

Ramanujan S. Hegde

Contact Information

Cell Biology and Metabolism Branch
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Personal Information

Place of Birth: Kumta, Karnataka, India
Date of Birth: April 1, 1970
Citizenship: USA

Education

M.D., University of California, San Francisco, CA, 1999.

Ph.D., University of California, San Francisco, CA, 1997.

B.A. (with General and Special Honors), University of Chicago, Chicago, IL, 1991.

Research Chronology

July 2008 to present	Senior Investigator, Cell Biology and Metabolism Program NICHD, National Institutes of Health, Bethesda, MD.
July 2002 to July 2008	Investigator, National Institutes of Health, Bethesda, MD.
Sept. 1999 to June 2002	National Cancer Institute Scholar, National Cancer Institute National Institutes of Health, Bethesda, MD.
Nov. 1991 to Aug. 1999	MD/PhD student, Univ. of California, San Francisco Advisor: Vishwanath R. Lingappa
Nov. 1988 to Aug. 1991	Undergraduate student, University of Chicago Advisor: H. Clive Palfrey

Honors and Awards

- R.R. Bensley Award in Cell Biology, 2008, for “distinguished contribution to the advancement of anatomy through discovery, ingenuity, and publications in the field of cell biology.”
- Patent No. 6,015,659 (with Co-inventor W. J. Welch): "Inducement of thermotolerance with benzoquinonoid ansamycins."
- Patent No. 6,821,742 (with co-inventors V. R. Lingappa and D. T. Rutkowski), "Conformational and topological protein regulation."
- NIH pre-IRTA Mentorship Award, 2001, 2002, 2003, and 2004, in recognition for outstanding education and guidance for post-baccalaureate students.
- National Cancer Institute Scholar Award, 1999.
- UCSF Chancellor's Award for Basic Research, 1996-1997.

Professional, teaching, and NIH Activities

- Co-organizer, FASEB meeting “From Unfolded Proteins in the Endoplasmic Reticulum to Disease” June, 2009.
- Associate Editor, *Molecular Biology of the Cell*, Jan. 2009 to present.
- Co-chairperson for “Organelle biology and dysfunction in disease” Symposium at 2007 NIH Research Festival.
- Co-Chairperson, Protein Trafficking Interest Group of the NIH, Jan. 2005-present.
- NICHD representative, NIH Ethics Committee, Jan. 2008-present
- NICHD representative, NIH Tenure-Track Investigators Committee, 2004-present.
- NIH study section member, Membrane Biology and Protein Processing, 2007, 2008.
- NIH study section member, Ischemic Injury and Neurodegeneration, 2007.
- Lecturer at “Cell Membranes” FAES course at NIH, 2008.
- Guest Lecturer, Medical College of Wisconsin, Cell Signaling Course, 2007.
- Guest Lecturer, Biophysical Chemistry Course, Colgate University, 2007.
- Lecturer at “Demystifying Medicine” course at NIH, January, 2007.
- Lecturer at “Cell Membranes and Protein Trafficking” FAES course at NIH, 2003.
- Invited Panelist, “Science and Technology: Frontiers of the 21st century”, Hugh O’Brien Youth Leadership Conference, National Academy of Sciences, July, 2001.
- Ad hoc reviewer for 5th edition of the textbook, *Molecular Biology of the Cell*.
- Ad hoc reviewer for grants by the NIH, NSF, MRC, Wellcome Trust, Israeli Science Foundation.
- Ad hoc reviewer for *Nature*, *Cell*, *Mol. Cell*, *Dev. Cell*, *J. Cell Biol.*, *PNAS*, *Mol. Biol. Cell*, *J. Biol. Chem.*, *J. Cell Sci.*, *EMBO J.*, *J. Neurosci.*, *Biochemistry*, and *Trends in Cell Biology*.

Publications (in reverse chronologic order)

Notes: Shared first authorship is indicated by *, and shared corresponding authorship by #.

Publications 1-15 were as a student; the remainder were as an independent investigator.

61. Ashok, A. and **Hegde, R.S.** (2009) Selective Processing and Metabolism of Disease-Causing Mutant Prion Proteins. *PLoS Pathogens*, 5:e1000479.
60. Chakrabarti, O. and **Hegde, R.S.** (2009) Functional depletion of Mahogunin by cytosolically exposed prion protein contributes to neurodegeneration. *Cell*, 137:1136-1147.
59. Chakrabarti, O., Ashok, A., and **Hegde, R.S.** (2009) Prion protein biosynthesis and its emerging role in neurodegeneration. *Trends Biochem. Sci.*, 34:287-95.

