Evangelos Papadopoulos, Ph.D.
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Major Accomplishments:

- Design and development of bivalent compounds for treatment of Cystic Fibrosis, Stablix Inc.
  - -Licensed to Vertex
- Design and development of allosteric protein-protein (eIF4E-eIF4G) interactions inhibitors, PIC tx.
  - -Promoted to IND enabling studies.
- Resolved co-crystal and liquid state NMR structure of inhibitor eIF4E complex, Harvard Medical School.
  - -Licensed to PIC tx.
- Worked in Molecular Dynamics, Machine Learning and AI projects for drug discovery, Stony Brook University.
  - -Work published in BioRxiv.

Professional Summary:
Biotech scientist with 15 years of combined industry and academic experience focused on drug discovery and development. Skilled in protein biochemistry, structural biology, and computational drug discovery, with hands-on expertise in molecular dynamics, machine learning, and advanced NMR/X-ray techniques. Recognized for managing high-impact projects, leading cross-functional teams, and achieving drug development milestones in complex biopharma environments.

- 15 years of extensive private sector and academic professional work experience in biotech science, with a global outlook based on time spent in various countries.
- Curated Benchling ELN databases, CRO quality control and high throughput assay data for hundreds of plasmids and proteins and thousands of experimental drug assay results.
- Produced DNA clones of significant mutations to be tested in cell lines.
- Screened in-silico millions of select chemical compounds potentially purchasable from MCULE against 10 target proteins and ordered hundreds to be assayed.
- Managed a team that performed DNA cloning, cell culture, western blots, and drug assays for the production, purification, drug assay and X-ray crystallography of proteins.

Skills Summary:

Skills	Experience
Protein Biochemistry and characterization (Cloning, expression, purification, bioconjugation)	10+ years (top expert)
Structural Biology (liquid state NMR, X-ray crystallography, isotope protein labelling)	10+ years (top expert)
Computational Biology (PyMol, GROMACS, NAMD-VMD, CHIMERA, MOE, Schrodinger)	10+ years (top expert)
ELN data management (Benchling, LiveDesign, CDD, DataWarrior, Scinamic)	5+ Years
Python, HTML, R, MATLAB, Bash Scripting	10+ years
Bioinformatics (AWS, Slurm, RNA-Seq)	5+ Years
SQL, Pandas, Matplotlib	5+ years

Summary:

- Conducted research for ten years at Harvard Medical School, Dana Farber Cancer Institute and Beth Israel Deaconess Medical Centre.
- Worked at PIC Tx, a spin-off startup company based on research involved in at Harvard.
- Developed bifunctional small molecule drugs while working at Stablix, Inc.
- Determined the crystal structure of many drug-protein complexes and identified various novel drug binding pockets.
- Explained the inhibition mechanism that saved significant time in the pursuit of new chemical matter for drug development.
- Reported findings in several publications, such as Nature Communications and PNAS.
- Received multiple major awards in mathematics.
- Also, awarded molecule of the month cover feature of the PDB website at Rutgers University.
- Recognized for collaboration with people from different cultures, backgrounds, levels, views; flexibility and ability to adapt to change quickly; complex analytical skills, implementing problem-solving methodology, and passion for projects that improve patients' lives.
- Strong interpersonal, verbal, written and presentation skills and an innovative thinker, as demonstrated by publications written and awards received for novel scientific discoveries.

Technical Skills:

- **Structural Biology-Biophysics (Top expert):** Liquid state NMR, X-ray crystallography, macromolecular visualization, drug discovery, structure prediction, genomics, proteomics structural and molecular informatics analysis, drugability, protein binding pockets analysis, computational and systems biology, docking, molecular dynamics simulations, High Throughput Screening, biophysical assays: MST, FP, TR-FRET, CD, DLS, ITC, SPR, FCS, HPLC, LC-MS.
- **Software-Computing:** Linux/ Windows scripting languages, Python, R, MATLAB, Fortran, html, Bioinformatics, Cheminformatics, Scientific computing simulations, predictive multivariate linear regression, statistical test analysis, algorithms development, datasets analysis, data sources integration and representation, single board computers, neural network deep learning applications, machine learning, AlphaFold, ColabFold, Rosetta.
- **Biochemistry-Biology (Top expert):** Molecular Biology, oligonucleotide primer design, gene-DNA cloning, site directed mutagenesis, protein expression in E. Coli and insect cells, isotope protein expression, protein purification, bioconjugation, FPLC chromatography, membrane dialysis, ultracentrifugation, refolding, cell culture maintenance, transfection, and drug treatment. CRISPR/Cas-9 knock out, cell viability, protein pull down, luciferase expression profiling, western blots, drug assays, cell assays, chemical biology assays, enzyme design, enzyme activity.
- **Computational-Biology (Top expert):** CDD Vault, LiveDesign, DataWarrior, Rdkit, obabel, Autodock, Schrödinger suite, PyMol, MOE, cell growth and metabolism models, model-based control, lux balance analysis, genome-scale metabolic models, cellular kinetics.
- **Languages:** Greek native speaker, basic to moderate proficiency in German, French, Swedish and Russian.

