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BIOGRAPHICAL SKETCH

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NAME: Acharya, Priyamvada

eRA COMMONS USER NAME (credential, e.g., agency login): Acharya001

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Jadavpur University, Kolkata, India	MSc	06/1996	Organic Chemistry
Center for Cellular and Molecular Biology, Hyderabad, India	PhD	09/2003	Biochemistry

A. Personal Statement

As Director of Division of Structural Biology, Duke Human Vaccine Initiative (DHVI), I lead the structural biology program at DHVI. We use cryo-electron microscopy (cryo-EM) and x-ray crystallography for structural determination of antibodies and their complexes with HIV-1 Env immunogens. The Division also runs a core facility for high throughput characterization of immunogens and antibody complexes by negative stain EM. Before joining DHVI on July 1st 2018, working at the Vaccine Research Center (VRC), I used X-ray crystallography to study HIV-1 entry, specifically studying the interactions of HIV-1 Envelope (Env) with its receptors and with antibodies, and applying insights gained from these studies to vaccine design. As part of the CD4 binding site team, I led structural efforts to define Env interactions and the development of neutralization efficacy of antibodies derived from the VH1-46 heavy chain lineage. I co-led structure-guided stabilization of HIV-1 Env that led to the stabilized, and now widely used, Env immunogen DS-SOSIP. I initiated and led structural investigations into antibodies that mediate non-neutralizing functions such as antibody-dependent cell-mediated cytotoxicity (ADCC). I also led structural studies on small molecule interactions of HIV-1 Env and structure-guided drug design, before moving to New York in 2015 (as still a member of the NIH VRC) to join the Simons Electron Microscopy Center (SEMC) at the New York Structural Biology Center (NYSBC) as an embedded scientist to incorporate cryo-EM studies into the VRC vaccine development programs. At NYSBC, I determined the structure of an early HIV-1 entry intermediate with Env bound to a single CD4, and went on to determine more than 10 atomic level structures of HIV-1 Env in complex with antibodies targeting the fusion peptide, V3 glycan region, V1V2 cap, and the CD4 binding site, as well as structures of human parainfluenza virus 3 (hPIV3) Env-antibody complexes. In this application, I will serve as the PI and will lead the team that will determine structures of HIV-1 Env complexes of DH270-lineage antibodies to decipher the structural basis for development of breadth in this lineage..

Positions and Honors

Positions and Employment

2003-2005 Visiting Scientist, Max Planck Institute of Biophysics, Frankfurt, Germany, and Max Planck Institute for Terrestrial Microbiology, Marburg, Germany

2005-2009 Visiting Fellow, Structural Biology Section (SBS), Vaccine Research Center (VRC), National Institutes of Allergy and Infectious diseases (NIAID), National Institutes of Health (NIH), Bethesda, Maryland, USA

2009-2013 Research Fellow, SBS/VRC/NIAID/NIH, Bethesda, Maryland, USA

2013-2015 SBS/VRC/NIAID/NIH Bethesda, Maryland, USA
2015-June 29, 2018 Research Scientist, Simons Electron Microscopy Center (SEMC), New York Structural Biology Center (NYSBC), New York, and SBS/VRC/NIAID/NIH, Bethesda, Maryland, USA
July 1, 2018- present- Associate Professor and Director of Structural Biology, Duke Human Vaccine Institute, Department of Surgery, Duke School of Medicine, Durham, NC, USA

Honors

1997 Junior Research Fellowship, Council of Scientific and Industrial Research (CSIR), India
1999 Senior Research Fellowship, CSIR, India
2017 Robert P. Apkarian Memorial Scholarship, Microscopy and Microanalysis Meeting
2017 Distinguished Achievement Award, NIH/Kelly Government Solutions
2018 Distinguished Achievement Award, NIH/Kelly Government Solutions
2018 Young Faculty Award, Duke Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery (CHAVI-ID)

