



## Shirit Einav

Associate Professor of Medicine (Infectious Diseases) and of Microbiology and Immunology

Medicine - Infectious Diseases

### CLINICAL OFFICES

- **Infectious Disease**

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### Bio

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### BIO

Shirit Einav is an infectious disease doctor. Her special interest is diagnosis and treatment of emerging viral infections.

### CLINICAL FOCUS

- Infectious Disease

### ACADEMIC APPOINTMENTS

- Associate Professor, Medicine - Infectious Diseases
- Associate Professor, Microbiology & Immunology
- Member, Bio-X
- Member, Maternal & Child Health Research Institute (MCHRI)
- Member, Wu Tsai Neurosciences Institute

### ADMINISTRATIVE APPOINTMENTS

- Rotating internship (part of the M.D. requirements in Israel), Suraski Medical Center, Tel-Aviv, Israel, (1997-1998)
- Research Studentship, Supervisor: Dr. Michael C. Carroll., Brigham and Women's Hospital and the Center for Blood Research, Harvard Medical School, Boston, MA, (1999-1999)
- Medical Internship and Residency, Internal Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, (1999-2002)
- Postdoctoral Fellowship. Supervisor: Dr. Jeffrey S. Glenn, Division of Gastroenterology and Hepatology, Stanford University School of Medicine, (2003-2004)
- Infectious Diseases Fellowship, Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, (2004-2008)
- Instructor of Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, (2009-2011)
- Assistant Professor (UTL), Department of Medicine, Department of Microbiology and Immunology, (2011- present)

### HONORS AND AWARDS

- B.A. graduation magna cum laude, Sackler School of Medicine, Tel-Aviv University (1994)

- Dean's Honor List (in four consecutive years), Sackler School of Medicine, Tel-Aviv University (1994-1997)
- M.D. graduation magna cum laude, Sackler School of Medicine, Tel-Aviv University (1997)
- Outstanding Thesis Award, Sackler School of Medicine, Tel-Aviv University (1999)
- Excellence in Teaching Housestaff Award, Harvard Medical School, Boston, MA (2002)
- Dean's Fellowship Award, Stanford University School of Medicine, Stanford, CA (2004)
- Fellow Travel Award, International Symposium on Hepatitis C Virus & Related Viruses (2004)
- American Liver Foundation Postdoctoral Fellowship Award, American Liver Foundation (ALF) (2006)
- ITI Young Investigator Innovation Award, Stanford Institute for Immunity, Transplantation, and Infection (ITI) (2008)
- Mentored Clinical Scientist Development Award (KO8), NIH/NIAID (2008 - 2013)
- DDC Pilot/Feasibility Award, Stanford Digestive Disease Center (DDC) (2009)
- IDSA 2009 Program Committee Choice Award, Infectious Diseases Society of America (IDSA) (2009)
- IDSA 2012 IDWeek Investigator Award, Infectious Diseases Society of America (IDSA) (2012)
- Stanford Bio-X Interdisciplinary Initiative Program Award, Stanford, Bio-X (2012)
- Clinical Scientist Development Award, Doris Duke Charitable Foundation (2013)
- Research Scholar Grant, American Cancer Society (2014)
- McCormick Faculty Award, Stanford University School of Medicine, Office of Diversity and Leadership (2015)
- Interdisciplinary Initiative Program Award, Stanford Bio-X (2016)
- Investigator-Initiated Research Award, Department of Defense (2016)
- Catalyst Award, Dr. Ralph & Marian Falk Medical Research Trust (2018)

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

- Member, Stanford Biosafety committee (2016 - present)
- Faculty Fellow, Center for Innovation in Global Health (2016 - present)
- Member, Bio-X Leadership Council (2016 - present)

## **PROFESSIONAL EDUCATION**

- Medical Education: Sackler School of Medicine (1998) Israel
- Fellowship: Stanford University Pediatric Infectious Disease Fellowship (2009) CA
- Residency: Beth Israel Deaconess Med Center/Harvard (2002) MA
- Board Certification: Infectious Disease, American Board of Internal Medicine (2006)
- Internship: Beth Israel Deaconess Med Center/Harvard (2000) MA
- BA, Sackler School of Medicine, Israel , Medical sciences (1994)
- MD, Sackler School of Medicine, Israel , Medicine (1999)

