

# **CHRISTOPHER S FRASER**

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## **EDUCATION**

Ph.D. (1999), Biochemistry, University of Sussex (Adviser, Simon Morley)  
B.Sc (First Class Honours) (1995), University of Sussex, England

## **ACADEMIC POSITIONS**

Professor (2020-present) University of California, Davis.  
Associate Professor (2015-2020) University of California, Davis.  
Assistant Professor (2008–2015) University of California, Davis.  
Postdoctoral researcher (2003–2008), Howard Hughes Medical Institute, University of California, Berkeley (Adviser, Jennifer Doudna)  
Postdoctoral researcher (1999–2002) University of California, Davis (Adviser, John Hershey)

## **FELLOWSHIPS AND AWARDS**

Wellcome Trust Prize Studentship 1995-1998

## **JOURNAL ACTIVITIES**

Editorial Board, Journal of Biological Chemistry (2013-2023)  
Editorial Board, Molecular and Cellular Biology (2014-2019)

## **GRANT REVIEW SERVICE**

Ad Hoc reviewer, BBSRC (2010)  
Ad Hoc reviewer, National Science Foundation (2010, 2014, 2019)  
Undergraduate research fellowship reviewer, American Heart Foundation (2013–2015)  
Ad Hoc reviewer, National Institutes of Health (MGA study section; June 2015, Feb 2016)

Ad Hoc reviewer, National Institutes of Health (GGG R15 study section; July 2016)

Permanent member of MGA study section, National Institutes of Health (July 2017–2021)

## **TEACHING EXPERIENCE**

### UC Davis

#### Undergraduate Course:

MCB 123 – Behavior and Analysis of Enzyme and Receptor Systems.

This is a 3 hour a week lecture-based course that typically enrolls ~130 students. The course runs every year for 10 weeks in the Spring Quarter.

#### Graduate Courses:

MCB 214 – Molecular Biology.

I co-teach this class with two other faculty (Wolf Heyer and Fred Chedin). I give 5 two-hour lectures in this course, which is usually taken by ~30 students. In my section, I discuss various topics in RNA biology that include the genetic code, translation (bacteria and eukaryotes), mRNA splicing, and RNAi. I teach this class every year.

BCB 251 – Molecular Mechanisms in Early Development.

I co-teach this class and give three 1.5 hour lectures on the regulation of translation in developmental systems. This class is usually taken by ~10 students. I teach this class every other year.

### Other teaching

I designed and taught a graduate class on the regulation of protein synthesis at São Paulo State University, Brazil (Sep 2013). This course lasted for five days and was attended by ~15 graduate students. The course comprised of seminars, journal club reviews and student presentations.

I designed and taught a graduate class on the regulation of protein synthesis at the Nara Institute of Science and Technology (NAIST), Japan (Dec 2013). This course lasted for two days and was attended by ~30 graduate students. The course comprised of three 2-hour seminars and a 1-hour seminar on my research.

## **CONFERENCES, SYMPOSIA, AND PLENARY LECTURES (Since 2008)**

2008: Invited speaker, Negotiating your first faculty position (Pathways Career Symposium; University of California, Davis).

2010: Invited speaker, RNA symposium. Ames Iowa.

2011: Invited speaker, Chico State University.

2012: Invited speaker, Virginia Commonwealth University.

2013: Invited speaker, Ribosomes Conference. Napa.

2013: Invited speaker, University of California, Berkeley.

2015: Invited speaker, National Institutes of Health.

2016: Invited speaker, Cliff Soll lecture, Hunter College.

2016: Session Chair, Translational Control Meeting, Cold Spring Harbor Laboratory.  
2016: Invited speaker, Columbia University.  
2017: Invited speaker, University of California, Riverside.  
2017: Invited speaker, Case Western Reserve University, Cleveland.  
2019: Invited speaker, Ohio State University, Columbus.  
2019: Invited speaker, Emory University, Atlanta.  
2019: Invited speaker, National Cancer Institute (NCI) Workshop: Dysregulation of Ribosome Biogenesis and Protein Synthesis in Cancer.

## **ACADEMIC SERVICES:**

### **Department.**

2010-2011	Member of MCB department work in progress seminar committee.
2012	Department representative for information technology committee.
2010-2015	Research and Space Committee; member.
2015	Member of MCB department faculty search committee.
2018	Member of MCB department faculty search committee.
2019-present	Vice Chair of MCB department for academic personnel.
2019-present	MCB department executive committee.

