Sophia Pfister, Ph.D.

UCSF Helen Diller Cancer Center (669) 243-9524 sophia@pfister.fi Residency Status: Green Card

SUMMARY

- Translational immuno-oncologist with expertise in T cell biology & oncology drug discovery.
- Discovered & patented 3 novel cancer treatments; translated one treatment into two phase II clinical trials.
- Invented an immune screening platform and identified novel targets that modulate tumor immunogenicity & immune cell activity. Received licensing interest for the platform and molecules.
- Strong hands-on immunology skills in T cell functional assays, *in vitro*, *in vivo* & *ex vivo* models, multi-color FACS, engineering primary human T cells, signaling pathways, PD-1/PD-L1 combination therapy.
- 3 first-author publications (*Cancer Cell, Cell Reports, Nature Reviews Drug Discovery*), 3 oral presentations in international conferences (to 1500+ audiences), 4 grants ($800k total) & 4 research awards.
- 5-year successful track record in leading drug discovery projects; leading cross-functional teams & working in collaboration with Genentech, AstraZeneca and Clovis.

RESEARCH EXPERIENCE

UCSF Helen Diller Family Comprehensive Cancer Center, Postdoctoral Fellow (Sep 2015 – present)

Mentor: Alan Ashworth (in close collaboration with Wendell Lim)

Identifying novel immunotherapies using high-throughput screening

- Developed a novel *in vitro* high-throughput tumor-immune cell screening platform, and used it to successfully identify novel molecules that modulate T cell killing of cancer cells.
- Received licensing interest from biotech and pharmaceutical companies for the platform and molecules.
- Unveiled the drug's effect on IFN, TLR, STING pathways by FACS, RNAi, CyTOF, SILAC, RNAseq.
- 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.

Leading industry collaborations to develop new cancer treatments

- Led collaborations with Genentech, AstraZeneca and Clovis to co-develop new immunotherapeutic agents and biomarkers. Work includes screening, functional studies and *in vivo* models.
- Awarded NIH grant & drug support from AstraZeneca to run a 30-person phase II trial in U.S. based on my previous publication, where patients with *SETD2* mutations are treated with AZD1775.

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).

CRUK/MRC Oxford Institute for Radiation Oncology, Postdoctoral Fellow (Sep 2014 – Sep 2015)

Mentor: Timothy Humphrey

Developing patient stratification biomarkers for AZD1775

- Generated *in vivo* mouse models and validated my PhD finding that tumors with *SETD2* gene mutations can be targeted by checkpoint kinase inhibitors including AZD1775.
- Initiated and led collaborations with 20 scientists from 6 labs to publish the findings in *Cancer Cell*.
- Moved this discovery to a clinical trial in the U.K. funded by AstraZeneca; led patent licensing talks.

Department of Oncology, University of Oxford, Ph.D. Research (Sep 2010 – Sep 2014)

Mentors: Timothy Humphrey & Thomas Helleday

Finding novel therapies that target epigenetic mutations in cancer

- Discovered that cancers with mutation in the *SETD2* gene are hypersensitive to the small molecule inhibitors of 3 checkpoint proteins. Elucidated the molecular mechanism of this genetic interaction.
- Translated this finding to 3 potential therapies that are less toxic, more effective and apply to over 10% of all cancer patients.

- Composed and filed the patent with patent attorneys & technology transfer office.

Identifying 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*.

Department of Pathology, University of Cambridge, B.A. Thesis (Jun 2009 – Mar 2010)

Mentor: Nick Coleman

Understanding the Oncostatin M signalling pathway in cervical cancer

- Identified that cervical cancer metastasis is controlled by the signalling pathway of a cell surface receptor OSMR. The research led to a paper published in the *Journal of Pathology*.

EDUCATION

University of Oxford, Ph.D., Oncology (2010 – 2014)

- Dissertation: The function and therapeutic potential of histone H3K36 trimethylation.
- Topics: Target identification, drug discovery, biomarkers, epigenetics, pre-clinical & clinical validation.

University of Cambridge, BA (class 2.1/GPA 3.67), major: Immunology & Cancer (2007 – 2010)

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

RESEARCH SKILLS

Immuno-oncology: primary human T cell functional assays (activation, proliferation and cytotoxicity), adoptive T-cell therapy (CAR & TCR), 10-color FACS, checkpoint blockade combination therapy, tumor & immune cell co-culture, CyTOF, SILAC, CODEX, Luminex, *in vitro*, *in vivo* & *ex-vivo* assays.

