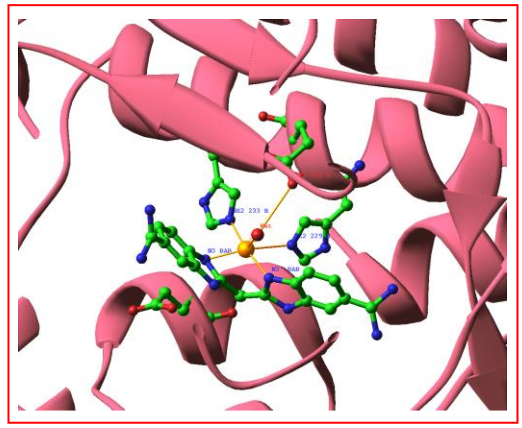
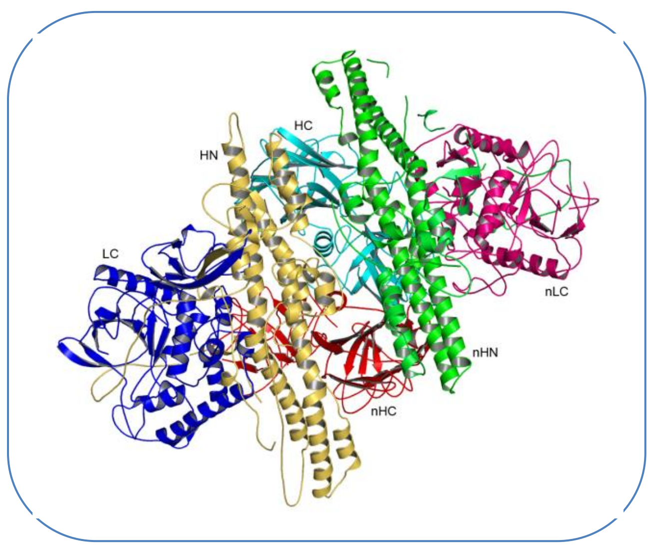
# S. Eswaramoorthy Ph.D.

## Research Interests

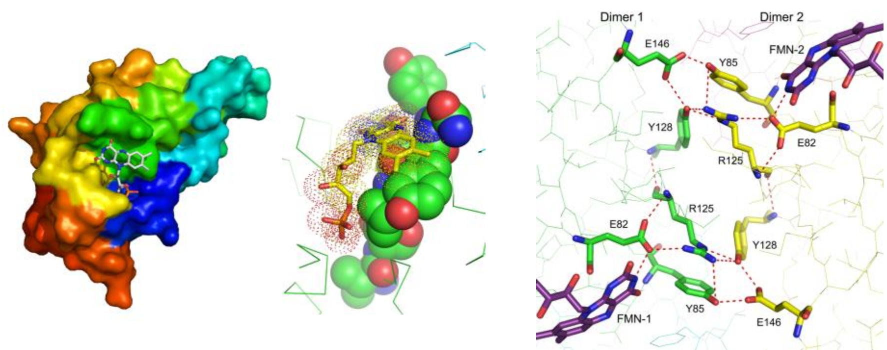
I

Botulism is a dangerous disease caused by seven different serotypes of *Clostridium botulinum* neurotoxin. It needs long term intensive care treatment to the infected otherwise the disease becomes fatal. The disease causing agent is a 150kDa protein expressed along with nontoxic nonhemeagglutinin (NTNH) and a few other associated proteins. All these proteins together form variable complexes like large, medium and small, and facilitate the toxin entry through the digestion system. With expertize in X-ray crystallography, I am interested in understanding the complex formation and the functional mechanism of these proteins through crystal structure analysis. We have solved the structures of toxins, toxin fragments, and toxin-ligand complexes and contributed to the understanding of the functional mechanism of these toxins. The focus now is studying the functional mechanism of the progenitor toxin complexes through small angle X-ray scattering (SAXS), X-ray crystallography and cryo-electron microscopy (Cryo-EM). When the complexes grow bigger cryo-electron microscopy (Cryo-EM) would be more helpful and SAXS studies will help in understanding the solution state. Protein-ligand complex studies are the other focus area of my research that is essential for drug discovery against the toxin.





**II** Environmental pollution plays a significant role in public health especially in diseases like cancer and asthma. Heavy metal contamination in soil and water is a potential hazard for humans and wild-life. People living around the area previously used for heavy metal processing have increased risk of developing cancer. Extended exposure to even mild radioactive materials will have significant impact on inducing cancer like diseases. Since this is an unavoidable problem we have to increase our effort to clean up and control such pollution. One of the effective ways to remove heavy metal contamination from soil and water is bacterial bioremediation. Soluble form of the metals like Uranium and Chromium are able to sweep and spread through the water flow. Converting the soluble form of these metals into insoluble form is proved to be a successful bioremediation process. I worked in collaboration with Stanford University on bacterial enzymes that are very effective in bioremediation. Our study on flavoproteins showed that protein engineering is very helpful in enhancing the enzyme activity.