B. Contributions to Science

1. Working on interactions of HIV-1 Env with coreceptors, I combined information from X-ray crystallography and NMR to determine structure of CCR5 N terminus bound to HIV-1 Env. I then used this structural information, and developed a high-throughput ELISA-based assay in collaboration with Dr. Carole Bewley, to discover small molecule mimetics of the CCR5 N terminus that inhibited entry of diverse HIV-1 strains. I went on to collaborate with the Bewley lab to reveal interactions of the second extracellular loop of CCR5 with HIV-1 Env.
    a. Huang CC, Lam SN, Acharya P, Tang M, Xiang SH, Hussan SS, Stanfield RL, Robinson J, Sodroski J, Wilson IA, Wyatt R, Bewley CA, Kwong PD. **Structures of the CCR5 N terminus and of a tyrosine-sulfated antibody with HIV-1 gp120 and CD4.** *Science*, 317(5846):1930-1934, Sep 2007. PMCID: PMC2278242
    b. Lam SN, Acharya P, Wyatt RT, Kwong PD, Bewley CA. **Tyrosine-sulfate isosteres of CCR5 N-terminus as tools for studying HIV-1 entry.** *Bioorganic and Medicinal Chemistry*, 16(23):10113-10120, Dec 2008. PMCID: PMC2650494
    c. Acharya P, Dogo-Isonagie C, LaLonde JM, Lam SN, Leslie GJ, Louder MK, Frye LL, Debnath AK, Greenwood JR, Luongo TS, Martin L, Watts KS, Hoxie JA, Mascola JR, Bewley CA, Kwong PD. **Structure-based identification and neutralization mechanism of tyrosine sulfate mimetics that inhibit HIV-1 entry.** *ACS Chemical Biol*, 6(10):1069-1077, Oct 2011. PMCID: PMC2650494
    d. Dogo-Isonagie C, Lam S, Gustchina E, Acharya P, Yang Y, Shahzad-ul-Hussan S, Clore GM, Kwong PD, Bewley CA. **Peptides from second extracellular loop of C-C chemokine receptor type 5 (CCR5) inhibit diverse strains of HIV-1.** *J Biol Chem*, 287(18):15076-15086, Apr 2012. PMCID: PMC3340262

2. Led structural investigations in a multi-institutional collaboration that developed a highly potent HIV-1 entry inhibitor M48U1. I solved the structure of M48U1 bound to HIV-1 gp120 at 1.5 Å resolution, which is the highest resolution structure determined for an HIV-1 Env complex to date. This structure formd the basis for structure-guided design of M48U12, an inhibitor with further improved HIV-1 neutraliation efficacy.
    a. Acharya P, Luongo TS, Louder MK, McKee K, Yang Y, Do Kwon Y, Mascola JR, Kessler P, Martin L, Kwong PD. **Structural basis for highly effective HIV-1 neutralization by CD4-mimetic miniproteins revealed by 1.5 Å cocrystal structure of gp120 and M48U1.** *Structure*, 21(6):1018-1029, Jun 2013. PMCID: PMC4140785
    b. Morellato-Castillo L§, Acharya P§, Combes O, Michiels J, Descours A, Ramos OH, Yang Y, Vanham G, Ariën KK, Kwong PD, Martin L, Kessler P. **Interfacial Cavity Filling To Optimize CD4-Mimetic Miniprotein Interactions with HIV-1 Surface Glycoprotein.** *J Med Chem*, 56(12):5033-5047, Jun 2013. (§ Co-first author). PMCID: PMC3812931

3. Working with the CD4 binding site team of the Structural Biology Section at VRC, I led structural investigations into HIV-1 neutralizing antibodies derived from the .VH1-46 heavy chain germline, and demonstrated a mode of binding distinct from the VRC01-class that derived from the VH1-2 germline.

