Sophia Pfister, Ph.D.

Director of Immuno-Oncology Foster City, CA sophia@pfister.fi Residency Status: Green Card

SUMMARY

- Director of Immuno-Oncology with expertise in T cell biology, drug discovery and precision medicine
- Successful experience in progressing immuno-oncology drug candidates from early research to IND filing
- 9+ years leading drug discovery programs (antibodies, small molecules & CAR-T); 5 years managing cross-functional teams (20+ people); 5 years recruiting & managing Ph.D./non-Ph.D. level direct reports
- Lead inventor on 2 patents: (1) a patient stratification biomarker for AstraZeneca, now tested in 2 phase II clinical trials; (2) the discovery and development of a key I-O drug in the pipeline of Pfizer
- 3 first-author publications (*Cancer Cell, Cell Reports, Nature Reviews Drug Discovery*) with 500+ citations, 3 oral presentations in AACR conferences (1,500+ audience), 5 grants ($1M+), 7 research awards

EDUCATION

UNIVERSITY OF OXFORD, Ph.D. in Oncology 2010 – 2014

- Topics: Cancer genetics & epigenetics, kinase inhibitors, combination therapies, patient stratification
- Dissertation: The function and therapeutic potential of histone H3K36 trimethylation

UNIVERSITY OF CAMBRIDGE, B.A. (Hons.) in Immunology & Oncology 2007 – 2010

- Courses: Innate and adaptive immunity, immune tolerance, molecular biology of cancer, pathology
- Thesis: The pro-malignant effects of OSM receptor overexpression in cervical cancer

RESEARCH EXPERIENCE

NOTABLE LABS – Lead scientific vision and strategy for the 40-person company **Foster City, CA**

Director of Immuno-Oncology, R&D lead **2019 – present**

Report to the CSO

Develop immuno-oncology roadmap for the company

- Led 3 direct reports to set up *ex vivo* platforms for T cell targeted therapeutics including CAR-T, CD3-bispecific antibodies and checkpoint blockade on primary human cancer samples
- Designed and implemented the roadmap for expanding the I-O research capabilities of the company to enable the discovery and development of in-licensed drug candidates

Develop a clinical-grade platform for personalized cancer therapies

- Led the 10-person R&D department to enhance a research-use-only functional screening platform to meet CLIA standards for identifying optimal therapies for individual cancer patients
- Led cross-functional teams (science, engineering, business development and CROs) to integrate robotics, AI and bioinformatics into the flow cytometry-based diagnostic platform

PFIZER – Lead immuno-oncology drug discovery and translational research **South San Francisco, CA**

Principal Scientist & Research Team Lead **2017 – 2019**

Report to the Senior Director of Cancer Immunology

Discover and develop a novel antibody immunotherapy targeting co-stim receptors on T cells

- Discovered and patented a method that improves efficacy and eliminates toxicity of a key I-O drug
- Advanced the program from exploratory stage to pipeline Lead selection in just 1 year
- Motivated a cross-functional team of 20+ scientists in engineering, pharmacology, toxicology, bioinformatics, biomarker and clinical research; and accelerated the program towards IND filing
- Awarded fast track promotion and 3 Pfizer Upjohn Awards for outstanding performance and leadership
- Recognized as the go-to person who provides mentoring and troubleshooting for junior scientists

Establish vision and strategy for Pfizer's precision immunotherapy initiative

- Established the first immuno-oncology screening platforms for Pfizer West Coast, including the NY-ESO-1 screening platform, *ex vivo* screening platform and a patient-derived organoids system
- Developed biomarkers and combination strategies for 2 clinical and 3 pre-clinical programs
- Led strategic collaborations with academia and industry in the field of I-O & managed multiple CROs

UCSF HELEN DILLER CANCER CENTER – Improve TCR-T cell therapy **San Francisco, CA**
Postdoctoral Fellow **2015 – 2017**
Mentors: Alan Ashworth & Wendell Lim

Identify novel regulators of human TCR-T cell function using high-throughput screening

- Invented a novel *ex vivo* high-throughput TCR-T + cancer cell screening platform and used it to successfully identify novel targets that modulate the cytotoxicity of TCR-T cells
- Received licensing interest from biotechs and pharmaceutical companies for the platform and targets
- Awarded the Parker Institute for Cancer Immunotherapies (PICI) grant ($250k) and the Cancer Target Discovery and Development (CTD^2) grant ($400k) for new technology development

Early cancer detection from blood using deep learning/artificial intelligence

- Led a cross-functional team of computer scientists, bioinformaticians and clinicians to develop a novel tool that uses deep learning to detect cancer from blood samples. Achieved 95% accuracy
- Selected as the finalist from 60+ applications in the UCSF Impact Grant ($250k)

UNIVERSITY OF OXFORD – Develop clinical biomarkers for AstraZeneca **Oxford, UK**
Postdoctoral Fellow **2014 – 2015**

Develop biomarkers for patient stratification for adavosertib (small molecule WEE1 inhibitor by AZ)

- Translated my Ph.D. project on SETD2 and WEE1 to a biomarker-driven therapeutic strategy that is potentially less toxic, more effective and applies to over 10% of all cancer patients
- Developed two biomarkers that AstraZeneca is now using in 2 Phase II clinical trials for adavosertib
- Filed a patent around the invention and led patent licensing negotiations with major pharma companies

UNIVERSITY OF OXFORD – Discover novel therapies targeting tumor-specific mutations **Oxford, UK**
Ph.D. Research, Oncology **2010 – 2014**

