

## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.

Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Gowda, Channe D	POSITION TITLE Professor of Biochemistry and Molecular Biology		
eRA COMMONS USER NAME: cgowda			
EDUCATION/TRAINING ( <i>Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Mysore, Mysore, India	BS	1971	Physics, Chem, Math
University of Mysore, Mysore, India	MS	1973	Organic Chemistry
University of Mysore, Mysore, India	PhD	1978	Organic Chemistry

### A. Personal Statement

Research in my laboratory focuses on molecular mechanisms involved in malaria parasite-human host interactions governing malaria immunology and pathophysiology. Specifically, over the past two decades, we have made several important contributions in delineating molecular interactions in the (i) adherence of *Plasmodium falciparum*-infected red blood cells (IRBCs) in the placenta that contributes to placental malaria pathogenesis, and (ii) malaria parasite-induced activation of the immune system, cell signaling, and initiation of innate immune responses. In both fronts, our work has been productive and represents impactful original contributions to the malaria field. We initiated studies on Toll-like receptor (TLR)-mediated interactions and cell signaling in immune responses to malaria. We have shown that parasite polysomes target TLR9 and mononucleosome is sufficient for TLR-mediated robust immune responses. In cytoadherence studies, we have identified and structurally characterized the chondroitin sulfate proteoglycan (CSPG) receptor involved in the adherence of *P. falciparum* in human placenta, established CSPG's localization in the placenta, elucidated the chondroitin 4-sulfate (C4S) structural motif that interacts with IRBCs, and identified various functional groups of the C4S motif involved in IRBC binding. Additionally, we have developed C4S oligomer-based photoreactive reagents that can covalently link to amino acid residues in the C4S-binding site VAR2CSA. Recently, in collaboration with Drs. Flanagan and Maria Bewely, we have expressed and purified the N- and C-terminal portions of VAR2CSA, the parasite protein that mediates IRBC adherence to CSPG. We have also developed a novel, sensitive, carbohydrate-based assay, which allows development of high through screening assay to identify small molecule inhibitors of C4S binding to VAR2CSA from drug libraries. More recently, we initiated collaboration with Dr. Geert-Jan Boons, CCRC, Georgia, to chemically synthesize chondroitin sulfate oligosaccharides for determining the precise location of sulfate group in oligosaccharides, which optimally interact with IRBCs and for structure-activity relationship studies in VAR2CSA-C4S binding. Additionally, we have reagents and resources from previous studies that are essential for the proposed studies. Thus, we are well suited to undertake the studies proposed in this grant application.

### B. Positions and Honors

#### Positions and Employment

1975-1986	Lecturer, Department of Chemistry, University of Mysore, Mysore, India.
1980-1981	Alexander von Humboldt Foundation Fellow, Institute of Biochemistry, Univ. of Kiel, Germany.
1983-1985	Postdoctoral Scholar, Dept of Biological Chemistry, PSU College of Medicine, Hershey, PA.
1986-1989	Instructor, Dept. of Pharmacology, New York University Medical Center, New York, NY.
1989-1994	Assistant Professor, Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC.
1994-2000	Associate Professor, Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC.
2001-present	Professor, Department of Biological Chemistry and Molecular Biology, Penn State University College of Medicine, Hershey, PA.

## **Other Experience and Professional Memberships**

### **Society Membership**

1987-present	Society for Glycobiology, USA.
1995-present	American Society for Biochemistry and Molecular Biology.
1999-present	American Association for the Advancement of Science.
2011-present	American Association of Immunologists.
2000-present	American Society of Tropical Medicine and Hygiene.
2003-present	American Society of Microbiology.
1995-2012	American Chemical Society.
2004-2012	American Society for Investigative Pathology.

### **Study Sections and Grant Review Panels**

1996	Ad-hoc Member, Cell Biology 2 Study Section, US Army Breast Cancer Program.
2000	Ad-hoc Member, Comparative Medicine Study Section, NIH.
2000	Ad-hoc Member, Molecular Targeted Drug Discovery for Cancer Study Section, NCI, NIH
2001	Ad-hoc Member, Biochemistry Study Section, NIGM, NIH.
2002-	Grant Review, The Wellcome Trust, London, UK – three times during this period
2005	Member, GCRC Site Visit to University of Rochester, Rochester, NY, NCRR, NIH.
2005	Ad-hoc Member, Pathogenic Eukaryotes (PTHE) Study Section, NIAID, NIH.
2005-present	Member, Promotion and Tenure Committee, Department of Biological Chemistry, Penn State University College of Medicine, Hershey, PA, Hershey.
2006	Member, Study Section, Special Panel for Innate Immune Response to Parasite NIAID, NIH.
2006 and 09	Grant Reviewer, Swiss National Science Foundation, Switzerland.
2007	Member, Special Panel for Infectious, Reproductive, Asthma & Pulmonary Study Section, NIH.
2008	Member, Study Section on Special Emphasis Panel for Development of Novel Interventions and Tools for the Control of Malaria, Neglected Tropical Diseases and their Vectors, NIH.
2009	Grant Reviewer, Maryland Industry and Maryland University Joint Research Program, MD.
2010	Program Grant Reviewer, The Netherlands Organization for Health Research and Development
2011-present	Member, Scientific-Advisory groups, International Center of Excellence in Malaria Research, Thailand.
2013	Ad-hoc Member, Clinical Neuroimmunology and Brain Tumors (CNBT) Study Section, NIH
2014	Member, Cooperative Centers on Human Immunology (U19) - Special Emphasis Review Panel, NIAID, NIH.

