PRABAKARAN (PRABA) PONRAJ, Ph.D.

Email: praba.ponraj@gmail.com | Tel.: 301-606-1828
https://www.linkedin.com/in/prabakaran-ponraj/

EXECUTIVE SUMMARY

Accomplished scientific leader in AI/ML-driven antibody discovery and structural biology, with a proven record of advancing therapeutic protein engineering from concept to clinical development. Led computational design initiatives delivering a patented CD4 HIV inhibitor (Phase I) and patented HBV/HPV vaccine technologies, demonstrating the ability to translate innovation into impact. Expert in integrating deep learning, antibody repertoire analytics, and structure-guided design to develop next-generation biologics, including multispecifics, VHHs, and engineered scaffolds. Built and scaled pipelines leveraging AlphaFold, ProteinMPNN, diffusion models, and geometric deep learning to drive data-informed antibody design and developability optimization. Editorial Board Member (Frontiers in Immunology, Antibodies); published 70+ research papers in prestigious journals including Nature Communications, Cell Reports, Journal of Molecular Biology, and Journal of Biological Chemistry (4,700+ citations); authored correspondence in Nature and co-authored News & Views in Nature Biotechnology.

TECHNICAL SKILLS

- **AI/ML & Deep Learning**: Generative models (RFDiffusion, ProteinMPNN, EvoDiff), diffusion models, VAEs, GANs, Graph Neural Networks, protein language models (ESM-2), AlphaFold
- **Computational Biology**: Structure-based protein design, multi-property optimization, sequence-structure relationships, high-throughput computational screening
- **Protein Engineering**: Antibody design and optimization, developability, VHHs, multispecifics, CARs, TCRs
- **Programming & Infrastructure**: Python, PyTorch, TensorFlow, AWS, HPC, ML pipeline development
- **Structural Biology**: X-ray crystallography, molecular modeling, AlphaFold, RosettaFold, PDB and CSD
- **Data Analysis**: NGS data analysis, high-dimensional data analysis, statistical modeling, bioinformatics pipelines

KEY ACHIEVEMENTS

- First X-ray structure of SARS-CoV antibody complex (PDB 2DD8)
- Built computational pipelines for antibody discovery and AI-driven big data analysis for drug development
- Sanofi “We R Hope Award” and NIH Technology Transfer Award recipient

PROFESSIONAL EXPERIENCE

Independent Consultant - AI/ML in Protein Engineering (July 2024 - Present) *Moderna, Cambridge, MA and Galapagous NV*

- Implementing GAN, VAE, and diffusion models for therapeutic antibody design and optimization
- Developing deep learning frameworks for antibody developability assessment and clinical-likeness prediction
- Creating automated workflows for AI/ML-driven antibody library design and screening

Senior Principal Scientist, AI Innovation - Antibodies (2018 - 2024) *Sanofi, Cambridge, MA*

- Led analysis of 150M+ antibody sequences using ML for novel diversity discovery and pattern recognition
- Developed and validated 100k in-silico common light chain library using AI-powered screening
- Created ML models for antigen-antibody binding prediction and antibody expression optimization
- Spearheaded collaborations with EMBL, MIT, and Harvard on innovative AI initiatives
- Established workflows integrating structural biology with deep learning for de novo antibody generation

Senior Scientist, Human Therapeutics Development (2015 - 2018) *Intrexon Corporation, Germantown, MD*

- Developed computational platform for antibody humanization and optimization
- Designed novel protein scaffolds using structure-based computational approaches
- Created high-throughput screening workflows for therapeutic candidates

Earlier Career Highlights:

- Engineered an HIV inhibitor advancing to Phase 1 trials using computational design (Leidos/NIH)
- Pioneered antibodyome analysis and Virology using advanced bioinformatics (Duke, UT SouthWestern)
- Solved multiple therapeutic protein structures, including first SARS-CoV antibody complex (NCI-NIH)
- Developed novel protein-DNA interaction classification systems, ProNIT Database (RIKEN)

EDUCATION

- **Doctor of Philosophy (PhD) in Physics (X-ray Crystallogrphy),** Bharathidasan University, India
- **Post Graduate Diploma, Computer Science,** Bharathidasan University, India

PATENTS

- Dimiter S. Dimitrov DS, Chen W, **Prabakaran P**. "Stabilized single human cd4 domains and fusion proteins" (2014) (US20160039904A1; WO2014150748A2).
- Brough DE, Bolinger CG, Yarlagadda R, Kurella V, **Prabakaran P,** Metenou S, Ding K-F. "Human papillomavirus vaccines and uses of the same" (2018) (WO2019173465A1).