a. Zhou T, Zhu J, Wu X, Moquin S, Zhang B, Acharya P, Georgiev IS, Altae-Tran HR, Chuang GY, Joyce MG, Do Kwon Y, Longo NS, Louder MK, Luongo TS, McKee K, Schramm CA, Skinner J, Yang Y, Yang Z, Zhang Z, Zheng A, Bonsignori M, Haynes BF, Scheid JF, Nussenzweig MC, Simek M, Burton DR, Koff WC, NISC Comparative Sequencing Program, Mullikin JC, Connors M, Shapiro L, Nabel GJ, Mascola JR, Kwong PD. **Multidonor Analysis Reveals Structural Elements, Genetic Determinants, and Maturation Pathway for HIV-1 Neutralization by VRC01-Class Antibodies.** *Immunity*, 39(2):245-258, Aug 2013. PMCID: PMC3985390
b. Zhou T§, Lynch RM§, Chen L§, Acharya P§, Wu X, Doria-Rose NA, Joyce MG, Lingwood D, Soto C, Bailer RT, Ernandes MJ, Kong R, Longo NS, Louder MK, McKee K, O'Dell S, Schmidt SD, Tran L, Yang Z, Druz A, Luongo TS, Moquin S, Srivatsan S, Yang Y, Zhang B, Zheng A, Pancera M, Kirys T, Georgiev IS, Gindin T, Peng HP, Yang AS; NISC Comparative Sequencing Program, Mullikin JC, Gray MD, Stamatatos L, Burton DR, Koff WC, Cohen MS, Haynes BF, Casazza JP, Connors M, Corti D, Lanzavecchia A, Sattentau QJ, Weiss RA, West AP Jr, Bjorkman PJ, Scheid JF, Nussenzweig MC, Shapiro L, Mascola JR, Kwong PD. **Structural Repertoire of HIV-1-Neutralizing Antibodies Targeting the CD4 Supersite in 14 Donors.** *Cell*, 161(6):1280-1292, May 2015. (§ Co-first author). PMCID: PMC4683157
c. Bonsignori M, Zhou T, Sheng Z, Chen L, Gao F, Joyce MG, Ozorowski G, Chuang GY, Schramm CA, Wiehe K, Alam SM, Bradley T, Gladden MA, Hwang KK, Iyengar S, Kumar A, Lu X, Luo K, Mangiapani MC, Parks RJ, Song H, Acharya P, Bailer RT, Cao A, Druz A, Georgiev IS, Kwon YD, Louder MK, Zhang B, Zheng A, Hill BJ, Kong R, Soto C; NISC Comparative Sequencing Program, Mullikin JC, Douek DC, Montefiori DC, Moody MA, Shaw GM, Hahn BH, Kelsoe G, Hraber PT, Korber BT, Boyd SD, Fire AZ, Kepler TB, Shapiro L, Ward AB, Mascola JR, Liao HX, Kwong PD, Haynes BF. **Maturation Pathway from Germline to Broad HIV-1 Neutralizer of a CD4-Mimic Antibody.** *Cell*, 165(2):449-463, Apr 2016. PMCID: PMC4826291

4. Determined the structure of A32-like antibody 2.2c in complex with HIV-1 gp120. A32-like antibodies target the gp41-interactive region of gp120 at its N terminus, and become exposed on the surface of the native Env spike at the later stages of viral entry following receptor engagement. In a a subsequent collaboration with Dr. Marzena Pazgier I solved structures of other A32-like antibodies, studies from which we were able to glean insights into the recognition of antibodies that mediate potent antibody-dependent cellular cytotoxicity (ADCC).
    a. Acharya P, Tolbert WD, Gohain N, Wu X, Yu L, Liu T, Huang W, Huang CC, Do Kwon Y, Louder RK, Luongo TS, McLellan JS, Pancera M, Yang Y, Zhang B, Flinko R, Foulke JS Jr, Sajadi MM, Kamin-Lewis R, Robinson JE, Martin L, Kwong PD, Guan Y, DeVico AL, Lewis GK, Pazgier M. **Structural Definition of an Antibody-Dependent Cellular Cytotoxicity (ADCC) Response Implicated in Reduced Risk for HIV-1 Infection.** *J Virol*, 88(21):12895-12906, Aug 2014. PMCID: PMC4248932
    b. Gohain N, Tolbert WD, Acharya P, Yu L, Liu T, Zhao P, Orlandi C, Visciano ML, Kamin-Lewis R, Sajadi MM, Martin L, Robinson JE, Kwong PD, DeVico AL, Ray K, Lewis GK, Pazgier M. **Cocrystal Structures of Antibody N60-i3 and Antibody JR4 in Complex with gp120 Define More Cluster A Epitopes Involved in Effective Antibody-Dependent Effector Function against HIV-1.** *J Virol*, 89(17):8840-8854, Jun 2015. PMCID: PMC4524080