## **LINKS**

- Einav Lab Website: <http://med.stanford.edu/einavlab>
- In the news: <http://www.the-scientist.com/?articles.view/articleNo/33759/title/Macro--Mini--Micro/>
- In the news: <http://news.stanford.edu/news/2013/september/einav-quake-antiviral-092613.html>
- In the news: <https://med.stanford.edu/news/all-news/2017/02/drug-combination-defeats-dengue-ebola-in-mice-study-finds.html>
- In the news: <http://www.fiercebiotech.com/research/cancer-drugs-tarceva-and-sutent-hold-ebola-and-dengue-at-bay-mice>

## Research & Scholarship

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### CURRENT RESEARCH AND SCHOLARLY INTERESTS

The goals of my lab are to better understand virus-host protein interactions, identify host factors conservatively required by multiple viruses, and develop broad-spectrum host-centered antiviral approaches with a high genetic barrier for resistance. We combine novel proteomic approaches, including microfluidics platforms, with molecular virology, biochemical, and genomic approaches to achieve these goals. We focus on emerging viruses from the Flaviviridae family (hepatitis C, dengue, Zika), as well as unrelated viruses, such as Ebola.

Ongoing projects:

1. Mechanisms by which emerging viruses hijack intracellular membrane trafficking pathways for mediating viral assembly, release, and direct cell-to-cell spread. We have identified several sorting signals within Flaviviridae proteins that are involved in mediating key steps in the viral cycle. We are currently mapping the interaction networks of these signals with human proteins, and investigating the functional relevance, regulatory mechanisms, and inhibition of these interactions. Additional projects involve interactions with cytoskeleton dynamics proteins, ESCRT machinery and more.
2. Mechanisms of HCV-related cancer. Chronic HCV infection is a major cause of hepatocellular carcinoma and is also associated with non-Hodgkin lymphoma. We study virus-host interactions involved in facilitating viral persistence (a precursor to HCV-related oncogenesis).
3. Furthering novel high-throughput proteomic technologies for screening and mapping virus-host interactomes and for screening small molecule libraries for inhibitors of protein-protein interactions.
4. Development of selective kinase inhibitors to combat emerging viral infections.
5. Monitoring immune responses to dengue virus infection in a new cohort of patients from Colombia.

## Teaching

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### COURSES

#### 2017-18

- Discovery and Innovation in Emerging Viral Infections: BIOS 253 (Win)

#### 2016-17

- Discovery and Innovation in Emerging Viral Infections: BIOS 253 (Win)

### STANFORD ADVISEES

#### Med Scholar Project Advisor

Stanford Schor, Praveen Tummalapalli

#### Postdoctoral Faculty Sponsor

Sathish Kumar, Sirls Saul, Zhiyuan Yao

#### Doctoral Dissertation Advisor (AC)

Makeda Robinson, Stanford Schor

#### Postdoctoral Research Mentor

Sathish Kumar, Sirls Saul, Zhiyuan Yao

### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Microbiology and Immunology (Phd Program)

