



## Karla Kirkegaard

Violetta L. Horton Professor and Professor of Microbiology and Immunology  
Genetics

### Bio

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#### ACADEMIC APPOINTMENTS

- Professor, Genetics
- Professor, Microbiology & Immunology
- Member, Bio-X

#### ADMINISTRATIVE APPOINTMENTS

- Chair, Stanford University School of Medicine - Microbiology & Immunology, (2006-2010)

#### LINKS

- My Lab's Web Site: <https://web.stanford.edu/group/kirkegaard>

### Research & Scholarship

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#### CURRENT RESEARCH AND SCHOLARLY INTERESTS

For many subcellular viruses and parasites, RNA, not DNA, is the carrier of genetic information. This has several interesting consequences for the genetics and biology of the virus. Poliovirus serves as a model to increase our understanding of positive-strand RNA viruses for which no vaccine is available and which remain a significant health hazard: examples include other picornaviruses, such as rhinoviruses, coxsackieviruses and the deadly enterovirus 71 as well as more distantly related positive-strand RNA viruses such as hepatitis C and Dengue fever.

Questions currently under scrutiny are posed below, and discussed in greater detail in our web site.

1. How does the biochemistry of RNA-dependent RNA polymerases affect the biology of RNA viruses?
2. How are the membranous structures on which viral RNA replication complexes assemble form, and from what intracellular organelles do they derive?
3. Why are the genetic properties of many RNA genomes different from DNA genomes? How does the error-prone nature of RNA-dependent RNA replication and the membrane association of the RNA replication complexes affect these genetic properties?

4. How does the inhibition of the protein secretory apparatus by the 3A and 2B proteins of picornaviruses such as poliovirus affect their pathogenesis? What would happen to the secretion of interferons, and to the presentation of antigens in the context of MHC class I molecules, if the host secretory pathway were not inhibited during infection by polioviruses, rhinoviruses and coxsackieviruses?

## Teaching

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### COURSES

#### 2021-22

- Genetics of Viral Emergence and Emerging Viruses: GENE 242 (Win)

#### 2019-20

- Advanced Cell Biology: BIO 214, BIOC 224, MCP 221 (Win)

### STANFORD ADVISEES

#### Doctoral Dissertation Reader (AC)

David Chmielewski, Alyssa Lyn Fortier, Christine Peters

#### Doctoral Dissertation Advisor (AC)

Jennifer Doherty, Brian Ho, Jasmine Moshiri, Makena Pule, Dorothy Tovar

### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biomedical Informatics (Phd Program)
- Genetics (Phd Program)
- Immunology (Phd Program)
- Microbiology and Immunology (Phd Program)

## Publications

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### PUBLICATIONS

- **The Hepatitis C Virus-Induced Membranous Web and Associated Nuclear Transport Machinery Limit Access of Pattern Recognition Receptors to Viral Replication Sites.** *PLoS pathogens*  
Neufeldt, C. J., Joyce, M. A., Van Buuren, N., Levin, A., Kirkegaard, K., Gale, M., Tyrrell, D. L., Wozniak, R. W.  
2016; 12 (2)
- **Escape of non-enveloped virus from intact cells** *VIROLOGY*  
Bird, S. W., Kirkegaard, K.  
2015; 479: 444-449
- **Escape of non-enveloped virus from intact cells.** *Virology*  
Bird, S. W., Kirkegaard, K.  
2015; 479-480: 444-449
- **Nonlytic spread of naked viruses.** *Autophagy*  
Bird, S. W., Kirkegaard, K.  
2015; 11 (2): 430-431
- **Dominant Drug Targets Suppress the Emergence of Antiviral Resistance** *ELIFE*  
Tanner, E. J., Liu, H., Oberste, M. S., Pallansch, M., Collett, M. S., Kirkegaard, K.  
2014; 3
- **Nonlytic viral spread enhanced by autophagy components** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*