Oncology drug discovery: drug library screens, CRISPR screens, drug combinations, drug resistance, whole genome sequencing, Foundation Medicine, synthetic lethality, inhibitors (PARP, kinases and epigenetics), animal models, biomarker development, tissue microarray, IHC, patient selection, clinical trial design.

Cell & molecular biology: CRISPRn/i, RNAi, DNA damage assays (comet, DNA repair foci, DNA fiber), cell cycle, drug dose response, ELISA, immunofluorescence imaging, qRT-PCR, western blotting, lentiviral packaging & transduction, stable gene integration, cloning, site-directed mutagenesis.

COMMUNICATION, TEAMWORK & LEADERSHIP

Reviewer (Mar 2016 – present)

- Invited reviewer for *Scientific Reports*, *Oncotarget*, *Oncology Letters* and *Biomedical Reports*.

Consultant, Oxbridge Biotech Roundtable (Mar 2014 – Jun 2014)

- Led a team of 6 postdocs to research on academic entrepreneurship in UK vs. US.
- Interviewed 32 academic entrepreneurs and 11 technology transfer offices; identified key challenges for academic entrepreneurs and proposed mitigation strategies. Published in *Nature Biotechnology*.

Conference Organizer, Oxford University (Sep 2010 – Jun 2011)

- Led a team of 8 humanity scientists to organize the conference on child welfare.
- Secured 4 leading scientists to give keynotes & doubled the number of participants from previous year.

Fundraiser, Gonville and Caius College, Cambridge University (Mar 2008 – Apr 2008)

- Achieved the highest donation rate (87%) in the 30-person telephone fundraising team.
- Contributed to the most successful alumni fundraising in any Oxbridge college in 2008.

AWARDS

- 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, 2009
- Cambridge Overseas Trust scholarship, 2007 – 2010

PATENT

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

PEER REVIEWED PUBLICATIONS

(1) Marked for Death: Targeting Epigenetic Changes in Cancer.
Nature Reviews Drug Discovery. 2017 Apr;16(4):241-263
Pfister SX and Ashworth A.

(2) A role for human homologous recombination factors in suppressing microhomology-mediated end joining.
Nucleic Acids Research. 2016 Jul 8;44(12):5743-57.
Ahrabi S, Sarkar S, **Pfister SX**, Pirovano G, Higgins GS, Porter AC, Humphrey TC.

(3) Inhibiting WEE1 selectively kills histone H3K36me3-deficient cancers by dNTP starvation.
Cancer Cell. 2015 Nov 28(5):557-68.
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. **(Commented on by *Cancer Cell, Science Signaling*, *Cancer Discovery* and *European Journal of Cancer.*)**

(4) IGF-1R inhibition induces schedule-dependent sensitization of human melanoma to temozolomide.
Oncotarget. 2015 Nov 24;6(37):39877-90.
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.

(5) Keys to the kingdom.
Nature Biotechnology. 2015 Mar;33(3):232-6.
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.

(6) SET-ting the stage for DNA repair.
Nature Structural & Molecular Biology. 2014 Aug;21(8):655-7.
Jha DK, **Pfister SX**, Humphrey TC, Strahl BD.

(7) SETD2-dependent histone H3K36 trimethylation is required for homologous recombination repair and genome stability.
Cell Reports. 2014 Jun 26;7(6):2006-18.
Pfister SX, Ahrabi S, Zalmas LP, Sarkar S, Aymard F, Bachrati CZ, Helleday T, Legube G, La Thangue NB, Porter AC, Humphrey TC.

(8) 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. 2011 Nov;225(3):448-62.
Winder DM, Chattopadhyay A, Muralidhar B, Bauer J, English WR, **Zhang SX**, Karagavriilidou K, Roberts I, Pett MR, Murphy G, Coleman N.

CONFERENCE PRESENTATIONS

(1) A novel synthetic lethal interaction between the histone mark H3K36me3 and checkpoint kinases.
Oral presentation, EORTC-NCI-AACR symposium on Molecular Targets and Cancer Therapeutics, 2014.

(2) Targeting DNA replication stress for cancer therapy.
Oral presentation, Cancer Research UK Radiation Oncology Symposium, 2015.

(3) Exploiting synthetic lethality to kill H3K36me3-deficient cancers by WEE1 inhibition.
Oral presentation, UK National Cancer Research Institute (NCRI) Cancer Conference, 2015.

(4) WEE1 inhibition selectively kills histone H3K36me3-deficient cancers by dNTP starvation.
Poster, AACR conference on Chromatin and Epigenetics in Cancer, 2015.

(5) A novel role of histone methylation in maintaining genome stability.
Poster, Chromatin, Replication and Chromosomal Stability, 2013.