## Publications

### PUBLICATIONS

- **A 20-Gene Set Predictive of Progression to Severe Dengue.** *Cell reports*  
Robinson, M., Sweeney, T. E., Barouch-Bentov, R., Sahoo, M. K., Kalesinskas, L., Vallania, F., Sanz, A. M., Ortiz-Lasso, E., Albornoz, L. L., Rosso, F., Montoya, J. G., Pinsky, B. A., Khatri, et al  
2019; 26 (5): 1104
- **Screening of Interactions with the ESCRT Machinery by a *Gaussia princeps* Split Luciferase-Based Complementation Assay.** *Methods in molecular biology (Clifton, N.J.)*  
Barouch-Bentov, R., Jacob, Y., Einav, S.  
2019; 1998: 291–304
- **MARCH8 Ubiquitinates the Hepatitis C Virus Nonstructural 2 Protein and Mediates Viral Envelopment.** *Cell reports*  
Kumar, S., Barouch-Bentov, R., Xiao, F., Schor, S., Pu, S., Biquand, E., Lu, A., Lindenbach, B. D., Jacob, Y., Demeret, C., Einav, S.  
2019; 26 (7): 1800–1814.e5
- **Synthesis and Structure-Activity Relationships of 3,5-Disubstituted-pyrrolo[2,3- b]pyridines as Inhibitors of Adaptor-Associated Kinase 1 with Antiviral Activity.** *Journal of medicinal chemistry*  
Verdonck, S., Pu, S. Y., Sorrell, F. J., Elkins, J. M., Froeyen, M., Gao, L. J., Prugar, L. I., Dorosky, D. E., Brannan, J. M., Barouch-Bentov, R., Knapp, S., Dye, J. M., Herdewijn, et al  
2019
- **Virus-inclusive single-cell RNA sequencing reveals the molecular signature of progression to severe dengue.** *Proceedings of the National Academy of Sciences of the United States of America*  
Zanini, F., Robinson, M. L., Croote, D., Sahoo, M. K., Sanz, A. M., Ortiz-Lasso, E., Albornoz, L. L., Rosso, F., Montoya, J. G., Goo, L., Pinsky, B. A., Quake, S. R., Einav, et al  
2018
- **Cyclin G-associated kinase (GAK) affinity and antiviral activity studies of a series of 3-C-substituted isothiazolo[4,3-b]pyridines.** *European journal of medicinal chemistry*  
Wouters, R., Pu, S., Froeyen, M., Lescrinier, E., Einav, S., Herdewijn, P., De Jonghe, S.  
2018; 163: 256–65
- **Viral journeys on the intracellular highways.** *Cellular and molecular life sciences : CMLS*  
Robinson, M., Schor, S., Barouch-Bentov, R., Einav, S.  
2018
- **Single-cell transcriptional dynamics of flavivirus infection.** *eLife*  
Zanini, F., Pu, S. Y., Bekerman, E., Einav, S., Quake, S. R.  
2018; 7
- **Repurposing of Kinase Inhibitors as Broad-Spectrum Antiviral Drugs.** *DNA and cell biology*  
Schor, S., Einav, S.  
2018; 37 (2): 63–69
- **Hepatitis C Virus Proteins Interact with the Endosomal Sorting Complex Required for Transport (ESCRT) Machinery via Ubiquitination To Facilitate Viral Envelopment (vol 47, e01456-16, 2016)** *MBIO*  
Barouch-Bentov, R., Neveu, G., Xiao, F., Beer, M., Bekerman, E., Schor, S., Campbell, J., Boonyaratankornkit, J., Lindenbach, B., Lu, A., Jacob, Y., Einav, S.  
2018; 9 (1)
- **Feasibility and biological rationale of repurposing sunitinib and erlotinib for dengue treatment.** *Antiviral research*  
Pu, S. Y., Xiao, F., Schor, S., Bekerman, E., Zanini, F., Barouch-Bentov, R., Nagamine, C. M., Einav, S.  
2018; 155: 67–75
- **Optimization of Isothiazolo[4,3- b]pyridine-Based Inhibitors of Cyclin G Associated Kinase (GAK) with Broad-Spectrum Antiviral Activity.** *Journal of medicinal chemistry*  
Pu, S. Y., Wouters, R., Schor, S., Rozenski, J., Barouch-Bentov, R., Prugar, L. I., O'Brien, C. M., Brannan, J. M., Dye, J. M., Herdewijn, P., De Jonghe, S., Einav, S.