### **Graduate groups.**

2010-present	Graduate advisor (BMCDB graduate program)
2011-2015	Graduate student Admissions Committee (BMCDB, 2011-2012 as member and 2012-2015 as chair).
2012-2015	Member, Executive Committee (BMCDB; served again 2017-2020).
2017-2020	Member, Executive Committee for T32 Training Grant in Molecular Biology.

### **College and University.**

2012-2016	Joint seminars in Molecular Biology. Member from 2012-2013 and Chair from 2013-2016.
2014	Member of Events Manager search committee.
2014	College vivarium committee.
2015-2017	Faculty Executive Committee. Member from 2015-2016 and Chair from 2016-2017.
2016-present	College faculty research award committee.
2016-2017	Member of senate committee on undergraduate scholarships, honors and prizes (CUSHP).

## **PUBLICATIONS**

### **C. Peer-reviewed publications (in chronological order).**

1. Fraser, C. S., Pain, V. M., and Morley, S. J. The association of initiation factor 4F with poly(A)-binding protein is enhanced in serum-stimulated *Xenopus* kidney cells. **J. Biol. Chem.** 1999 Jan 1; 274(1):196-204.
2. Fraser, C. S., Pain, V. M., and Morley, S. J. Cellular stress in *Xenopus* kidney cells

- enhances the phosphorylation of eukaryotic translation initiation factor (eIF)4E and the association of eIF4F with poly(A)-binding protein. **Biochem. J.** 1999 Sep 15; 342 Pt 3:519-26.
- Daughenbaugh, K. F., Fraser, C. S., Hershey, J. W. B., and Hardy, M. E. The genome-linked protein VPg of the Norwalk virus binds eIF3, suggesting its role in translation initiation complex recruitment. **EMBO J.** 2003 Jun 2;22(11):2852-9.
  - Mayeur, G. L., Fraser, C. S., Pieretti, F., Block, K. L., and Hershey, J. W. B. Characterization of eIF3k, a newly discovered subunit of mammalian translation initiation factor eIF3. **Eur. J. Biochem.** 2003 Oct 15; 270(20): 4133-4139.
  - Fraser, C. S., Lee, J. Y., Mayeur, G. L., Bushell, M., Doudna, J. A., and Hershey, J. W. B. The j-subunit of human translation initiation factor eIF3 is required for the stable binding of eIF3 and its subcomplexes to 40S ribosomal subunits in vitro. **J. Biol. Chem.** 2004 Mar 5;279(10):8946-56.
  - Ji, H., Fraser, C. S., Yu, Y., Leary, J., and Doudna, J. A. Coordinated assembly of human translation initiation complexes by the Hepatitis C Virus internal ribosome entry site RNA. **Proc. Natl. Acad. Sci. U. S. A.** 2004 Dec 7;101(49):16990-5.
  - Siridechadilok, B., Fraser, C. S., Hall, R. J., Doudna, J. A., and Nogales, E. Structural Roles for Human Translation Factor eIF3 in Initiation of Protein Synthesis. **Science.** 2005 Dec 2;310(5753):1513-5.
  - Damoc, E., Fraser, C. S., Zhou, M., Videler, H., Mayeur, G. L., Hershey, J. W., Doudna, J. A., Robinson, C. V., and Leary, J. A. Structural Characterization of the Human Eukaryotic Initiation Factor 3 Protein Complex by Mass Spectrometry. **Mol. Cell Proteomics.** 2007 Jul;6(7):1135-1146.
  - Fraser, C. S., Berry, K. E., Hershey, J. W., and Doudna, J. A. eIF3j is located in the decoding center of the human 40S ribosomal subunit. **Mol. Cell.** 2007 Jun 22;26(6):811-9.
  - Pöyry, T. A. A., Kaminski, A., Connell, E., Fraser, C. S., and Jackson, R. J. The mechanism of an exceptional case of reinitiation after translation of a long open-reading frame reveals why such events do not generally occur in mammalian mRNA translation. **Genes Dev.** 2007 Dec 1;21(23):3149-62.
  - Zhou, M., Sandercock, A. M., Fraser, C. S., Ridlova, G., Stephens, E., Schenauer, M. R., Yokoi-Fong, T., Barsky, D., Leary, J. A., Hershey, J. W., Doudna, J. A., and Robinson, C. V. Mass Spectrometry reveals modularity and a complete subunit interaction map of the eukaryotic translation factor eIF3. **Proc. Natl. Acad. Sci. U. S. A.** 2008 Nov 25;105(47): 18139-44.
  - Fraser, C. S., Hershey, J. W., and Doudna, J. A. The pathway of HCV mRNA recruitment to the human ribosome. **Nat. Struct. Mol. Biol.** 2009. April; 16(4): 397-404.
  - Lee, S. B., Park, J. H., Folk, J. E., Deck, J.A., Pegg, A. E., Sokabe, M., Fraser, C. S., and Park, M.H. Inactivation of eukaryotic initiation factor 5A (eIF5A) by specific acetylation of its hypusine residue by spermidine/spermine acetyltransferase 1 (SSAT1). **Biochem J.** 2010 Dec 15;433(1):205-13.
  - Lindqvist, L., Robert, F., Merrick, W., Kakeya, H., Fraser, C., Osada, H., and Pelletier, J. Inhibition of translation by cytotrienin A—a member of the ansamycin family. **RNA**

