UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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We are recruiting four Staff Research Associates (SRAs)/Specialists to assist with ongoing multidisciplinary cellular engineering projects. Our lab has pioneered the application of novel genetic engineering technologies such as CRISPR to primary human immune cells (Schumann et al., *PNAS* 2015). These new technical abilities have furthered our labs research into the genetic underpinnings of autoimmune disease and T cell biology (Farh and Marson et al., *Nature* 2015), as well as opened the door to novel cancer immunotherapies based on engineered human immune cells (Roth et al., *Nature* 2018). In addition to cell editing, our lab integrates genomic analysis (e.g. ChIP-seq, ATAC-seq, RNA-seq), human disease genetics, and high dimensional screening approaches for *in vitro* and *in vivo* studies of T cell function (Simeonov et al. *Nature* 2017; Shifrut and Carnevale et al. *Cell* 2018).

We are recruiting SRAs/Specialists for four different projects:

Mapping Trans-regulatory Networks in Primary Immune Cells (SRA)
Interpreting genome wide association studies and understanding the genetic basis of disease requires understanding trans-regulatory networks in primary human cells. We are using high throughput CRISPR/Cas9 perturbations to map gene regulatory networks in human T cells. These regulatory maps will provide insights into the genetic architecture of complex traits, potential therapeutic targets for autoimmune diseases, and how to manipulate immune cells for cell therapies. The SRA will get extensive experience with CRISPR/Cas9 screening and next generation sequencing.

Primary responsibilities will include isolating and culturing of primary human immune cells, genetic editing of immune cells using CRISPR/Cas9, performing flow cytometry, and producing next generation sequencing libraries. Additional responsibilities will include supporting the development of novel single cell sequencing methods. Responsibilities will also involve basic molecular biology (PCR, cloning, preparing plasmid constructs, etc.). Strong organizational and communication skills are required. This position represents an excellent opportunity to gain exposure to basic laboratory skills, genomics, and genome engineering in a dynamic, well-established research environment.

Pooled Knock-in Screens (SRA)
Our lab recently established CRISPR/Cas9-based high throughput pooled knock-in screens in primary T cells (Roth et al., Biorxiv DOI 10.1101/604561): T cells are edited to express a tumor-specific T cell receptor and a variety of modulatory or potentially therapeutic molecules (such as immune checkpoint chimera). Aim of this project is to enhance T cell functionality in inhibitory conditions and to identify key players of anti-tumor efficacy.

Working as part of a multidisciplinary group, the SRA will utilize various protocols to generate the molecular components, such as DNA constructs, necessary for specific cellular engineering experiments. Additional major responsibilities will include the preparation, sequencing, and analysis of next-generation sequencing libraries to support pooled screening experiments. Further responsibilities will consist of isolation and culture of primary human immune cells, as well as functional analysis of engineered cells via Sanger sequencing and flow cytometry. Strong organizational and communication skills are required. For exceptionally skilled applicants, opportunity exists to extend the SRA's role to include the design and completion of cellular editing experiments, as well as *in vivo* analysis of novel cellular cancer immunotherapies. This position represents an excellent opportunity to gain exposure to basic laboratory skills as well as genetics and genome engineering skills in a dynamic, well-established research environment.

Therapeutic applications of primary human T cell editing (Junior or Assistant Specialist)
This position will support preclinical development for novel gene and cellular therapies. You will have the opportunity to work on true "bench-to-bedside" projects translating basic research in CRISPR-mediated editing of human T cells toward actual patient therapeutics. This work may lead to publications in scientific journals and will support clinical trials for treatment of patients with autoimmune disease, cancer, and other types of disease. Specific tasks include molecular biology, cell culture, flow cytometry, FACS, new assay development, and experimental design. You will also gain expertise in clinical trial design, preclinical development, and cGMP manufacturing for experimental cellular therapies.

Developing alternative Cas9 delivery methods (SRA)
Current approaches for Cas9 delivery include RNP electroporation, plasmid-based transfection, or viral transduction. While these methods are effective for *in vitro* editing of purified cell populations, improved methods that directly target and modify the cell of interest are highly desirable for generating the next generation of *in vitro* and *in vivo* genome editing tools. This position will support a collaborative effort to develop such approaches between the Marson lab at UCSF and the labs of Ross Wilson and Jennifer Doudna at UC Berkeley. Under direct supervision and training, the SRA will utilize various protocols performing molecular biology such as preparing samples for sequencing (DNA purification/RNA purification/PCR/sequencing library generation) or performing CRISPR/Cas9 gene editing in cell culture. The SRA will also perform cell culture and differentiation of hematopoietic stem cells and cell lines. The candidate will interact closely with other laboratory members and will be responsible for meticulous handling and processing of research and clinical samples. The candidate will also aid in new and ongoing research projects involving other sample types including primary human T cells. Strong organization skills are required. This position represents an excellent opportunity to gain exposure to basic laboratory skills as well as genetics and genome engineering skills in a dynamic, well-established functional and therapeutic genomics research environment.

Required Qualifications:
• BA/BS degree and one or more years of laboratory experience utilizing techniques or methods required by the position; or an equivalent combination of education and experience
• Experience with general laboratory techniques, especially basic molecular and cellular biology techniques (including but not limited to DNA and RNA isolation, PCR, gel electrophoresis, DNA assembly, bacterial transformation, mammalian cell culture, etc.)
• Excellent organizational and interpersonal communication skills (verbal and written)
• Willingness and ability to learn new methods and skills for changing research priorities
• Ability to work independently and as a member of a research team
• Ability to prioritize tasks, coordinate work tasks with others, and meet multiple deadlines

Preferred Qualifications
• Prior experience with mammalian cell culture, especially T cell culture
• Prior experience with DNA sequencing technologies, including Sanger and NGS
• Prior experience with next-generation sequencing library preparations and quality control
• Prior experience in the design and assembly of DNA constructs (via restriction digestion and ligation, Gibson assemblies, Golden-Gate assemblies, etc.)

Payment is according to the UCSF pay scale. UCSF is an equal opportunity/affirmative action employer. All qualified candidates are encouraged to apply. Please email Brian.Shy@ucsf.edu, Jacob.Freimer@ucsf.edu, David.Nguyen@ucsf.edu, and Franziska.Blaeschke@ucsf.edu for additional questions about any of the positions or to submit your complete application documents including CV, references. Please also note whether you are interested in all posted positions or, alternatively, which individual projects you are interested in.

Sincerely,

Alex Marson, MD, PhD
University of California, San Francisco