Deciphering cell-to-cell communication in perturbed whole blood using single-cell RNA sequencing

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Introduction: Recent single-cell RNA sequencing (scRNA-seq) studies of fresh samples from healthy and diseased patients have revealed new insights into the communication patterns between different immune cells. However, these studies can only describe a snapshot of the very dynamic process within the immune system. To further resolve the kinetics of cellular interactions most studies use simplistic cell cultures with predefined subsets of the immune landscape. For instance, stimulating only highly purified individual immune cell types such as monocytes, T, B or NK cells not only disregards important cell-cell interactions, but additionally cell isolation strategies may also pre-activate cells.
Methods: To mimic a more realistic and less artificial perturbation of immune regulation and communication in human blood cells, we utilized a commercial whole blood culturing system called TruCulture® in close collaboration with HOT Screen GmbH. Cells were stimulated using lipopolysaccharide, dexamethasone and a combination of both as a model for sepsis and one of its therapies. The transcriptional response of single CD45+ immune cells was examined during 32h using the scRNA-seq technology Seq-Well.
Results: This time kinetics experiment provides data of about 120.000 single cells over seven different time points (0, 2, 4, 8, 16, 24, 32h) and four different conditions. Using state-of-the-art algorithms, we were able to classify the different cell types and mapped their activation states upon different perturbations. We were able to identify transcriptional responses first in the myeloid compartment followed by an activation of lymphoid cells. Clear inter- & intracellular communication patterns were found in the different subsets.
Conclusion: Our results indicate that this approach can be used to study perturbation and cell-cell interactions within the blood-derived immune cell compartment ex vivo while overcoming the limitations of classical co-culture experiments. We anticipate the combination of whole-blood culture systems with single cell analysis to be used to define the immune system's reactivity in many pathophysiological conditions and diseases.

Keywords : scRNA-seq, Human, Cellular interaction, Stimulation, Blood
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