### **Journal's Editorial Board member**

2003-2008	<i>Journal of Biological Chemistry</i> , American society for Biochemistry and Molecular Biology.
2011-present	<i>Journal of Biological Chemistry</i> , American society for Biochemistry and Molecular Biology.
2006-present	<i>Current Chemical Biology</i> , Bentham Publishers.
2008-present	<i>Open Glycosciences</i> , Bentham Publishers.
2009-present	<i>Pathology and Laboratory Medicine International</i> , Dove Med. Press.
2009-present	<i>Hematology Research and Reviews</i> , Dove Medical Press.
2009-present	Molecular Biology International, SAGE-Hindawi Publishers.
2010-present	<i>Infection and Immunity</i> , American Society for Microbiology.

### **Awards**

1974	Gold medalist and cash award by the University of Mysore, India, for First Rank in MS.
1980-1981	The Alexander von Humboldt Foundation Fellowship, Germany
1993	Shannon Award from NIH.

1998-2000      Burroughs Wellcome Fund award for New Initiatives in Malaria Research.  
 2006-08        Outstanding Mentor Award for serving in American Society Microbiology. Mentoring Program.  
 2007 and 08    Star Award Recognition for Teaching by PSU Hershey Medical Students.

**C. Selected Peer-reviewed Publications** (Selected from total of 130 peer-reviewed publications)

**Most relevant to the current application**

1. Alkhalil, A., Achur, R.N., Valiyaveettil, M., Ockenhouse, C.F., and **Gowda, D.C.** (2000) Structural requirements for the adherence of *Plasmodium falciparum*-infected erythrocytes to chondroitin sulfate proteoglycan of human placenta. *J. Biol. Chem.* **275**, 40357–40364. PMID: 11005815
2. Achur, R.N., Valiyaveettil, M., Alkhalil, A., Ockenhouse, C.F., and **Gowda, D.C.** (2000) Characterization of proteoglycans of human placenta and identification of unique chondroitin sulfate proteoglycans of the intervillous spaces that mediate the adherence of *Plasmodium falciparum*-infected erythrocytes to the placenta. *J. Biol. Chem.* **275**, 40344–40356. PMID: 11005814
3. O'Neil-Dunne, I., Achur, R.N., Agbor-Enoh, S.T., Valiyaveettil, M., Naik, R.S., Ockenhouse, C.F., Zhou, A., Megnekou, R., Leke, R., Taylor, D.W., and **Gowda, D.C.** (2001) Gravidity-dependent production of antibodies that inhibit binding of *Plasmodium falciparum*-infected erythrocytes to placental chondroitin sulfate proteoglycan during pregnancy. *Infect. Immun.* **69**, 7487–7492. PMID: 11705924.
4. Agbor-Enoh, S.T., Achur, R.N., Valiyaveettil, M., Taylor, D.W., and **Gowda, D.C.** (2002) Expression of chondroitin sulfate proteoglycan and binding of *Plasmodium falciparum*-infected erythrocytes in human placenta during pregnancy. *Infect. Immun.* **71**, 2455–2461. PMID: 12704116
5. Achur, R.N. Valiyaveettil, M., and **Gowda, D.C.** (2003) The low sulfated chondroitin sulfate proteoglycans of human placenta have sulfate group-clustered domains that can efficiently bind *Plasmodium falciparum*-infected erythrocytes. *J. Biol. Chem.* **278**, 11705–11713.
6. Muthusamy, A., Achur, R.N., Bhavanandan, V.P., Fouda, G.G., Taylor, D. W., and **Gowda, D.C.** (2004) *Plasmodium falciparum*-infected erythrocytes adhere both in the intervillous space and on the villous Surface of human placenta by binding to the chondroitin sulfate proteoglycan receptor. *Am. J. Pathol.* **164**, 2013–2025. PMID: 15161637
7. **Gowda, D.C.** (2006) Role of chondroitin 4-sulfate in pregnancy-associated malaria. *Adv. Pharmacol.* **53**, 375–400. PMID: 17239776.
8. Muthusamy, Achur, R.N., Valiyaveettil, M., Botti, J.J., Taylor, D.W., Leke, R.F., and **Gowda, D.C.** (2007) Chondroitin sulfate proteoglycan but not hyaluronic acid is the receptor for the adherence of *Plasmodium falciparum*-infected erythrocytes in human placenta and IRBC adherence upregulates the receptor expression. *Am. J. Pathol.* **170**, 1989-2000. PMID: 17525266; PMCID: PMC1899447.
9. Parkasha Gowda, A.S., Madhunapantula, Acxhur, R. N., S.V., Valiyaveettil, M., Bhavanadhan, V.P., and **Gowda, D.C** (2007) Structural basis for the adherence of *Plasmodium falciparum* infected erythrocytes to chondroitin 4-sulfate and design of novel photoactivable reagents for the identification of parasite adhesive proteins. *J. Biol. Chem.* **282**, 916-928. PMID: 17085451.
10. Singh, K., Gittis, A. G., Nguyen, P., **Gowda, D. C.**, Miller, L. H., Garboczi, D. N. (2008) Structure of the DBL3X domain of pregnancy-associated malaria protein VAR2CSA complexed with chondroitin sulfate A. *Nat Struct Mol Biol.* **15**, 932-938. PMCID: PMC2658892, NIHMSID: NIHMS67061.
11. Achur, R. N., Kakizaki, I., Goel, S., Kaoru Kojima, K., Madhunapantula, S.V., Goyal, A., Ohta, M., Kumar, S., Takagaki, K., and **Gowda, D.C.** (2008) Structural interactions in chondroitin 4-sulfate mediated adherence of *Plasmodium falciparum* infected erythrocytes in human placenta during pregnancy malaria. *Biochemistry*, **47**, 12635-12643. PMCID: PMC2645940, NIHMS72201.
12. Goyal, A., Goel, S., and **Gowda, D. C.** (2009) *Plasmodium falciparum*: assessment of parasite-infected red blood cell binding to placental chondroitin proteoglycan and bovine tracheal chondroitin sulfate A. *Exp. Parasitol.* **123**, 105-110, PMID: 19392627; PMCID: PMC2854576 and NIHMSID: NIHMS191159.