Professional Experience:

Dana Farber Cancer Institute, Boston, MA **2020 – Current**
Research Scientist – Medical Oncology

- Dr. Mitsiades' lab specializes in cancer cell therapy and personalized medicine for mainly multiple myeloma and breast cancer.
- Report to Dr. Mitsiades and managed a team that performed DNA cloning, cell culture, western blots, and drug assays for engineered and patients' primary cells. Analysed CRISPR/Cas-9 derived bioinformatics data about disease relevant mutations, visualized the respective protein structures and determined the importance of the mutations in relation to drug therapies.
- Illustrated hundreds of significant protein mutations and analysed them against a panel of FDA approved drugs.
- Produced DNA clones of significant mutations to be tested in cell lines.
- Docked millions of purchasable compounds against the significant proteins for Multiple Myeloma to find novel drugs.
- Docked thousands of FDA approved compounds against the significant proteins for Multiple Myeloma for potential drug repurposing.

Stablix Inc, New York City, NY and Boston, MA **2021 – 2023**
Senior Scientist – (Biomolecular and Computational Sciences)

- Developed bifunctional chemical molecules for targeted de-ubiquitination as novel therapeutic drugs.
- Reported to the head of the BMS department and led a team. Worked with integrated CROs for the production, purification, drug assay and X-ray crystallography of proteins and bioconjugation.
- Partnered with multiple chemists for the analysis of active chemical matter space derived by DEL (DNA Encoded Libraries) and ASMS (Affinity Selection Mass Spectrometry). Led effort to identify novel binding pockets, ran high throughput virtual screens and ordered chemical matter of interest based on activity, chemical similarity, core hopping and substructure.
- Identified and implemented a streamlined process for managing production, purification, and inventory of more than a hundred different protein constructs expressed in E. Coli and insect cells.
- Curated ELN databases for hundreds of plasmids and proteins and thousands of experimental drug assay results.
- Characterized more than 6000 small molecules for binding and activity on DUBs (Deubiquitinases) and protein targets. Including techniques like SPR, MST, liquid state NMR.
- Screened in-silico 5 million select chemical compounds potentially purchasable from MCULE against 10 target proteins and ordered hundreds to be assayed.
- Introduced tools to look for similar chemicals in libraries containing billions of compounds available to purchase like ZINC, ENAMINE and ordered diversity sets of hundreds of compounds to be tested for SAR (Structure Activity Relationship) analysis.

PIC therapeutics, Boston, MA **2017 – 2020**
Research Scientist – Drug Development

- Develops protein translation inhibitors as small molecule drugs for cancer.
- Developed high throughput drug assays performed in house and with the CRO CEPTER. Worked on the cell culture and drug assays to test the drugs efficiency in protein translation inhibition in live cell lines and cell extracts.
- Tested -approximately three hundred compounds by FP and TR-FRET activity assay.
- Verified the protein translation inhibition in a dozen different cell lines.
- Docked 100 million purchasable compounds from the ENAMINE chemical library to crystal structures.

Harvard Medical School, Boston, MA **2009 – 2017**
Research Scholar

- Professor Wagner's lab specializes in the research of protein translation initiation factors and inhibitors as antitumor agents.
- Reported to Professor Wagner and managed a team. Cloned, expressed, and purified proteins. Purified isotope labelled proteins for liquid state NMR. Performed drug assays by FP, NMR, and set-up crystallization, bioconjugation. Focused on the protein translation factor eIF4E that leads the RNA from the nucleus to the ribosome and the inhibitor 4EGI1 (protein translation is hyperactivated in cancer cells and inhibition can be therapeutic).
- Analysed drug 4EGI1 binding mechanism to protein eIF4E by liquid state NMR.
- Collected X-ray diffraction data at the APS Synchrotron in Argonne Lab for the eIF4E-4EGI1 complex.
- Studied AGO2 interactions with eIF1A by Western Blot and NMR assays.
- Discovered the first structure of eIF4E with the novel drug 4EGI (PDB molecule of the month February 2019).
- Designed and collaborated for the synthesis and testing of a PROTAC E3 ligase recruiter bifunctional analogue of 4EGI(these molecules can destroy eIF4E and halt protein translation initiation).
- Modified antibodies to attach fluorescent and paramagnetic metals, functional groups for TR-FRET and NMR.