58. **Hegde, R.S.** (2009) Protein maturation and processing at the endoplasmic reticulum. In: *The Liver: Biology and Pathobiology*. 5th Edition. Edited by I. A. Arias et al., Wiley-Blackwell, In press.
57. Sharma, A.S., Mariappan, M., Appathurai, S., and **Hegde, R.S.** (2009) In vitro dissection of protein translocation into the mammalian endoplasmic reticulum. *Methods Mol. Biol.* In press.
56. Polgar, O., Ediriwickrema, L.S., Robey, R.W., Sharma, A., **Hegde, R.S.**, Li, Y., Xia, D., Ward, Y., Dean, M., Ozvegy-Laczka, C., Sarkadi, B., and Bates, S.E. (2009) Arginine 383 is a crucial residue in ABCG2 biogenesis. *Biochim. Biophys. Acta*, 1788(7):1434-43.
55. Kang, S.W. and **Hegde, R.S.** (2008) Lighting up the stressed ER. *Cell*, 135(5):787-9.
54. Rane, N.S., Kang, S.W., Chakrabarti, O., Feigenbaum, L., and **Hegde, R.S.** (2008) Chronic prion protein degradation via pre-emptive quality control causes neurodegeneration. *Dev. Cell*, 15:359-370.
53. **Hegde, R.S.** and Kang, S.W. (2008) The concept of translocational regulation. *J. Cell Biol.* 182:225-232.
52. Menetret, J.F., **Hegde, R.S.**, Aguiar, M., Gygi, S.P., Park, E., Rapoport, T.A., and Akey, C.W. (2008) Single copies of Sec61 and TRAP associate with a non-translating mammalian ribosome. *Structure*, 16:1126-1137.
51. Ashok, A. and **Hegde, R.S.** (2008) Retrotranslocation of prion proteins from the ER by inhibition of GPI signal sequence transamidation. *Mol. Biol. Cell.* 19:3463-3476.
50. Ashok, A. and **Hegde, R.S.** (2008) Cytotoxicity of aberrant proteins. In: *Encyclopedia of Life Sciences (ELS)*. John Wiley & Sons, Ltd: DOI: 10.1002/9780470015902.a0020887.
49. MacKinnon, A.L., Garrison, J.L., **Hegde, R.S.**, and Taunton J. (2007) Photo-leucine incorporation reveals the target of a cyclodepsipeptide inhibitor of cotranslational translocation. *J. Am. Chem. Soc.* 129:14560-1.
48. *Rutkowski, D.T., *Kang, S.W., Goodman, A.G., Garrison, J.L., Taunton, J., Katze, M.G., Kaufman, R.J., and **Hegde, R.S.** (2007) The Role of p58IPK in Protecting the Stressed Endoplasmic Reticulum. *Mol. Biol. Cell*, 18:3681-91.
47. Ong, H. L., Liu, X., Tsaneva-Atanasova, K., Singh, B. B., Bandyopadhyay, B. C., Swaim, W. D., Russell, J. T., **Hegde, R. S.**, Sherman, A., and Ambudkar, I. S. (2007) Relocalization of STIM1 for activation of store-operated Ca²⁺ entry is determined by the depletion of subplasma membrane endoplasmic reticulum Ca²⁺ store. *J. Biol. Chem.*, 282:12176-85.

46. Stefanovic, S. and **Hegde, R. S.** (2007) Identification of a targeting factor for post-translational membrane protein insertion into the ER. *Cell*, 128:1147-1159.
45. Alken, M. and **Hegde, R. S.** (2007) The translocation apparatus of the endoplasmic reticulum. In: *Molecular machines involved in protein transport across cellular membranes*, ed. R. Dalbey, C. Koehler, and F. Tamanoi. Academic press/Elsevier.
44. Ong, H. L., Liu, X., Sharma, A., **Hegde, R. S.**, and Ambudkar, I. (2007) Intracellular Ca²⁺ release via the ER translocon activates store-operated calcium entry. *Pflugers Arch.* 453:797-808.
43. *Kang, S. W., *Rane, N. S., Kim, S. J., Garrison, J. L., Taunton, J., and **Hegde, R. S.** (2006) Substrate-specific translocational attenuation during ER stress defines a pre-emptive quality control pathway. *Cell*, 127:999-1013.
42. Bernstein, H. D. and **Hegde, R. S.** (2006) The surprising complexity of signal sequences. *Trends Biochem. Sci.* 31:563-71.
41. Ashok, A. and **Hegde, R. S.** (2006) Prions and retroviruses: an endosomal rendezvous? *EMBO Rep.* 7:685-687.
40. Snapp, E. L. and **Hegde, R. S.** (2006) Rational design and evaluation of FRET experiments to measure protein proximities in cells. In *Curr. Prot. in Cell Biol.*, ed. J. S. Bonifacino et al., Chapter 17:Unit 17.9, Wiley.
39. Snapp, E. L., Sharma, A., Lippincott-Schwartz, J., and **Hegde, R. S.** (2006) Monitoring chaperone engagement of substrates in the endoplasmic reticulum of live cells. *Proc. Natl. Acad. Sci.*, 103(17):6536-6541.
38. Chakrabarti, O. and **Hegde, R. S.** (2006) Trafficking of the cellular Prion protein and its role in neurodegeneration. In: *Protein trafficking in the neuron*, ed. A. Bean, Elsevier, 413-436.
37. *Shaffer, K. L., *Sharma, A., Snapp, E. L., and **Hegde, R. S.** (2005) Regulation of protein compartmentalization expands the diversity of protein function. *Dev. Cell*, 9:545-554.
36. Brambillasca, S., Yabal, M., Soffientini, P., Stefanovic, S., Makarow, M., **Hegde, R. S.**, and #Borgese, N. (2005) Transmembrane topogenesis of a tail-anchored protein is modulated by membrane lipid composition. *EMBO J.*, 24:2533-2542.
35. Garrison, J. L., Kunkel, E. J., **Hegde, R. S.**, and #Taunton, J. (2005) A substrate-specific inhibitor of protein translocation into the endoplasmic reticulum. *Nature*, 436:285-289.
34. *Menetret, J. F., **Hegde, R. S.**, Heinrich, S. U., Chandramouli, P., Ludtke, S. J., Rapoport, T. A., and Akey, C. W. (2005) Architecture of the ribosome-channel complex derived from native membranes. *J. Mol. Biol.*, 348:445-457.