13. Goel, S., Valiyaveetil, M., Achur, R.N., Goyal, A., Mattei, D., Salanti, A., Trenholme, K.R., Gardiner, D.L., D. **Gowda, D.C.** (2010) Dual stage synthesis and crucial role of CLAG9 in the surface expression of malaria parasite *var* proteins. *Proc. Natl. Acad. Sci. USA.* 107, 16643-16648. PMCID: PMC2944715.
14. Singh, K., Gitti, R.K., Diouf, A., Zhou, H., **Gowda, D.C.**, Miura, K., Ostazeski, S.A., Fairhurst R.M., Garboczi, D.N., and Long. C.A. (2010) Subdomain 3 of *Plasmodium falciparum* VAR2CSA DBL3X is identified as a minimal chondroitin sulfate A binding region. *J. Biol. Chem.* 285, 24855-24862. PMCID: PMC2915721
15. Goel, S., and **Gowda, D.C.** (2011) How specific is *Plasmodium falciparum* adherence to chondroitin 4-sulfate? *Trends Parasitol.* **27**, 375-381. PMCID: PMC3153608, NIHMS290564.

## **D. Research Support**

### **Ongoing Research Support**

**D43TW008268**

6/1/2010-5/31/2016

Fogarty International Center, NIH

**Title:** Malaria Research Training in South India

Role: PI

The goal of this project is to train and mentor Indian graduate students, who study malaria epidemiological in Mangalore city, India, for their PhD degree.

**R01 AI041139-17**

01/01/2013-12/31/2017

NIH/NIAID

Innate Immune Responses to Malaria Parasite

Role: PI

The goal of this project is to identify the IL-4-inducing malaria parasite protein, and gain mechanistic insight into the modulation of malaria-induced immune responses by IL-4 and inhibitors of ERK signaling using a cerebral malaria model.

### **Completed Research Support**

**Penn State Department of Health**

3/1/2013-12/31/20113

**Bridge support**

Role: PI

The goal of this project is to express N-and C-terminal portion, and full length VAR2CSA in mammalian cells, purify proteins and study C4S interactions with VAR2CSA.

**Penn State Department of Health**

9/1/2010-12/31/2012

**Bridge support**

Role: PI

The role of this project is to express VAR2CSA DBL domains and study domain interactions.

**R01 AI045086-13**

01/01/2005-12/31/2011

NIH/NIAID

Cytoadherence in Maternal Malaria

Role: PI

The goal of this project is to determine the structural basis for the adhesion of *Plasmodium falciparum*-infected red blood cells to chondroitin sulfate proteoglycan in human placenta.