2010 Dec;16(12):2404-13.

15. Park, J. H., Dias, C., Lee, S. B., Valentini, S., Sokabe, M., Fraser, C. S., and Park, M. H. Production of active recombinant eIF5A: reconstitution in E.coli of eukaryotic hypusine modification of eIF5A by its coexpression with modifying enzymes. **Protein Eng. Des. Sel.** 2011 Mar;24(3):301-9.
16. Özeş, A. R., Feoktistova, K., Avanzino, B. C., and Fraser, C. S. Duplex unwinding and ATPase activities of the DEAD-box helicase eIF4A are coupled by eIF4G and eIF4B. **J. Mol. Biol.** 2011 Sep 30;412(4):674-87.
17. Andaya, A., Jia, W., Sokabe, M., Fraser, C. S., Hershey, J. W., and Leary, J.A. Phosphorylation of human eukaryotic initiation factor 2 $\gamma$ : Novel site identification and targeted PKC involvement. **J. Proteome Res.** 2011 Oct 7;10(10):4613-23.
18. Sun, C., Todorovic, A., Querol-Audí, J., Bai, Y., Villa, N., Snyder, M., Ashchyan, J., Lewis, C. S., Hartland, A., Gradia, S., Fraser, C. S., Doudna, J. A., Nogales, E., and Cate, J. H. Functional reconstitution of human eukaryotic translation initiation factor 3 (eIF3). **Proc. Natl. Acad. Sci. U. S. A.** 2011 Dec 20;108(51):20473-8.
19. Sokabe, M., Fraser, C. S., and Hershey, J. W. The human translation initiation multi-factor complex promotes methionyl-tRNA<sub>i</sub> binding to the 40S ribosomal subunit. **Nucleic Acids Res.** 2012 Jan;40(2):905-13.
20. Virgili, G., Frank, F., Feoktistova, K., Sawicki, M., Sonenberg, N., Fraser, C. S., and Nagar, B. Structural Analysis of the DAP5 MIF4G Domain and Its Interaction with eIF4A. **Structure.** 2013 Apr 2;21(4):517-27.
21. Feoktistova, K., Tuvshintogs, E., Do, A., and Fraser, C. S. Human eIF4E promotes mRNA restructuring by stimulating eIF4A helicase activity. **Proc. Natl. Acad. Sci. U. S. A.** 2013 Aug 13;110(33):13339-44.
22. Villa, N., Do, A., Hershey, J. W., and Fraser, C. S. Human eukaryotic initiation factor 4G (eIF4G) binds to eIF3c, -d, and -e to promote mRNA recruitment to the ribosome. **J. Biol. Chem.** 2013 Nov 15;288(46):32932-40.
23. Özeş, A. R., Feoktistova, K., Avanzino, B. C., Baldwin, E. P., and Fraser, C. S. Real-time fluorescence assays to monitor duplex unwinding and ATPase activities of helicase proteins. **Nature Protoc.** 2014 Jun 19;9(7):1645-61.
24. Sokabe, M., and Fraser, C. S. Human Eukaryotic Initiation Factor 2 (eIF2)-GTP-Met-tRNA<sub>i</sub> Ternary Complex and eIF3 Stabilize the 43S Preinitiation Complex. **J. Biol. Chem.** 2014 Nov 14;289(46):31827-36.
25. Sidrauski, C., Tsai, J. C., Kampmann, M., Hearn, B. R., Vedantham, P., Jaishankar, P., Sokabe, M., Mendez, A. S., Newton, B. W., Tang, E. L., Verschueren, E., Johnson, J. R., Krogan, N. J., Fraser, C. S., Weissman, J. S., Renslo, A. R., and Walter, P. Pharmacological dimerization and activation of the exchange factor eIF2B antagonizes the integrated stress response. **Elife.** 2015 Apr 15;4.
26. García-García, C., Frieda, K. L., Feoktistova, K., Fraser, C. S., and Block, S. M. Factor-Dependent Processivity in the Human eIF4A DEAD-box Helicase. **Science.** 2015 Jun 26;348(6242):1486-8.
27. Rossi, D., Barbosa, N. M., Galvão, F. C., Boldrin, P. E., Hershey, J. W., Zanelli, C. F., Fraser, C. S., and Valentini, S. R. Evidence for a Negative Cooperativity between eIF5A and eEF2 on Binding to the Ribosome. **PLoS One.** 2016 Apr