Flavodoxins are flavin-dependent oxidoreductases involved in the process of electron transfer. Bacteria utilize this enzyme to handle the stress induced by heavy metals and other chemical contamination in the soil. These proteins reduce soluble form of heavy metals like Cr(VI) into an insoluble Cr(III). Identifying these bacterial enzymes that are useful for different bioremediation processes and optimizing their catalytic activity through protein engineering is our strategy to help environmental protection. Bioremediation using bacteria will be an efficient tool for controlling pollution.

# Publications

1. **Eswaramoorthy S**, Sun J, Lu H, Singh B.R. and Swaminathan S. Molecular Assembly of *Clostridium botulinum* progenitor M complex of type E. Scientific Reports (Nature Publishing Group). 2015. 5:17795 DOI: 10.1038/srep17795.
2. Ghasempur S, **Eswaramoorthy S**, Hillerich BS, Seidel RD, Swaminathan S, Almo SC, Gerlt JA. Discovery of a novel L-lyxonate degradation pathway in Pseudomonas aeruginosa PAO1. Biochemistry. 2014 May 27;53(20):3357-66.
3. Goble AM, Toro R, Li X, Ornelas A, Fan H, **Eswaramoorthy S**, Patskovsky Y, Hillerich B, Seidel R, Sali A, Shoichet BK, Almo SC, Swaminathan S, Tanner ME, Raushel FM.Deamination of 6-aminodeoxyfutalosine in menaquinone biosynthesis by distantly related enzymes. Biochemistry. 2013 Sep 17;52(37):6525-36.
4. **Eswaramoorthy S**, Poulain S, Hienerwadel R, Bremond N, Sylvester MD, Zhang YB, Berthomieu C, Van Der Lelie D, Matin A. Crystal structure of ChrR--a quinone reductase with the capacity to reduce chromate. PLoS One. 2012. 7(4):e36017.
5. Kumari SS, **Eswaramoorthy S**, Mathias RT, Varadaraj K. Unique and analogous functions of aquaporin 0 for fiber cell architecture and ocular lens transparency. Biochim Biophys Acta. 2011 Sep;1812(9):1089-97.
6. Lakshminarasimhan D, **Eswaramoorthy S**, Burley SK, Swaminathan S. Structure of YqgQ protein from Bacillus subtilis, a conserved hypothetical protein. Acta Crystallogr Sect F Struct Biol Cryst Commun. 2010 Jan 1;66(Pt 1):8-11.
7. Kumaran D, **Eswaramoorthy S**, Furey W, Navaza J, Sax M, Swaminathan S. Domain organization in Clostridium botulinum neurotoxin type E is unique: its implication in faster translocation. J Mol Biol. 2009 Feb 13;386(1):233-45.
8. Tyagi R, **Eswaramoorthy S**, Burley SK, Raushel FM, Swaminathan S. A common catalytic mechanism for proteins of the HutI family. Biochemistry. 2008 May 20;47(20):5608-15.
9. Madegowda M, **Eswaramoorthy S**, Burley SK, Swaminathan S. X-ray crystal structure of the B component of Hemolysin BL from Bacillus cereus. Proteins. 2008 May 1;71(2):534-40.
10. Almo SC, Bonanno JB, Sauder JM, Emtage S, Dilorenzo TP, Malashkevich V, Wasserman SR, Swaminathan S, **Eswaramoorthy S**, Agarwal R, Kumaran D, Madegowda M, Ragumani S, Patskovsky Y, Alvarado J, Ramagopal UA, Faber-Barata J, Chance MR, Sali A, Fiser A, Zhang ZY, Lawrence DS, Burley SK. Structural genomics of protein phosphatases. J Struct Funct Genomics. 2007 Sep;8(2-3):121-40. Review.
11. **Eswaramoorthy S**, Bonanno JB, Burley SK, Swaminathan S. Mechanism of action of a flavin-containing monooxygenase. Proc Natl Acad Sci U S A. 2006 Jun 27;103(26):9832-7. Epub 2006 Jun 15. Erratum in: Proc Natl Acad Sci U S A. 2007 Sep 4;104(36):14543.
12. Jayaraman S, **Eswaramoorthy S**, Kumaran D, Swaminathan S. Common binding site for disialyllactose and tri-peptide in C-fragment of tetanus neurotoxin. Proteins. 2005 Nov 1;61(2):288-95.
13. Jayaraman S, **Eswaramoorthy S**, Ahmed SA, Smith LA, Swaminathan S. N-terminal helix reorients in recombinant C-fragment of Clostridium botulinum type B. Biochem Biophys Res Commun. 2005 Apr 29;330(1):97-103.
14. Kumaran D, **Eswaramoorthy S**, Studier FW, Swaminathan S. Structure and mechanism of ADP-ribose-1"-monophosphatase (Appr-1"-pase), a ubiquitous cellular processing enzyme. Protein Sci. 2005 Mar;14(3):719-26.
15. Agarwal R, **Eswaramoorthy S**, Kumaran D, Binz T, Swaminathan S. Structural analysis of botulinum neurotoxin type E catalytic domain and its mutant Glu212-->Gln reveals the pivotal role of the Glu212 carboxylate in the catalytic pathway. Biochemistry. 2004 Jun 1;43(21):6637-44.