33. **Hegde, R. S.** (2005) Protein translocation across the endoplasmic reticulum. In: Protein movement across membranes, pp. 1-18. ed. J. Eichler, Landes Bioscience, Georgetown, TX.
32. Levine, C. G., Mitra, D., Sharma, A., Smith, C. L., and **Hegde, R. S.** (2005) The efficiency of protein compartmentalization into the secretory pathway. *Mol. Biol. Cell*, 16:279-291.
31. **Hegde, R. S.** and Rane, N. S. (2005) The molecular basis of prion protein-mediated neuronal damage. In: Neurodegeneration and Prion Disease, pp. 407-450, ed. D. R. Brown, Springer, NY, NY.
30. Rane, N., Yonkovich, J., and **Hegde, R. S.** (2004) Protection from cytosolic prion protein toxicity by modulation of protein translocation. *EMBO J.*, 23:4550-4559.
29. *Karsten, V., ***Hegde, R. S.**, Sinai, A. P., Yang, M., and Joiner, K. (2004) Transmembrane domain modulates sorting of membrane proteins in toxoplasma gondii. *J. Biol. Chem.* 279:26052-26057.
28. Snapp, E. L., Reinhart, G. A., Bogert, B. A., Lippincott-Schwartz, J., and **Hegde, R. S.** (2004) The organization of engaged and quiescent translocons in the endoplasmic reticulum of mammalian cells. *J. Cell Biol.* 164:997-1007.
27. Tremblay P., Ball, H. L., Kaneko, K., Groth, D., **Hegde, R. S.**, Cohen, F. E., DeArmond, S. J., Prusiner, S. B., and Safar, J. G. (2004) Mutant PrPSc conformers induced by a synthetic peptide and various prion strains. *J. Virol.*, 78:2088-2099.
26. Snapp, E. L., **Hegde, R. S.**, Francolini, M., Lombardo, F., Colombo, S., Pedrazzini, E., Borgese, N., and Lippincott-Schwartz, J. (2003) Formation of stacked ER cisternae by low affinity protein interactions. *J. Cell Biol.*, 163:257-69.
25. **Hegde, R. S.** and Rane, N. S. (2003) Prion protein trafficking and the development of neurodegeneration. *Trends Neurol. Sci.* 26:337-339.
24. Fons, R. D., Bogert, B. A., and **Hegde, R. S.** (2003) Substrate-specific function of the translocon-associated protein complex during translocation across the ER membrane. *J. Cell Biol.* 160:529-539.
23. **Hegde, R. S.** (2002) Targeting and beyond: new roles for old signal sequences. *Mol. Cell*, 10:697-698.
22. Kim, S. J. and **Hegde, R. S.** (2002) Cotranslational partitioning of nascent prion protein into multiple populations at the translocation channel. *Mol. Biol. Cell*, 13:3775-3786.
21. Lingappa, V. R., Rutkowski, D. T., **Hegde, R. S.**, and Andersen, O. S. (2002) Conformational control through translocational regulation: a new view of secretory and membrane protein folding. *Bioessays*, 24:741-748.