26;11(4):e0154205.

28. Barbosa, N. M., Boldrin, P. E., Rossi, D., Yamamoto, P. A., Watanabe, T. F., Serrão, V. H., Hershey, J. W., Fraser, C. S., Valentini, S. R., and Zanelli, C. F. Mapping surface residues of eIF5A that are important for binding to the ribosome using alanine scanning mutagenesis. **Amino Acids**. 2016 Oct;48(10):2363-74.
29. Sokabe, M., and Fraser, C. S. A helicase-independent activity of eIF4A in promoting mRNA recruitment to the human ribosome. **Proc. Natl. Acad. Sci. U. S. A.** 2017 Jun 13;114(24):6304-6309.
30. Avanzino, B. C., Fuchs, G., and Fraser, C. S. Cellular cap-binding protein, eIF4E, promotes picornavirus genome restructuring and translation. **Proc. Natl. Acad. Sci. U. S. A.** 2017 Sep 5;114(36):9611-9616.
31. Avanzino, B. C., Jue, H., Miller, C. M., Cheung, E., Fuchs, G., and Fraser, C. S. Molecular mechanism of poliovirus Sabin vaccine strain attenuation. **J. Biol. Chem.** 2018 Oct 5;293(40):15471-15482.
32. Sokabe, M., and Fraser, C. S. Toward a Kinetic Understanding of Eukaryotic Translation. **Cold Spring Harb. Perspect. Biol.** 2019 Feb 1;11(2).
33. Howard, C. M., Bearss, N., Subramanian, B., Tilley, A., Sridharan, S., Villa N., Fraser, C. S., and Raman, D. The CXCR4-LASP1-eIF4F Axis Promotes Translation of Oncogenic Proteins in Triple-Negative Breast Cancer Cells. **Front. Oncol.** 2019 Apr 24;9:284.
34. Querido, J. B., Sokabe, M., Kraatz, S., Gordiyenko, Y., Skehel, J. M., Fraser, C. S., and Ramakrishnan, V. Structure of a human 48S translational initiation complex. **Science**. 2020 Sep 4;369(6508):1220-1227.

Complete list of published work in Pubmed:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=fraser+cs>

#### **CURRENT FUNDING:**

1) R01 GM092927 (Fraser) 3/1/10-4/30/23

NIGMS (NIH)

Title: The mechanism of mRNA recruitment to the human ribosome.

The objective of this project is to study the molecular details of initiation factor interactions that stabilize mRNA on the human ribosome. This project focuses on the role of the cap-binding complex in promoting mRNA recruitment to the 40S subunit.

2) R01 AI146245 (Isberg) 2/20/20-1/31/25

NIAID (NIH)

Title: The Interface between L. Pneumophila manipulation of host endoplasmic

reticulum and innate immune subterfuge.

The objective of this project from the perspective of the Fraser lab is to determine the mechanism by which infection of human cells by Legionnaire's pneumonia reprograms the translation machinery of the host cell.

**3) W. M. Keck Foundation (Montpetit, Shah, Fraser, Wozniak) 7/1/18-6/30/21**

Flaviviridae viral RNA in the host cell nucleus – a new paradigm and opportunity.

The objective of this project is to study the molecular details of why Zika, Hepatitis C, Dengue, and West Nile virus genomic RNAs engage nuclear processes, and how this benefits the viruses.