5. Co-led the team that developed DS-SOSIP – an Env construct stabilized by disulfides designed to resist CD4-induced structural changes. DS-SOSIP is currently being manufactured at the VRC for use as an immunogen, and is widely used in the field for vaccine studies. We also used DS-SOSIP as the basis for developing further stabilized immunogens. I led the antigenic analyses in this study, which involved development of a screening assay that could be implemented in a medium to high-throughput format on 100s of constructs, implementation of the assay in both rapid, ELISA-based formats for screening, and for use in surface plasmon resonance and biolayer interferometry studies to precisely define interaction parameters. It also involved analyzing the results of the antigenicity screens to make decisions on which constructs to take to the next steps of design and development. I performed mechanistic studies on DS-SOSIP and showed that it binds only one CD4 molecule, likely mimicking a very early entry intermediate. Using cryo-EM, I determined the structure of BG505 DS-SOSIP bound to a single CD4 – a structure that revealed quaternary contacts made by CD4 on HIV-1 Env and a larger interactive surface for CD4 interaction than was known from earlier structures of gp120-bound CD4. These studies impact our

understanding of the CD4-binding site with implications for vaccine development targeting this site.

a. Kwon YD§, Pancera M§, Acharya P§, Georgiev IS§, Crooks ET, Gorman J, Joyce MG, Guttman M, Ma X, Narpala S, Soto C, Terry DS, Yang Y, Zhou T, Ahlsen G, Bailer RT, Chambers M, Chuang GY, Doria-Rose NA, Druz A, Hallen MA, Harned A, Kirys T, Louder MK, O'Dell S, Ofek G, Osawa K, Prabhakaran M, Sastry M, Stewart-Jones GB, Stuckey J, Thomas PV, Tittley T, Williams C, Zhang B, Zhao H, Zhou Z, Donald BR, Lee LK, Zolla-Pazner S, Baxa U, Schön A, Freire E, Shapiro L, Lee KK, Arthos J, Munro JB, Blanchard SC, Mothes W, Binley JM, McDermott AB, Mascola JR, Kwong PD. **Crystal structure, conformational fixation and entry-related interactions of mature ligand-free HIV-1 Env.** *Nat Struct Mol Biol*, 22(7):522-531, Jul 2015. (§ Co-first author). PMCID: PMC4706170
b. Liu Q§, Acharya P§, Dolan MA, Zhang P, Guzzo C, Lu J, Kwon A, Gururani D, Miao H, Bylund T, Chuang GY, Druz A, Zhou T, Rice W, Wigge C, Carragher B, Potter CS, Kwong PD, Lusso P. **Structure and functional characterization of the initial quaternary contact of CD4 with the HIV-1 envelope trimer.** *Nat Struc Mol Biol*, 24(4):370-378, Apr 2017. (§ Co-first author). PMCID: PMC
c. Chuang GY, Geng H, Pancera M, Xu K, Cheng C, Acharya P, Chambers M, Druz A, Tsybovsky Y, Wanninger T, Yang Y, Doria-Rose N, Georgiev I, Gorman J, Joyce MG, O'Dell S, Zhou T, McDermott A, Mascola J, Kwong PD. **Structure-Based Design of a Soluble Prefusion-Closed HIV-1-Env Trimer with Reduced CD4 Affinity and Improved Immunogenicity.** *J Virol*, 91(10): e02268-16, May, 2017. PMCID: PMC
d. Georgiev IS, Joyce MG, Chen RE, Leung K, McKee K, Druz A, Van Galen JG, Kanekiyo M, Tsybovsky Y, Yang ES, Yang Y, Acharya P, Pancera M, Thomas PV, Wanninger T, Yassine HM, Baxa U, Doria-Rose NA, Cheng C, Graham BS, Mascola JR, Kwong PD. **Two-Component Ferritin Nanoparticles for Multimerization of Diverse Trimeric Antigens.** *ACS Infect Dis*, doi: 10.1021/acsinfecdis.7b00192, Mar 2018. [Epub ahead of print].

