AMIR TAHERI GHAHFAROKHI

Genome Editing Expert

PROFILE

Amir is a Genome Editing specialist with 15 years of experience across the pharma and biotech industries. He is highly skilled in wet lab techniques and bioinformatics and is passionate about translating gene editing advances into transformative genetic medicines. He is experienced in building and leading efficient teams that deliver high-quality results in pre-clinical settings.

WORK EXPERIENCES

Immitra Bio GmbH (Zurich, Switzerland) *Mar 2024 – Present*

- [**Leadership**] Led the research team of 5 scientists toward establishing a gene and cell therapy platform, combining CRISPR-Cas9 and Hematopoietic Stem and Progenitor Cells (HSPCs) technologies.
- Achieved over 50% promoter editing (30 nucleotide insertion) and over 25% gene insertions in HSPCs.

Vector BioPharma AG (Basel, Switzerland) *Mar 2022 – Nov 2023*

- [**Leadership**] Led the genome editing team and contributed to the leadership team, set short and long-term strategic milestones, managed the team budget and priorities, delivered quarterly progress reports to the senior management team, and supported the professional development of direct reports.
- [**Innovation**] Developed a novel method for Adenovirus-based Virus-Like Particle (VLP) production, reducing the turnaround time from 6 weeks to 11 days.
- [**Innovation**] Established a comprehensive Cas9 discovery pipeline, encompassing bioinformatics search and in-vitro characterization, resulting in patented advancements.
- Achieved efficacious in-vivo Prime Editing using proprietary VLP technology and benchmarked against Adeno-Associated Virus (AAV) delivery.
- Procured an Illumina next-generation sequencing machine and established standard operating procedures for targeted sequencing.
- Established and implemented an Amazon Web Services-based cloud computing platform, eliminating the costs associated with procurement and maintenance of in-house computing servers.
- Developed bioinformatics pipelines accompanied with html tools for intranet-based visualization of sequencing outputs, enabling streamlined data analysis and interpretation.
- Developed a de-novo assembly and annotation pipeline for nanopore sequencing reads of large plasmid constructs.

AstraZeneca (Gothenburg, Sweden) *Mar 2015 – Feb 2022*

- Held diverse roles in the Discovery Sciences department, including three years as a Postdoctoral researcher (Genome Editing), two years as a Senior Research Scientist (Translational Genomics), and two years as a Senior Bioinformatician (Quantitative Biology).
- Designed CRISPR-based Therapeutic Genome-Editing strategies to treat rare genetic diseases.
- Developed and maintained bioinformatics pipelines for *in-silico* prediction of CRISPR off-target effects, ranking target sites, and assessing their activity.
- Designed DNA and RNA editing libraries and developed constructs for High-Throughput Screening assays (arrayed and pooled).
- Developed innovative cell-based assays to validate DNA repair inhibitory compounds.
- Developed and implemented the Rational Off-target Ranking Algorithm and confirmation by Sequencing (RORA-Seq), enhancing CRISPR off-target detection through deep sequencing.
- Characterized Cas9 nuclease activity in human cells and profiled their DNA repair capacity using RIMA (published in Nucleic Acids Research).
- Led comprehensive bioinformatics analysis of Cas9s from the IIB family, resulting in the discovery of novel Cas9 variants with unique nuclease activity (patented) for potential application in curing rare genetic diseases.
- Provided bioinformatics solutions for Target Identification and Target Validation in drug discovery programs, enabling Target Annotation and Prioritization.
- Established a co-targeting enrichment strategy in Cas9-targeted cells (patented).
- Recognized as PostDoc of the year in 2017 among 130 AstraZeneca's PostDocs across the US, UK, and SE.

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EDUCATION

PhD (2009 - 2014)

- **Molecular Genetics**, Ferdowsi University of Mashhad, Iran.
- **Dissertation title**: Engineering and validation of TALENs for Targeted Disruption of Myostatin Gene in Mouse Embryonic Stem Cells.
- **Thesis work**: Joined Prof. Paul Verma's research team at Monash University, Melbourne, Australia (2012-2013). Additionally contributed to the ongoing lab project including targeted integration into mouse ChrY, SLC11A1 conditional gene knockout line generation.

MSc (2007 - 2009)

- **Molecular Genetics**, Ferdowsi University of Mashhad, Iran.
- **Thesis title**: Development of an absolute-based Quantitative Competitive PCR (qcPCR) and Real-Time PCR Assays for Quantification of Butyrate Producing Bacterium: *Butyrivibrio fibrisolvens*.

BSc (2001 - 2006)

- **Animal Sciences**, Kurdistan University, Sanandaj, Iran.

CORE SKILLS

Leadership (developing skills)

- **Communication**: distilling complex matters and effective presentation to senior management. Engaging with Key Opinion Leaders, Subject Matter Experts, and other stakeholders. Ensuring the effective flow of information within the managerial line and with peers.
- **Decision-making**: autonomous actions within the defined boundaries, capable of proposing and setting pre-clinical milestones and defining strategies and roadmaps.
- **Adaptability**: open to adapt to radical changes in dynamic and fast-paced environments.
- Empowerment of team members and delegation of project leads.