- Bird, S. W., Maynard, N. D., Covert, M. W., Kirkegaard, K.  
2014; 111 (36): 13081-13086
- **The Ins and Outs of Viral Infection: Keystone Meeting Review** *VIRUSES-BASEL*  
Bird, S. W., Kirkegaard, K., Agbandje-McKenna, M., Freed, E. O.  
2014; 6 (9): 3652-3662
  - **Dominant drug targets suppress the emergence of antiviral resistance.** *eLife*  
Tanner, E. J., Liu, H., Oberste, M. S., Pallansch, M., Collett, M. S., Kirkegaard, K.  
2014; 3
  - **Double-membraned Liposomes Sculpted by Poliovirus 3AB Protein** *JOURNAL OF BIOLOGICAL CHEMISTRY*  
Wang, J., Ptacek, J. B., Kirkegaard, K., Bullitt, E.  
2013; 288 (38): 27287-27298
  - **The NeST Long ncRNA Controls Microbial Susceptibility and Epigenetic Activation of the Interferon-gamma Locus** *CELL*  
Gomez, J. A., Wapinski, O. L., Yang, Y. W., Bureau, J., Gopinath, S., Monack, D. M., Chang, H. Y., Brahic, M., Kirkegaard, K.  
2013; 152 (4): 743-754
  - **Inhibition of Cellular Autophagy Deranges Dengue Virion Maturation** *JOURNAL OF VIROLOGY*  
Mateo, R., Nagamine, C. M., Spagnolo, J., Mendez, E., Rahe, M., Gale, M., Yuan, J., Kirkegaard, K.  
2013; 87 (3): 1312-1321
  - **Neuron-to-neuron transmission of alpha-synuclein fibrils through axonal transport** *ANNALS OF NEUROLOGY*  
Freundt, E. C., Maynard, N., Clancy, E. K., Roy, S., Bousset, L., Sourigues, Y., Covert, M., Melki, R., Kirkegaard, K., Brahic, M.  
2012; 72 (4): 517-524
  - **Competing pathways control host resistance to virus via tRNA modification and programmed ribosomal frameshifting** *MOLECULAR SYSTEMS BIOLOGY*  
Maynard, N. D., Macklin, D. N., Kirkegaard, K., Covert, M. W.  
2012; 8
  - **Interstitial Contacts in an RNA-Dependent RNA Polymerase Lattice** *JOURNAL OF MOLECULAR BIOLOGY*  
Tellez, A. B., Wang, J., Tanner, E. J., Spagnolo, J. F., Kirkegaard, K., Bullitt, E.  
2011; 412 (4): 737-750
  - **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)
  - **Enzymatic and nonenzymatic functions of viral RNA-dependent RNA polymerases within oligomeric arrays** *RNA-A PUBLICATION OF THE RNA SOCIETY*  
Spagnolo, J. F., Rossignol, E., Bullitt, E., Kirkegaard, K.  
2010; 16 (2): 382-393
  - **Bypass Suppression of Small-Plaque Phenotypes by a Mutation in Poliovirus 2A That Enhances Apoptosis** *JOURNAL OF VIROLOGY*  
Burgon, T. B., Jenkins, J. A., Deitz, S. B., Spagnolo, J. F., Kirkegaard, K.  
2009; 83 (19): 10129-10139
  - **Role of Microtubules in Extracellular Release of Poliovirus** *JOURNAL OF VIROLOGY*  
Taylor, M. P., Burgon, T. B., Kirkegaard, K., Jackson, W. T.  
2009; 83 (13): 6599-6609
  - **Subversion of the Cellular Autophagy Pathway by Viruses** *AUTOPHAGY IN INFECTION AND IMMUNITY*  
Kirkegaard, K.  
2009; 335: 323-333
  - **Potential subversion of autophagosomal pathway by picornaviruses** *AUTOPHAGY*  
Taylor, M. P., Kirkegaard, K.  
2008; 4 (3): 286-289

