Benchmarking of Single Cell transcriptomics technologies to determine the cutaneous Lupus Erythematosus immune cell transcriptomic atlas and provide additional insights into BIIB059 mechanism of action

Abstract

Single Cell Sequencing (ScSeq) enables characterization of subtle differences at cellular level that are masked in bulk approaches. We are using this technology to identify effector molecules produced by Plasmacytoid dendritic cells (pDCs) in human Cutaneous Lupus Erythematosus (CLE) which are shown to drive disease progression.

Our goal is to benchmark both 10x genomics Single cell platform and SmartSeqV4 protocol to identify the most robust and sensitive technology to characterize pDCs in disease setting.
We purified closely related human primary immune subsets (pDCs, Monocytes and B cells) and completed ScSeq on pure populations and equal cellular pools using 10x genomics system. These results were benchmarked to recently published data for ability to distinguish cell types and assess signal to noise.

Our current plan is to optimize SmartSeqV4 protocol to improve detection of transcripts that are uniquely expressed by pDCs in Lupus skin

Conclusions

- Using 10x system, B cells – pDC – Monocyte populations could be distinguished in a mixed culture
- However, key pDC and Monocyte markers SLC15A4, NRP1 and ITGAM were not detected and fold changes of other markers were suppressed in contrast to recent publication
- SmartSeqV4 offers lower throughput but may provide better sensitivity for detection of key marker transcripts that distinguish pDC populations

Next Steps

We hypothesize that an optimized SmartSeqV4 method will provide best option for detection of transcripts that are uniquely expressed by pDCs in Lupus skin