6. Led mechanistic investigations and cryo-EM structural determination of antibodies that target the HIV-1 Env fusion peptide. Here I solved the structures of 4 fusion peptide-directed antibodies, at resolutions ranging from 3.6-4.4 Å, by cryo-EM. These structure-function studies revealed distinct modes of antibody recognition of the fusion peptide, wherein naturally elicited antibody VRC34 recognizes an extended conformation of the fusion peptide and makes functional contacts with regions outside the fusion peptide, whereas, antibodies elicited through vaccination of mice recognize a helical fusion peptide with recognition focused on the fusion peptide, with little contributions from other Env regions.
    a. Kong R, Xu K, Zhou T, Acharya P, Lemmin T, Liu K, Ozorowski G, Soto C, Taft JD, Bailer RT, Cale EM, Chen L, Choi CW, Chuang GY, Doria-Rose NA, Druz A, Georgiev IS, Gorman J, Huang J, Joyce MG, Louder MK, Ma X, McKee K, O'Dell S, Pancera M, Yang Y, Blanchard SC, Mothes W, Burton DR, Koff WC, Connors M, Ward AB, Kwong PD, Mascola JR. **Fusion peptide of HIV-1 as a site of vulnerability to neutralizing antibody.** *Science*, 352(6287):828-833, May 2016. PMCID: PMC4917739
    b. Kai X§, Acharya P§, Kong R§, Cheng Cheng§, Chuang G, Liu K, Louder MK, O'Dell S, Rawi R, Sastry M, Shen C, Zhang, B, Zhou T, Asokan M, Bailer RT, Chambers M, Chen X, hoi CW, Dandey VP, Doria-Rose N, Druz A, Eng ET, Farney K, Foulds KE, Geng H, Georgiev IS, Gorman J, Hill KR, Jafari AJ, Kwon YD, Lai YT, Lemmin T, McKee K, Ohr TY, Ou L, Peng D, Roshan AP, Sheng Z, Todd JP, Tsybovsky Y, Viox EG, Wang Y, Wei H, Yang Y, Zhou AF, Chen R, Yang L, Scorpio DG, McDermott AB, Shapiro L, Carragher B, Potter CS, Mascola JR, Kwong PD. **Epitope-based vaccine design yields fusion peptide-directed antibodies that neutralize diverse strains of HIV-1.** *Nat Med*, 24(6):857-867, June 2018 (§ Co-first author)
    c. Dingens AS§, Acharya P§, Haddox HK, Rawi R, Xu K, Chuang G, Wei H, Mascola JR, Carragher B, Potter CS, Overbaugh J, Kwong PD, Bloom, JD. (2018) **Epitope-based vaccine design yields fusion peptide-directed antibodies that neutralize diverse strains of HIV-1.** Plos Pathogens, 14(7):e1007159, Jul 2018. (§ Co-first author)

Complete Listing of Published Work: https://tinyurl.com/y7aml25x