2018

- **Combating Intracellular Pathogens with Repurposed Host-Targeted Drugs.** *ACS infectious diseases*  
Schor, S., Einav, S.  
2018; 4 (2): 88–92
- **Turning Up Your Nose for a Flaviviral Encephalitis Cure.** *Cell host & microbe*  
Barouch-Bentov, R., Einav, S.  
2018; 23 (4): 427–29
- **Interactions between the Hepatitis C Virus Nonstructural 2 Protein and Host Adaptor Proteins 1 and 4 Orchestrate Virus Release.** *mBio*  
Xiao, F., Wang, S., Barouch-Bentov, R., Neveu, G., Pu, S., Beer, M., Schor, S., Kumar, S., Nicolaescu, V., Lindenbach, B. D., Randall, G., Einav, S.  
2018; 9 (2)
- **Anticancer kinase inhibitors impair intracellular viral trafficking and exert broad-spectrum antiviral effects** *JOURNAL OF CLINICAL INVESTIGATION*  
Bekerman, E., Neveu, G., Shulla, A., Brannan, J., Pu, S., Wang, S., Xiao, F., Barouch-Bentov, R., Bakken, R. R., Mateo, R., Govero, J., Nagamine, C. M., Diamond, et al  
2017; 127 (4): 1338-1352
- **Repurposing of Kinase Inhibitors as Broad-Spectrum Antiviral Drugs.** *DNA Cell Biol.*  
Schor, S., Einav, S.  
2017: 63–69
- **Hepatitis C Virus Proteins Interact with the Endosomal Sorting Complex Required for Transport (ESCRT) Machinery via Ubiquitination To Facilitate Viral Envelopment.** *mBio*  
Barouch-Bentov, R., Neveu, G., Xiao, F., Beer, M., Bekerman, E., Schor, S., Campbell, J., Boonyaratanakornkit, J., Lindenbach, B., Lu, A., Jacob, Y., Einav, S.  
2016; 7 (6)
- **Pathogen receptor discovery with a microfluidic human membrane protein array** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Glick, Y., Ben-Ari, Y., Drayman, N., Pellach, M., Neveu, G., Boonyaratanakornkit, J., Avrahami, D., Einav, S., Oppenheim, A., Gerber, D.  
2016; 113 (16): 4344-4349
- **Epidermal Growth Factor Receptor-Dependent Mutual Amplification between Netrin-1 and the Hepatitis C Virus** *PLOS BIOLOGY*  
Plissonnier, M., Lahlali, T., Michelet, M., Lebosse, F., Cottarel, J., Beer, M., Neveu, G., Durantel, D., Bartosch, B., Accardi, R., Clement, S., Paradisi, A., Devouassoux-Shisheboran, et al  
2016; 14 (3)
- **Response—Applying antibiotics lessons to antivirals.** *Science*  
Bekerman, E., Einav, S.  
2015; 348 (6242): 1437-?
- **Selective Inhibitors of Cyclin G Associated Kinase (GAK) as Anti-Hepatitis C Agents** *JOURNAL OF MEDICINAL CHEMISTRY*  
Kovackova, S., Chang, L., Bekerman, E., Neveu, G., Barouch-Bentov, R., Chaikuad, A., Heroven, C., Sala, M., De Jonghe, S., Knapp, S., Einav, S., Herdewijn, P.  
2015; 58 (8): 3393-3410
- **Infectious disease. Combating emerging viral threats.** *Science*  
Bekerman, E., Einav, S.  
2015; 348 (6232): 282-283
- **AP-2-Associated Protein Kinase 1 and Cyclin G-Associated Kinase Regulate Hepatitis C Virus Entry and Are Potential Drug Targets** *JOURNAL OF VIROLOGY*  
Neveu, G., Ziv-Av, A., Barouch-Bentov, R., Bekerman, E., Mulholland, J., Einav, S.  
2015; 89 (8): 4387-4404
- **Isothiazolo[4,3-b]pyridines as inhibitors of cyclin G associated kinase: synthesis, structure-activity relationship studies and antiviral activity** *MEDCHEMCOMM*  
Li, J., Kovackova, S., Pu, S., Rozenski, J., De Jonghe, S., Einav, S., Herdewijn, P.  
2015; 6 (9): 1666-1672
- **B-cell receptors expressed by lymphomas of hepatitis C virus (HCV)-infected patients rarely react with the viral proteins.** *Blood*

Ng, P. P., Kuo, C., Wang, S., Einav, S., Arcaini, L., Paulli, M., Portlock, C. S., Marcotrigiano, J., Tarr, A., Ball, J., Levy, R., Levy, S.  
2014; 123 (10): 1512-1515