SELECTED PUBLICATIONS (from 70+ peer-reviewed papers, *-corresponding author**)**

1. **Prabakaran P***, Gupta A, Rao SP, Rajpal D, Wendt M, **Qiu Y***, **Chowdhury PS***. "Unveiling inverted D genes and D-D fusions in human antibody repertoires unlocks novel antibody diversity." **Commun. Biol.** 2025, 133.
2. Shahsavarian M, Watkins T, **Prabakaran P***, Carr A, Wendt M and Qiu Y. "Bioinformatics Analyses of Antibody Repertoires and Their Roles in Modern Antibody Drug Discovery". **Biopharmaceutical Informatics: Learning How to Discover Developable Biotherapeutics**, Taylor & Francis 2025. Editors: Sandeep Kumar and Andrew E. Nixon.
3. **Prabakaran P***, Rao SP and Wendt M. "Animal immunization merges with innovative technologies: A new paradigm shift in antibody discovery". **mAbs** 2021. Jan-Dec 2021;13(1):1924347.
4. **Prabakaran P*** and **Chowdhury PS***. "Immunogenetic Analysis Reveals a Novel Landscape of Non-Canonical Cysteines in Human VH Repertoire." **Cell Reports** 2020. 31(13):107831
5. Haque A, Mahendra A, **Prabakaran P**, Mackness BC, Wang YH, Amatya N, Yu X, Hopke J, Zhang N, Cho HS, Zhang R, Sancho J, Saleh J, Rao SP, Wendt M, Chowdhury, PS. "Honing-in antigen-specific cells during antibody discovery: a user-friendly process to mine a deeper repertoire". **Commun. Biol**. 2022; 30;5(1):1157.
6. Zhang R, **Prabakaran P**, Yu X, Mackness BC, Boudanova E, Hopke J, Sancho J, Saleh J, Cho HS, Zhang N, Mannes HS, Stimple S, Hoffmann D, Park A, Chowdhury PS, Rao SP "A platform-agnostic, function first-based antibody discovery strategy using plasmid-free mammalian expression of antibodies" **mAbs** 2021;13(1):1904546.
7. Jung J, Mundle ST, Ustyugova IV, Andrew P. Horton AP, Daniel R. Boutz DR, Pougatcheva S, **Prabakaran P**, Jonathan R. McDaniel JR, Gregory R. King GR, Park D, Maria D. Person MD, Ye C, Tan B, Tanno Y, DiNapoli J, Delagrave S, Wilson PC, Ross TM, Ippolito GC, Kleanthous H, Lee J, Georgiou G. "High Prevalence of Serum Monoclonal Antibodies to Non-Hemagglutinin Antigens Including Sulfated Glycans in the Elderly after Seasonal Influenza Vaccination" **Journal of Clinical Investigation** 2021. 131(13): e148763.
8. **Prabakaran P***, Glanville J, Ippolito GC. "Next-Generation Sequencing of Human Antibody Repertoires for Exploring B-cell Landscape, Antibody Discovery and Vaccine Development." **Front. Immunol.** 2020, 11:1344
9. **Prabakaran P***. "Next-generation sequencing may challenge antibody patent claims." **Nature** 2018, 557(7704), 166
10. **Prabakaran P** and Dimitrov DS. "Human Antibody Structure and Function", **Protein Therapeutics, Wiley-VCH**. 2017. Editors: Tristan Vaughan, Jane Osbourn, Bahija Jallal.
11. Li W, **Prabakaran P**, Chen W, Zhu Z, Feng Y and Dimitrov DS. "Antibody Aggregation: Insights from Sequence and Structure" **Antibodies** 2016, 5(3), 19.
12. Ying T, **Prabakaran P**, Dimitrov DS. "A systems approach to HIV-1 vaccines." **Nature Biotechnol.** 2016, 34(1):44-6
13. Ying T, **Prabakaran P**, Du L, et al. "A novel critical role in MERS-CoV neutralization by an exceptionally potent germline-like antibody." **Nature Commun.** 2015, 15;6:8223
14. **Prabakaran P***, Chen W, Dimitrov DS. "Elicitation of broadly neutralizing antibodies against HIV-1 – the germline/maturation hypothesis." **Front. Immunol.** 2014, 28;5:398
15. Xiao M, **Prabakaran P***, Chen W, Kessing B*, Dimitrov DS. "Deep Sequencing and Circos Analyses of Antibody Libraries Reveal Antigen-driven Selection of Ig VH Genes during HIV-1 Infection." **Exp Mol Pathol.** 2013, 95(3):357-63 [Cover article]
16. **Prabakaran P**, Gan J, Feng Y, et al. "Structure of SARS Coronavirus Receptor-Binding Domain Complexed with Neutralizing Antibody." **J Biol. Chem.** 2006, 281(23): 15829-36
17. **Prabakaran P**, Gan J, Wu Y, et al. "Structural mimicry of CD4 by a cross-reactive HIV-1 neutralizing antibody with CDR-H2 and H3 containing unique motifs." **J. Mol. Biol.** 2006, 357(1): 82-99

Google Scholar Citations: 4500+, h-index: 32
Full list: https://scholar.google.com/citations?user=s1UkTM0AAAAJ&hl=en