Find novel therapies that target epigenetic mutations in cancer

- Discovered that human cancers with mutation in the *SETD2* gene can be selectively killed by the checkpoint inhibitors including WEE1. Elucidated the molecular mechanism of this genetic interaction
- Published the finding in *Cancer Cell* which attracted extensive attention from the media and pharma

Identify novel genes in DNA damage repair pathway

- Discovered a novel human tumor suppressor gene involved in DNA repair and published the findings in *Cell Reports* and *Nature Structural & Molecular Biology*

UNIVERSITY OF CAMBRIDGE – Understand OSM signaling in cervical cancer **Cambridge, UK**
B.A. Thesis, Immunology & Oncology **2009 – 2010**

- Identified that cervical cancer development and metastasis is controlled by the signalling pathway of a cell surface receptor OSMR, leading to a paper published in the *Journal of Pathology*

RESEARCH SKILLS

Immuno-oncology drug discovery: Multi-color FACS, FlowJo analysis, *in vitro* & *ex-vivo* I-O screens, human T cell isolation & functional characterization, immune phenotyping, T cell activation/cytotoxicity/ memory formation assays, murine syngeneic and xenograft tumor models, PK, PD, toxicology, combination therapies, CyTOF, Luminex, ELISA, single-cell RNA-seq, t-SNE plots

Precision medicine / biomarker development: primary human tumor sample handling and functional assays, GCP, genetic determinants of drug response, drug resistance, whole genome sequencing, Foundation Medicine, tissue microarray, IHC/IF, clinical trial design

Cell & molecular biology: Genetic modification of primary T cells, single-cell analysis, CRISPR, RNAi, epigenetics, cell cycle, immunofluorescence imaging, western blotting, lentivirus, site-directed mutagenesis

AWARDS

- Pfizer Upjohn Awards for outstanding performance, leadership and teamwork, 2017, 2018 & 2019
- Pfizer Grant to Hire Postdoc (awarded to top 1% Pfizer applicants based on scientific impact), 2017
- Oxford Nautilus Award for research excellence (for discovering novel cancer therapies), 2015
- Nomination for the Oncology Sylvia Lawler Prize, Royal Society of Medicine, 2014
- Clarendon scholarship (received by top 3% of Oxford graduate students), 2010 – 2014
- British Biochemical Society summer internship scholarship (for research excellence), 2009
- Cambridge Overseas Trust scholarship (for academic excellence), 2007 – 2010

PATENTS

Medicaments for use in methods of treating cancers which comprise a decreased amount of H3K36me3
Pfister SX *et al*., PCT filed 2014, WO/2014/188201

Anti-41BB antibodies having improved efficacy and reduced toxicity
Pfister SX *et al*., filed by Pfizer 2018

PEER-REVIEWED PUBLICATIONS

1. **Pfister SX** and Ashworth A. (2017) Marked for Death: Targeting Epigenetic Changes in Cancer. *Nature Reviews Drug Discovery.* *
   * Article citations ranked Top 10% of all articles of similar age in *Nature Reviews Drug Discovery*

2. Ahrabi S, Sarkar S, **Pfister SX**, Pirovano G, Higgins GS, Porter AC, Humphrey TC. (2016) A role for human homologous recombination factors in suppressing microhomology-mediated end joining. *Nucleic Acids Research.*

3. **Pfister SX**, Markkanen E, Jiang Y, Sarkar S, Woodcock M, Orlando G, Mavrommati I, Pai CC, Zalmas LP, Drobnitzky N, Dianov GL, Verrill C, Macaulay VM, Ying S, La Thangue NB, D'Angiolella V, Ryan AJ, Humphrey TC. (2015) Inhibiting WEE1 selectively kills histone H3K36me3-deficient cancers by dNTP starvation. *Cancer Cell.* *
   * Article received commentaries in *Cancer Cell*, *Science Signaling*, *Cancer Discovery*, *Eur. J. Cancer*

4. Ramcharan R, Aleksic T, Kamdoum WP, Gao S, **Pfister SX**, Tanner J, Bridges E, Asher R, Watson AJ, Margison GP, Woodcock M, Repapi E, Li JL, Middleton MR, Macaulay VM. (2015) IGF-1R inhibition induces schedule-dependent sensitization of human melanoma to temozolomide. *Oncotarget.*

5. Wong S, Sasportas L, Richardson K, Gordon B, Jayatunga M, Shalizi A, **Pfister SX**, Stanzl E, Chui C, Mathur M, Thomsen S, Shetty S, Pliuskys L, Mehra A, Bahar H, Godec J, Jong S, Perez D. (2015) Keys to the kingdom. *Nature Biotechnology.*

6. Jha DK, **Pfister SX**, Humphrey TC, Strahl BD. (2014) SET-ting the stage for DNA repair. *Nature Structural & Molecular Biology*

7. **Pfister SX**, Ahrabi S, Zalmas LP, Sarkar S, Aymard F, Bachrati CZ, Helleday T, Legube G, La Thangue NB, Porter AC, Humphrey TC. (2014) SETD2-dependent histone H3K36 trimethylation is required for homologous recombination repair and genome stability. *Cell Reports.*

8. Winder DM, Chattopadhyay A, Muralidhar B, Bauer J, English WR, **Zhang SX**, Karagavriilidou K, Roberts I, Pett MR, Murphy G, Coleman N. (2011) Overexpression of the oncostatin M receptor in cervical squamous cell carcinoma cells is associated with a pro-angiogenic phenotype and increased cell motility and invasiveness. *Journal of Pathology.*