The 65th ASH Annual Meeting Abstracts

## ONLINE PUBLICATION ONLY

### 803.EMERGING TOOLS, TECHNIQUES AND ARTIFICIAL INTELLIGENCE IN HEMATOLOGY

### Automated Cut&run Brings Scalable Epigenomic Profiling to Hematology

*Keith E Maier, PhD [1], Matthew R Marunde [1], Vishnu U. Sunitha Kumary, PhD [2], Carolina P Lin [2], Danielle N Maryanski [2], Liz Albertorio-Saez [2], Dughan J Ahimovic [3], Michael J Bale [3], Juliana J Lee [4], Bryan J Venters, PhD [2], Michael-Christopher Keogh, PhD [2]*

[1] EpiCypher Inc, Durham, NC
[2] EpiCyper, Inc, Durham, NC
[3] Weill Cornell Medicine, New York, NY
[4] Harvard Medical School, New York, NY

Genome-wide association studies (GWAS) and corresponding transcriptomics research have been leveraged to identify disease risk variants in hematological disorders with the hopes of developing more personalized treatment regimens. Interestingly, >90% of GWAS-identified variants are found in non-coding regions of the genome, indicating they likely affect the regulatory machinery that governs chromatin structure.

Non-coding elements, such as enhancers, play important roles in supporting chromatin mechanisms, including cell-type specific gene expression, cell fates and disease states. However, these variants are difficult to study compared to protein-coding mutations and have been challenging to directly associate with phenotypic readouts. To date, efforts to understand the effects of non-coding variants on chromatin dynamics have been focused on chromatin accessibility (ATAC-seq) and DNA methylation profiling. Notably, these assays can only provide a binary, "open-or-closed," view of chromatin and often fail to provide mechanistic insight into disease etiology.

Epigenomic features - such as histone post-translational modifications (PTMs) and chromatin-associated proteins - mark distinct genomic compartments (e.g., promoters, enhancers) and regulate chromatin structure, gene expression, and cell function. Mapping these features provides a rich context to study cell fate and has great potential for discovering new biomarkers and drug targets. Despite this, efforts to integrate epigenomics into large scale lymphatic and myeloid research have been hampered by the poor sensitivity, high background, and low throughput of traditional chromatin mapping technology (i.e., ChIP-seq).

Here, we present autoCUT&RUN, a high throughput assay for rapid, ultra-sensitive profiling of epigenomic features from FACS-isolated primary cells or tissues. This workflow generates reliable profiles from <10,000 cells per reaction, and is supported by a rigorous optimization strategy, high-quality antibodies, and quantitative spike-in controls. As part of a multi-site collaboration with the Immunological Genome Consortium, we used our autoCUT&RUN platform to build a comprehensive epigenomic database of mouse immune cells - composed of >1,500 epigenomic profiles from >100 different FACS-isolated primary immune cell types. These studies set the stage to leverage high-throughput epigenomics for multi-site clinical studies to identify and/or characterize novel biomarkers for precision medicine applications.

Further, we will discuss our integration of CUT&RUN and Enzymatic Methylation-sequencing (CUT&RUN-EM) to deliver a true multiomic view of the co-occurrence of epigenomic features and DNA methylation, which can reveal multivalent cellular mechanisms and deconvolute sample heterogeneity.

**Disclosures Maier:** *EpiCypher Inc:* Current Employment, Current equity holder in private company, Current holder of *stock options* in a privately-held company. **Marunde:** *EpiCypher Inc:* Current Employment, Current equity holder in private company, Current holder of *stock options* in a privately-held company. **U. Sunitha Kumary:** *EpiCypher Inc:* Current Employment, Current holder of *stock options* in a privately-held company; *New England Biolabs:* Ended employment in the past 24 months. **Lin:** *EpiCypher Inc:* Current Employment, Current holder of *stock options* in a privately-held company. **Maryanski:** *EpiCypher Inc:* Current Employment, Current equity holder in private company, Current holder of *stock options* in a privately-held company. **Albertorio-Saez:** *EpiCypher Inc:* Current Employment. **Venters:** *EpiCypher Inc:* Current Employment, Current holder

of *stock options* in a privately-held company. **Keogh:** *EpiCypher Inc:* Current Employment, Current holder of *stock options* in a privately-held company, Membership on an entity's Board of Directors or advisory committees.

https://doi.org/10.1182/blood-2023-186100