Molecular Biology (proven skills, in-depth knowledge)

- **CRISPR**: designing knockout, knock-in, base editing, and prime-editing experiments. Discovering and characterizing new Cas9 enzymes. Theoretical knowledge of CAST systems.
- **DNA Repair**: profiling the DNA repair capacity of the cells, exploiting MMEJ/NHEJ pathways for precise repair of the genes, and predicting the outcome of repair events.
- **Molecular Cloning**: conventional restriction enzyme cut and ligation, Golden-gate cloning, site-directed mutagenesis using various methodologies.
- **High-Throughput Sequencing**: Illumina-based deep targeted sequencing (certified user for Mini-Seq instrument), hands-on library preparation experience.
- **Assay development**: clonal cell line generation, arrayed and pooled functional genomics screens.
- **Gene delivery**: first generation and gutless Adenovirus production, AAV, Lentivirus production.
- **Cell Culture**: mammalian and bacterial cells, imaging, FACS, clonal cell isolation.
- **Databases and other skills**: NCBI, BioMart, HPA, Primer-BLAST, CLC, Geneious, Benchling, …

Bioinformatics (supplementary skills)

- **Programming**: R (advanced), Bash (advanced), VBA (advanced), Python (intermediate), C++ (intermediate), JavaScript (intermediate), HTML, and CSS.
- **Pipeline management**: Snakemake (advanced), NextFlow (beginner).
- **High-Performance Computing**: SLURM (advanced). Amazon Web Services (AWS, intermediate).
- **Reproducibility tools**: Conda (advanced), Git (advanced), Rmarkdown (advanced).
- **NGS data analysis**: targeted deep sequencing (advanced), RNA-seq (beginner), Oxford Nanopore (intermediate), GATK (intermediate), Bioconductor (used several packages).
- **CRISPR-specific tools**: CHANGE-Seq/CIRCLE-Seq (advanced), CasOFFinder (advanced), CRISPResso.
- **Data visualization**: ggplot, IGV, Blender, Adobe-illustrator, JMP.
- **Other**: *de-novo* assembly of ONT reads (whole plasmid sequencing, advanced), annotation of plasmids for coding and non-coding elements (advanced).

PUBLICATIONS

Peer-reviewed articles

1. S. Wimberger, N. Akrap, M. Firth, et al., **A. Taheri-Ghahfarokhi**, M. Maresca (2023) Simultaneous inhibition of DNA-PK and PolΘ improves integration efficiency and precision of genome editing. *Nature Communications (14) 4761*. Contribution: designed and conceived the study, performed compound screening screens, and developed bioinformatics tools.
2. B. Bestas, S. Wimberger, [17 co-authors], **A. Taheri-Ghahfarokhi**, [6 co-authors], M. Maresca (2023) Identification and Characterization of New Cas9 Variants within the Class II CRISPR-Cas Systems. *Nature Communications (4): 5474*. Contribution: co-inventor, performed bioinformatics search and proof-of-concept experiments, designed and generated several hundreds of plasmids for deep characterization of Cas9 leads.
3. [Book Chapter] Y. Shamshirgaran, J. Liu, H. Sumer, P.J. Verma, **A. Taheri-Ghahfarokhi** * (2022) Tools for efficient genome editing: ZFNs, TALENs, and CRISPRs. *Applications of Genome Modulation and Editing, 29-46*. * Corresponding author.
4. [Book Chapter] S. Wimberger, N. Akrab, **A. Taheri-Ghahfarokhi** * (2022) DNA repair pathways in the context of therapeutic genome editing. *Genome Editing in Drug Discovery, 177-192*. * Corresponding author.
5. **A. Taheri-Ghahfarokhi** *, B.J.M. Taylor, R. Nitsch, A. Lundin, et al., (2018) Decoding non-random mutational signatures at Cas9 targeted sites. *Nucleic Acids Research 46 (16), 8417-8434*. Contribution: designed and conceived the study, performed experiments and bioinformatics analysis, prepared figures, and drafted the manuscript. * Corresponding author.
6. M. Bjursell, M.J. Porritt, E. Ericson, **A. Taheri-Ghahfarokhi**, et al., (2018) Therapeutic genome editing with CRISPR/Cas9 in a humanized mouse model ameliorates α1-antitrypsin deficiency phenotype. *EBioMedicine 29, 104-111*. Contribution: designed and performed the off-target analysis for CRISPR gene targeting.
7. A. Carreras, L.S. Pane, R. Nitsch, K. Madeyski-Bengtson, M. Porritt, P. Akcakaya, **A. Taheri-Ghahfarokhi**, et al., (2019) In vivo genome and base editing of a human PCSK9 knock-in hypercholesterolemic mouse model. *BMC Biology 17 (1), 1-14*. Contribution: performed bioinformatics analysis.
8. The full list of publications is available on my *Google Scholar* page.

Conferences

1. **A. Taheri-Ghahfarokhi**, M. Porritt, M. Firth, et al., (2020) Rational Off-target Ranking Algorithm and confirmation by Sequencing (RORA-Seq). Oral presentation. NextGen Omics Series UK: 6th Annual Genome Editing Congress. Contribution: developed RORA, performed experiments and bioinformatics analysis.

Patents

1. M. Maresca, A. Taheri-Ghahfarokhi, F. Karlsson, M. Bohlooly, L. Mayr (2019) Compositions and methods for improving the efficacy of cas9-based knock-in strategies. Issued May 23, 2019, Patent number: *WO2019099943A1*.
2. M. Maresca, A. Taheri-Ghahfarokhi, M. Bohlooly, L. Mayr (2017) Gene modification assays. Issued Jul 20, 2017, Patent number: *WO2017122096A1*.
3. Two additional patents were submitted (currently not in the public domain).

CONTACT

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- Website: https://amirtaheri.info

Contact QR card

PERSONAL INFO

- Born 1983, married, Iranian-Swedish.
- Occasional chess player (rapid peak rating 1900).