- **Modification of cellular autophagy protein LC3 by poliovirus** *JOURNAL OF VIROLOGY*  
Taylor, M. P., Kirkegaard, K.  
2007; 81 (22): 12543-12553
- **Poliovirus infection blocks ERGIC-to-Golgi trafficking and induces microtubule-dependent disruption of the Golgi complex** *JOURNAL OF CELL SCIENCE*  
Beske, O., Reichelt, M., Taylor, M. P., Kirkegaard, K., Andino, R.  
2007; 120 (18): 3207-3218
- **Intramolecular and intermolecular uridylylation by poliovirus RNA-dependent RNA polymerase** *JOURNAL OF VIROLOGY*  
Richards, O. C., Spagnolo, J. F., Lyle, J. M., Vleck, S. E., Kuchta, R. D., Kirkegaard, K.  
2006; 80 (15): 7405-7415
- **Bottleneck-mediated quasispecies restriction during spread of an RNA virus from inoculation site to brain** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Pfeiffer, J. K., Kirkegaard, K.  
2006; 103 (14): 5520-5525
- **Nucleotide channel of RNA-dependent RNA polymerase used for intermolecular uridylylation of protein primer** *JOURNAL OF MOLECULAR BIOLOGY*  
Tellez, A. B., Crowder, S., Spagnolo, J. F., Thompson, A. A., Peersen, O. B., Brutlag, D. L., Kirkegaard, K.  
2006; 357 (2): 665-675
- **Increased fidelity reduces poliovirus fitness and virulence under selective pressure in mice** *PLOS PATHOGENS*  
Pfeiffer, J. K., Kirkegaard, K.  
2005; 1 (2): 102-110
- **Topology of double-membraned vesicles and the opportunity for non-lytic release of cytoplasm** *AUTOPHAGY*  
Kirkegaard, K., Jackson, W. T.  
2005; 1 (3): 182-184
- **Trans-dominant inhibition of RNA viral replication can slow growth of drug-resistant viruses** *NATURE GENETICS*  
Crowder, S., Kirkegaard, K.  
2005; 37 (7): 701-709
- **Inhibition of cellular protein secretion by picornaviral 3A proteins** *VIROLOGY*  
Choe, S. S., Dodd, D. A., Kirkegaard, K.  
2005; 337 (1): 18-29
- **Allosteric effects of ligands and mutations on poliovirus RNA-dependent RNA polymerase** *JOURNAL OF VIROLOGY*  
Boerner, J. E., Lyle, J. M., Daijogo, S., Semler, B. L., SCHULTZ, S. C., Kirkegaard, K., Richards, O. C.  
2005; 79 (12): 7803-7811
- **Subversion of cellular autophagosomal machinery by RNA viruses** *PLOS BIOLOGY*  
Jackson, W. T., Giddings, T. H., Taylor, M. P., Mulinyawe, S., RABINOVITCH, M., Kopito, R. R., Kirkegaard, K.  
2005; 3 (5): 861-871
- **Ribavirin resistance in hepatitis C virus replicon-containing cell lines conferred by changes in the cell line or mutations in the replicon RNA** *JOURNAL OF VIROLOGY*  
Pfeiffer, J. K., Kirkegaard, K.  
2005; 79 (4): 2346-2355
- **Intracellular topology and epitope shielding of poliovirus 3A protein** *JOURNAL OF VIROLOGY*  
Choe, S. S., Kirkegaard, K.  
2004; 78 (11): 5973-5982
- **Cellular autophagy: Surrender, avoidance and subversion by microorganisms** *NATURE REVIEWS MICROBIOLOGY*  
Kirkegaard, K., Taylor, M. P., Jackson, W. T.  
2004; 2 (4): 301-314
- **Nonstructural protein precursor NS4A/B from hepatitis C virus alters function and ultrastructure of host secretory apparatus** *JOURNAL OF VIROLOGY*