- **Identification and Targeting of an Interaction between a Tyrosine Motif within Hepatitis C Virus Core Protein and AP2M1 Essential for Viral Assembly** *PLOS PATHOGENS*  
Neveu, G., Barouch-Bentov, R., Ziv-Av, A., Gerber, D., Jacob, Y., Einav, S.  
2012; 8 (8)
- **The hepatitis C virus (HCV) NS4B RNA binding inhibitor clemizole is highly synergistic with HCV protease inhibitors.** *journal of infectious diseases*  
Einav, S., Sobol, H. D., Gehrig, E., Glenn, J. S.  
2010; 202 (1): 65-74
- **The Hepatitis C Virus (HCV) NS4B RNA Binding Inhibitor Clemizole Is Highly Synergistic with HCV Protease Inhibitors** *Annual Meeting of the Infectious-Diseases-Society-of-America*  
Einav, S., Dvory-Sobol, H., Gehrig, E., Glenn, J. S.  
OXFORD UNIV PRESS INC.2010: 65-74
- **A small molecule inhibits HCV replication and alters NS4B's subcellular distribution** *ANTIVIRAL RESEARCH*  
Bryson, P. D., Cho, N., Einav, S., Lee, C., Tai, V., Bechtel, J., Sivaraja, M., Roberts, C., Schmitz, U., Glenn, J. S.  
2010; 87 (1): 1-8
- **Six RNA Viruses and Forty-One Hosts: Viral Small RNAs and Modulation of Small RNA Repertoires in Vertebrate and Invertebrate Systems** *PLOS PATHOGENS*  
Parameswaran, P., Sklan, E., Wilkins, C., Burgon, T., Samuel, M. A., Lu, R., Ansel, K. M., Heissmeyer, V., Einav, S., Jackson, W., Doukas, T., Paranjape, S., Polacek, et al  
2010; 6 (2)
- **Discovery of a hepatitis C target and its pharmacological inhibitors by microfluidic affinity analysis** *NATURE BIOTECHNOLOGY*  
Einav, S., Gerber, D., Bryson, P. D., Sklan, E. H., Elazar, M., Maerkl, S. J., Glenn, J. S., Quake, S. R.  
2008; 26 (9): 1019-1027
- **The nucleotide binding motif of hepatitis C virus NS4B can mediate cellular transformation and tumor formation without ha-ras co-transfection** *HEPATOLOGY*  
Einav, S., Sklan, E. H., Moon, H. M., Gehrig, E., Liu, P., Hao, Y., Lowe, A. W., Glenn, J. S.  
2008; 47 (3): 827-835
- **TBC1D20 is a Rab1 GTPase-activating protein that mediates hepatitis C virus replication** *JOURNAL OF BIOLOGICAL CHEMISTRY*  
Sklan, E. H., Serrano, R. L., Einav, S., Pfeffer, S. R., Lambright, D. G., Glenn, J. S.  
2007; 282 (50): 36354-36361
- **Mechanisms of resistance to antiviral agents.** *In Manual of clinical microbiology, 9th edition, Murray PR ed, Baron EJ ed, Jorgensen JH ed, Pfaller MA ed, Tenover FC ed, and Tenover RH ed. American Society of Microbiology.*  
Shafer RW, Einav S, Chou S  
2007: 1689-04
- **A nucleotide binding motif in hepatitis C virus (HCV) NS4B mediates HCV RNA replication** *JOURNAL OF VIROLOGY*  
Einav, S., Elazar, M., Danieli, T., Glenn, J. S.  
2004; 78 (20): 11288-11295
- **Prenylation inhibitors: a novel class of antiviral agents** *JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY*  
Einav, S., Glenn, J. S.  
2003; 52 (6): 883-886
- **Immunopathogenesis of hepatitis C virus in the immunosuppressed host.** *Transplant infectious disease*  
Einav, S., Koziel, M. J.  
2002; 4 (2): 85-92
- **Complement C4 is protective for lupus disease independent of C3** *JOURNAL OF IMMUNOLOGY*  
Einav, S., Pozdnyakova, O. O., Ma, M. H., Carroll, M. C.  
2002; 168 (3): 1036-1041