Beth Israel Deaconess Medical Center, Boston, MA **2008 – 2012**
Post-doctoral Associate – Experimental Medicine

- Professor Ladias' lab specializing in the research of structural biology by X-ray crystallography.
- Reported to Professor Ladias and managed a team.. Cloned, expressed, purified, and crystallized protein KLC1 involved in binding of vesicle cargos and implicated in dementia patients.

Consultant Collaborations

Stony Brook University, Stony Brook, NY **2022 – Current**
Consultant – Molecular Dynamics and AI/ML drug discovery

- Dr. Yuefan Deng lab specialized in molecular dynamics and statistical analysis of proteins for drug development.
- Run and analysed molecular dynamics simulations of eIF4E in the presence or absence of cap and 4EGI1 ligands.
- Docked millions of select drug like compounds against protein translation regulator eIF4E using the Seawolf cluster.
- Identified important alternative conformations of eIF4E cap binding pocket to derive novel drug candidates.
- Designed and implemented AI/ML workflows to identify new drug candidates for BACE1 substrates.

Significant Awards

- PDB Molecule of the Month, http://pdb101.rcsb.org/motm/230
- Award on novel Mathematical theory, 6th European Union Contest for Young Scientists, Luxembourg.
- First place at "Lefkopoulio" contest in Statistics, Greek National Institute of Statistics.
- Silver medal at the 10th Balkan Mathematical Olympiad, Nicosia Cyprus

Education & Development:

- **Post Doctoral studies in Molecular Structural Biology at Beth Israel Deaconess Medical Centre and Harvard Medical School- BCMP (Biomolecular Chemistry and Molecular Pharmacology).**
  Received the Alexandros Onassis Foundation Scholarship based on PhD publications and performance.
- **PhD, MSc in Biophysics at Stockholm University, Sweden.**
  Studied under the secretaries of the Nobel committee for Chemistry, Astrid Gräslund and Physiology, Arne Holmgren. Received the National Scholarship Foundation awarded scholarship based on exams and publications. Techniques used: Liquid state heteronuclear and homonuclear NMR, Se NMR, solid state NMR, CD, ITC.
- **Bachelors, MSc in Physics, University of Athens, National Technical University of Athens, Greece.**
  Design and quality control of the muon Geiger detectors for the LHC experiment at CERN, Geneva, CH.
  After MSc received a Greek State Scholarships Foundation (I.K.Y.) scholarship by exams, 1st place in biophysics.

Select publications:

1) "An AI-Driven Framework for Discovery of BACE1 Inhibitors for Alzheimer's Disease." Biorxiv, May 15, 2024
2) "Structural and Dynamical Analyses of Apo and Cap-binding eIF4E: An in silico Study." Biorxiv, May 19, 2024
3) "A biphenyl inhibitor of eIF4E targeting an internal binding site enables the design of cell-permeable PROTAC-degraders." **Eur. J. Med. Chem.** 2021
4) "Molecular Landscape of the Ribosome Pre-initiation Complex during mRNA Scanning: Structural Role for eIF3c and Its Control by eIF5." **Cell Rep.** 2017
5) "Molecular mechanism of the dual activity of 4EGI-1: Dissociating eIF4G from eIF4E but stabilizing the binding of unphosphorylated 4E-BP1." **Proc. Natl. Acad. Sci. USA.** 2015
6) "eIF1A augments Ago2-mediated Dicer-independent miRNA biogenesis and RNA interference", **Nature Communications,** 2015
7) "4EGI-1 targets breast cancer stem cells by selective inhibition of translation that persists in CSC maintenance, proliferation and metastasis." **Oncotarget**. 2014
8) **"**Structure of the eukaryotic translation initiation factor eIF4E in complex with 4EGI-1 reveals an allosteric mechanism for dissociating eIF4G." **PNAS** 2014
9) "Essential role of eIF5-mimic protein in animal development is linked to control of ATF4 expression." **Nucleic Acids Res.** 2014

Complete List of Published Work in My Bibliography:

https://orcid.org/0000-0003-4050-4521

Nonprint Materials

- NMR constraints [Script Library]. Stockholm (SE); 2006 https://pymolwiki.org/index.php/Nmr_cnstr
- NMR solution structure of peptide from Doppel protein, in DHPC micelles. https://evanspap.w3spaces.com/
- GitHub scripts for Computational Structural Biology: https://github.com/evanspap/

Hobbies, free time activities

Sailing, hiking, designing electronics, design and building machines with practical applications, programming.