20. Kim, S. J., Mitra, D., Salerno, J. S., and **Hegde, R. S.** (2002) Signal sequences control gating of the protein translocation channel in a substrate-specific manner. *Dev. Cell*, 2:207-217.
19. Lingappa, V. R. and **Hegde, R. S.** (2001) Prion Protein Biogenesis: Implications for Neurodegeneration. In "Research and Perspectives in Alzheimer's Diseases". Beyreuther/Christen/Masters (Eds.) copyright Springer-Verlag Berlin Heidelberg.
18. Kim, S. J., Rahbar, R., and **Hegde, R. S.** (2001) Combinatorial control of prion protein biogenesis by the signal sequence and transmembrane domain. *J. Biol. Chem.* 276:26132-26140.
17. Rutkowski, D. T., Lingappa, V. R. and **Hegde, R. S.** (2001) Substrate-specific regulation of the ribosome-translocon junction by N-terminal signal sequences. *Proc. Natl. Acad. Sci.* 98:7823-7828.
16. Wilhelm, J. E., Vale, R. D., and **Hegde, R. S.** (2000) Coordinate control of translation and localization of Vg1 mRNA in *Xenopus* oocytes. *Proc. Natl. Acad. Sci.*, 97:13132-13137.
15. **Hegde, R. S.**, Tremblay, P., Groth, D., DeArmond, S. J., Prusiner, S. B. and Lingappa, V. R. (1999) Transmissible and genetic prion diseases share a common pathway of neurodegeneration. *Nature*, 402:822-826.
14. **Hegde, R. S.** and Lingappa, V. R. (1999) Regulation of protein biogenesis at the endoplasmic reticulum membrane. *Trends Cell Biol.*, 9:132-137.
13. **Hegde, R. S.**, Voigt, S., and Lingappa, V. R. (1998) Regulation of protein topology by *trans*-acting factors at the endoplasmic reticulum. *Mol. Cell*, 2:85-91.
12. **Hegde, R. S.**, Voigt, S., Rapoport, T. A., and Lingappa, V. R. (1998) TRAM regulates the exposure of nascent secretory proteins to the cytosol during translocation into the endoplasmic reticulum. *Cell*, 92:621-631.
11. **Hegde, R. S.**, Mastrianni, J. A., Scott, M. R., DeFea, K. A., Tremblay, P., Torchia, M., DeArmond, S. J., Prusiner, S. B., and Lingappa, V. R. (1998) A transmembrane form of the prion protein in neurodegenerative disease. *Science*, 279:827-834.
10. Rusinol, A. E., **Hegde, R. S.**, Chuck, S. L., Lingappa, V. R., and Vance, J. E. (1998) Translocational pausing of apolipoprotein can be regulated by membrane lipid composition. *J. Lipid. Res.*, 39:1287-1294.
9. **Hegde, R. S.** and Lingappa, V. R. (1997) Membrane protein biogenesis: regulated complexity at the endoplasmic reticulum. *Cell*, 91: 575-582.
8. Lingappa, J. R., Hill, R. L., Wong, M. L. and **Hegde, R. S.** (1997) A multi-step, ATP-dependent pathway for assembly of human Immunodeficiency (HIV) capsids in a cell-free system. *J. Cell Biol.*, 136:567-581.

7. Lingappa, V. R. and **Hegde, R.** (1997) Translocational pausing and the regulation of membrane protein biogenesis. in *Membrane Proteins: structure, function and expression control*. Edited by Naotaka Hamasaki and Katsuyoshi Mihara. Kyushu University Press (Japan), S. Karger AG (Switzerland).
6. Kivlen, M. H., Dorsey, C. A., Lingappa, V. R. and **Hegde, R. S.** (1997) Asymmetric distribution of pause transfer sequences in apolipoprotein B-100. *J. Lipid Res.*, 38: 1149-1162.
5. **Hegde, R. S.** and Lingappa, V. R. (1996) Sequence-specific alteration of the ribosome-membrane junction exposes nascent secretory proteins to the cytosol. *Cell*, 85:217-228.
4. **Hegde, R. S.**, Zuo, J., Voellmy, R. and Welch, W. J. (1995) Short circuiting stress protein expression via a tyrosine kinase inhibitor, Herbimycin A. *J. Cellular Physiology*, 165:186-200.
3. **Hegde, R. S.** and Palfrey, H. C. (1991) Ionic effects on bumetanide binding to the activated Na/K/2Cl Cotransporter: Selectivity and Kinetic properties of ion binding sites, *J. Membrane Biology*, 126:27-37.
2. Pewitt, E. B., **Hegde, R. S.**, Haas, M., and Palfrey, H. C. (1990) The Regulation of Na/K/2Cl cotransport and bumetanide binding by protein phosphorylation and dephosphorylation. *J. Biol. Chem.*, 265:20747-20756.
1. Pewitt, E. B., **Hegde, R. S.**, and Palfrey, H. C. (1990) [3H] Bumetanide binding to avian erythrocyte membranes. *J. Biol. Chem.*, 265:14364-14370.