
Annes, J. P., Chen, Y., Munger, J. S., Rifkin, D. B.  
2004; 165 (5): 723-734
  - **A genetic screen to identify latent transforming growth factor beta activators** *ANALYTICAL BIOCHEMISTRY*  
Annes, J., Vassallo, M., Munger, J. S., Rifkin, D. B.  
2004; 327 (1): 45-54
  - **Annexin II-mediated plasmin generation activates TGF-beta 3 during epithelial-mesenchymal transformation in the developing avian heart** *DEVELOPMENTAL BIOLOGY*  
Krishnan, S., Deora, A. B., Annes, J. P., Osoria, J., RIFKIN, D. B., Hajar, K. A.  
2004; 265 (1): 140-154
  - **Making sense of latent TGF beta activation** *JOURNAL OF CELL SCIENCE*  
Annes, J. P., Munger, J. S., RIFKIN, D. B.  
2003; 116 (2): 217-224
  - **Latent TGF-beta binding protein-3 (LTBP-3) requires binding to TGF-beta for secretion** *FEBS LETTERS*  
Chen, Y., Dabovic, B., Annes, J. P., Rifkin, D. B.  
2002; 517 (1-3): 277-280
  - **The integrin alpha(V)beta(6) binds and activates latent TGF beta 3** *FEBS LETTERS*  
Annes, J. P., RIFKIN, D. B., Munger, J. S.  
2002; 511 (1-3): 65-68
  - **The latent transforming growth factor-beta-binding protein-1 promotes in vitro differentiation of embryonic stem cells into endothelium** *MOLECULAR BIOLOGY OF THE CELL*  
Gualandris, A., Annes, J. P., Arese, M., Noguera, I., Jurukovski, V., Rifkin, D. B.  
2000; 11 (12): 4295-4308
  - **PKC-theta is required for TCR-induced NF-kappa B activation in mature but not immature T lymphocytes** *NATURE*  
Sun, Z. M., Arendt, C. W., Ellmeier, W., Schaeffer, E. M., Sunshine, M. J., Gandhi, L., Annes, J., Petrzilka, D., Kupfer, A., Schwartzberg, P. L., Littman, D. R.  
2000; 404 (6776): 402-407