

PRABAKARAN (PRABA) PONRAJ, Ph.D.

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SUMMARY

Innovative leader in antibody discovery and engineering with a robust track record in advancing therapeutic protein design. Expertise in antibody repertoire profiling, and integrating NGS techniques and analysis with in-vivo and in-vitro display-based antibody discovery and screening and novel library designs. Combining rational design, AI/ML applications, and evolutionary approaches to develop novel antibody modalities, including multispecifics and other advanced constructs. Leverage AlphaFold, ESM2, ProteinMPNN, protein language models, and geometric deep learning for modern antibody discovery. Led antibody/protein scaffolds and engineering for next-gen biologics discovery and improved developability. Proven ability to lead cross-functional teams, manage CROs, and drive projects from discovery to development.

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

- Led development of protein design platform using GAN, VAE, and diffusion models for therapeutic antibodies
- Implementing deep learning frameworks for assessing developability for antibody library and binders
- Developed 100k in-silico common light chain library using ML, resulting in target specific candidates
- Awarded Sanofi's "We R Hope Award" and NIH Technology Transfer Award for innovation in protein engineering
- Published 70+ papers in computational biology, structural modeling and protein/antibody engineering

PROFESSIONAL EXPERIENCE

Associate Director, Computational Biology & Bioinformatics (2025 - Present) Institute for Protein Innovation, *Boston, MA*

- Driving antibody discovery and protein engineering through AI, bioinformatics, and open science collaboration
- Developing integrative tools, leading scientific strategy, and advancing protein science innovation.

Independent Consultant, AI/ML in Protein Engineering (2024 - 2025) *Moderna, Cambridge, MA and Galapagos NV*

- Implemented GAN, VAE, and diffusion models for therapeutic antibody design and optimization
- Created automated workflows for AI/ML-driven antibody library design and screening

Senior Principal Scientist, AI Innovation & Antibody Discovery (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
- Established workflows integrating structural biology with deep learning for de novo antibody generation

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

- Developed computational platform for antibody humanization and optimization
- Designed novel protein scaffolds using structure-based computational approaches

Earlier Career Highlights:

- Engineered an HIV inhibitor advancing to Phase 1 trials using computational design (Leidos/NIH)
- Pioneered antibodyome analysis and Oversaw building X-ray core facility (Duke)
- 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 Crystallography)**, 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. Shamsavarian 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: 4750+, h-index: 33

Full list: <https://scholar.google.com/citations?user=s1UkTM0AAAAJ&hl=en>