- Konan, K. V., Giddings, T. H., Ikeda, M., Li, K., Lemon, S. M., Kirkegaard, K.  
2003; 77 (14): 7843-7855
- **A single mutation in poliovirus RNA-dependent RNA polymerase confers resistance to mutagenic nucleotide analogs via increased fidelity** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Pfeiffer, J. K., Kirkegaard, K.  
2003; 100 (12): 7289-7294
  - **Visualization and functional analysis of RNA-dependent RNA polymerase lattices** *SCIENCE*  
Lyle, J. M., Bullitt, E., Bienz, K., Kirkegaard, K.  
2002; 296 (5576): 2218-2222
  - **Similar structural basis for membrane localization and protein priming by an RNA-dependent RNA polymerase** *JOURNAL OF BIOLOGICAL CHEMISTRY*  
Lyle, J. M., Clewell, A., Richmond, K., Richards, O. C., Hope, D. A., SCHULTZ, S. C., Kirkegaard, K.  
2002; 277 (18): 16324-16331
  - **Oligomerization and cooperative RNA synthesis activity of hepatitis C virus RNA-dependent RNA polymerase** *JOURNAL OF VIROLOGY*  
Wang, Q. M., Hockman, M. A., Staschke, K., Johnson, R. B., Case, K. A., Lu, J. R., Parsons, S., Zhang, F. M., Rathnachalam, R., Kirkegaard, K., Colacino, J. M.  
2002; 76 (8): 3865-3872
  - **Poliovirus 3A protein limits interleukin-6 (IL-6), IL-8, and beta interferon secretion during viral infection** *JOURNAL OF VIROLOGY*  
Dodd, D. A., Giddings, T. H., Kirkegaard, K.  
2001; 75 (17): 8158-8165
  - **Oligomeric structures of poliovirus polymerase are important for function** *EMBO JOURNAL*  
Hobson, S. D., Rosenblum, E. S., Richards, O. C., Richmond, K., Kirkegaard, K., SCHULTZ, S. C.  
2001; 20 (5): 1153-1163
  - **MHC I-dependent antigen presentation is inhibited by poliovirus protein 3A** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Deitz, S. B., Dodd, D. A., Cooper, S., Parham, P., Kirkegaard, K.  
2000; 97 (25): 13790-13795
  - **Remodeling the endoplasmic reticulum by poliovirus infection and by individual viral proteins: an autophagy-like origin for virus-induced vesicles** *JOURNAL OF VIROLOGY*  
Suhy, D. A., Giddings, T. H., Kirkegaard, K.  
2000; 74 (19): 8953-8965
  - **Functional coupling between replication and packaging of poliovirus replicon RNA** *JOURNAL OF VIROLOGY*  
Nugent, C. I., Johnson, K. L., Sarnow, P., Kirkegaard, K.  
1999; 73 (1): 427-435
  - **Complete protein linkage map of poliovirus P3 proteins: Interaction of polymerase 3D(pol) with VPg and with genetic variants of 3AB** *JOURNAL OF VIROLOGY*  
Xiang, W. K., Cuconati, A., Hope, D., Kirkegaard, K., Wimmer, E.  
1998; 72 (8): 6732-6741
  - **KH domain integrity is required for wild-type localization of Sam68** *EXPERIMENTAL CELL RESEARCH*  
McBride, A. E., Taylor, S. J., Shalloway, D., Kirkegaard, K.  
1998; 241 (1): 84-95
  - **Site size of cooperative single-stranded RNA binding by poliovirus RNA-dependent RNA polymerase** *JOURNAL OF BIOLOGICAL CHEMISTRY*  
Beckman, M. T., Kirkegaard, K.  
1998; 273 (12): 6724-6730
  - **Inhibition of endoplasmic reticulum-to-Golgi traffic by poliovirus protein 3A: Genetic and ultrastructural analysis** *JOURNAL OF VIROLOGY*  
Doedens, J. R., Giddings, T. H., Kirkegaard, K.  
1997; 71 (12): 9054-9064
  - **Poliovirus RNA recombination in cell-free extracts** *RNA-A PUBLICATION OF THE RNA SOCIETY*  
Tang, R. S., Barton, D. J., Flanagan, J. B., Kirkegaard, K.

1997; 3 (6): 624-633

- **Cellular origin and ultrastructure of membranes induced during poliovirus infection** *JOURNAL OF VIROLOGY*  
Schlegel, A., Giddings, T. H., Ladinsky, M. S., Kirkegaard, K.  
1996; 70 (10): 6576-6588
- **INHIBITION OF CELLULAR PROTEIN SECRETION BY POLIOVIRUS PROTEINS 2B AND 3A** *EMBO JOURNAL*  
Doedens, J. R., Kirkegaard, K.  
1995; 14 (5): 894-907
- **SECRETORY PATHWAY FUNCTION, BUT NOT CYTOSKELETAL INTEGRITY, IS REQUIRED IN POLIOVIRUS INFECTION** *3rd International Symposium on Positive-Strand RNA Viruses*  
DOEDENS, J., MAYNELL, L. A., KLYMKOWSKY, M. W., Kirkegaard, K.  
SPRINGER WIEN.1994: 159-172