16. Swaminathan S, **Eswaramoorthy S**, Kumaran D. Structure and enzymatic activity of botulinum neurotoxins. Mov Disord. 2004 Mar;19 Suppl 8:S17-22.
17. **Eswaramoorthy S**, Kumaran D, Keller J, Swaminathan S. Role of metals in the biological activity of Clostridium botulinum neurotoxins. Biochemistry. 2004 Mar 2;43(8):2209-16.
18. Agarwal R, **Eswaramoorthy S**, Kumaran D, Dunn JJ, Swaminathan S. Cloning, high level expression, purification, and crystallization of the full length Clostridium botulinum neurotoxin type E light chain. Protein Expr Purif. 2004 Mar;34(1):95-102.
19. **Eswaramoorthy S**, Rao ST, Pan B, Sundaralingam M. Structure of the dodecamer r(GAUCACUUCGGU) with four 5'-overhang nucleotides. Acta Crystallogr D Biol Crystallogr. 2004 Jan;60(Pt 1):8-12.
20. Kumaran D, **Eswaramoorthy S**, Gerchman SE, Kycia H, Studier FW, Swaminathan S. Crystal structure of a putative CN hydrolase from yeast. Proteins. 2003 Aug 1;52(2):283-91.
21. **Eswaramoorthy S**, Gerchman S, Graziano V, Kycia H, Studier FW, Swaminathan S. Structure of a yeast hypothetical protein selected by a structural genomics approach. Acta Crystallogr D Biol Crystallogr. 2003 Jan;59(Pt 1):127-35.
22. **Eswaramoorthy S**, Kumaran D, Swaminathan S. A novel mechanism for Clostridium botulinum neurotoxin inhibition. Biochemistry. 2002 Aug 6;41(31):9795-802.
23. **Eswaramoorthy S**, Kumaran D, Swaminathan S. Crystallographic evidence for doxorubicin binding to the receptor-binding site in Clostridium botulinum neurotoxin B. Acta Crystallogr D Biol Crystallogr. 2001 Nov;57(Pt 11):1743-6.
24. Kumaran D, **Eswaramoorthy S**, Furey W, Sax M, Swaminathan S. Structure of staphylococcal enterotoxin C2 at various pH levels. Acta Crystallogr D Biol Crystallogr. 2001 Sep;57(Pt 9):1270-5.
25. Kumaran D, **Eswaramoorthy S**, Luft BJ, Koide S, Dunn JJ, Lawson CL, Swaminathan S. Crystal structure of outer surface protein C (OspC) from the Lyme disease spirochete, Borrelia burgdorferi. EMBO J. 2001 Mar 1;20(5):971-8.
26. Kumaran D, **Eswaramoorthy S**, Dunn JJ, Swaminathan S. Crystallization and preliminary X-ray analysis of Borrelia burgdorferi outer surface protein C (OspC). Acta Crystallogr D Biol Crystallogr. 2001 Feb;57(Pt 2):298-300.
27. Swaminathan S, **Eswaramoorthy S**. Crystallization and preliminary X-ray analysis of Clostridium botulinum neurotoxin type B. Acta Crystallogr D Biol Crystallogr. 2000 Aug;56(Pt 8):1024-6.
28. Swaminathan S, **Eswaramoorthy S**. Structural analysis of the catalytic and binding sites of Clostridium botulinum neurotoxin B. Nat Struct Biol. 2000 Aug;7(8):693-9.
29. Kumar PR, **Eswaramoorthy S**, Vithayathil PJ, Viswamitra MA. The tertiary structure at 1.59 A resolution and the proposed amino acid sequence of a family-11 xylanase from the thermophilic fungus Paecilomyces varioti bainier. J Mol Biol. 2000 Jan 21;295(3):581-93.
30. Sekar K, **Eswaramoorthy S**, Jain MK, Sundaralingam M. Crystal structure of the complex of bovine pancreatic phospholipase A2 with the inhibitor 1-hexadecyl-3-(trifluoroethyl)-sn-glycero-2-phosphomethanol,. Biochemistry. 1997 Nov 18;36(46):14186-91.
31. **Eswaramoorthy S**, Vithayathil PJ, Viswamitra MA. Crystallization and preliminary X-ray crystallographic studies of thermostable xylanase crystals isolated from Paecilomyces varioti. J Mol Biol. 1994 Nov 4;243(4):806-8.