Professional References

- Gerhard Wagner, Ph.D., Harvard Medical School.,
  Elkan Blout Professor of Biological Chemistry and Molecular Pharmacology.
  Phone: +1-617-432-3212, Email:gerhard_wagner@hms.harvard.edu
- Bertal H. Aktas, D.V.M., Ph.D., Brigham and Women's Hospital.
  Assistant Professor of Medicine.
  Phone: +1-617-525-3141, Email:huseyin_aktas@hms.harvard.edu
- Uddhav Shigdel, Hyku Biosciences
  Director, Biomolecular Sciences
  Phone: +1-773-957-5710, Email: ushigdel@gmail.com
- Astrid Gräslund, Stockholm University
  Professor emerita
  Secretary and Deputy Member of the Nobel Committee for Chemistry
  Phone: +46-816-2450, Email: astrid.graslund@dbb.su.se

One Page - Short Summary, Key Points:

• Developed bivalent compounds for treating Cystic Fibrosis; licensed to Vertex (Stablix Inc.).

• Designed allosteric inhibitors for eIF4E-eIF4G protein interactions; advanced to IND-enabling studies (PIC tx).

• Resolved eIF4E inhibitor co-crystal structure using liquid-state NMR; licensed to PIC tx (Harvard Medical School).

• Led machine learning and AI-driven molecular dynamics projects for novel drug discovery (Stony Brook University, work published in BioRxiv).

Protein Biochemistry: Cloning, expression, purification, bioconjugation | 10+ years (top expert)

Structural Biology: NMR, X-ray crystallography, isotope protein labelling | 10+ years (top expert)

Computational Biology: PyMol, GROMACS, NAMD-VMD, CHIMERA, MOE, Schrodinger | 10+ years (top expert)

Data Management: Benchling, LiveDesign, CDD, DataWarrior, Scinamic | 5+ Years

Programming: Python, HTML, R, MATLAB, Bash | 10+ years

Bioinformatics: AWS, Slurm, RNA-Seq | 5+ Years

Data Analysis: SQL, Pandas, Matplotlib | 5+ years

Dana Farber Cancer Institute, Boston, MA (2020 – Current)
Research Scientist – Medical Oncology
- Managed a team in cancer therapy research, focusing on CRISPR/Cas-9 bioinformatics data analysis to improve drug therapy response predictions.
- Illustrated and analysed hundreds of protein mutations, producing DNA clones tested in cell lines against FDA-approved drugs.

Stablix Inc, NY & Boston, MA (2021 – 2023)
Senior Scientist – Biomolecular & Computational Sciences
- Led bifunctional molecule development for targeted de-ubiquitination therapies.
- Curated ELN databases for thousands of proteins and plasmids; characterized over 6,000 small molecules using SPR, MST, and NMR assays.

PIC Therapeutics, Boston, MA (2017 – 2020)
Research Scientist – Drug Development
- Developed high-throughput drug assays, leading testing of ~300 compounds for translation inhibition in multiple cancer cell lines.
- Docked 100M compounds to analyse binding efficacy for cancer treatment.

Harvard Medical School, Boston, MA (2009 – 2020)
Research Scholar
- Specialized in protein translation initiation factor research, discovering new binding mechanisms for inhibitors like 4EGI1.
- Published findings in Nature Communications and PNAS; awarded PDB Molecule of the Month feature.

Beth Israel Deaconess Medical Centre, Boston, MA (2008 – 2012)
Postdoctoral Associate – Structural Biology
- Researched structural biology using X-ray crystallography; cloned, purified, and crystallized proteins implicated in dementia research.

Postdoctoral Studies in Molecular Structural Biology - Beth Israel Deaconess Medical Centre, Harvard Medical School

PhD, MSc in Biophysics - Stockholm University, Sweden (Awarded National Scholarship)

BSc, MSc in Physics - University of Athens, National Technical University of Athens (Awarded Greek State Scholarships)