Multimodal label-free microscopy for the detection of single-cell immune response

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Recent research has shown the importance of studying biological responses at single-cell level, as cellular behaviors are often highly heterogenous and can involve multiple mechanisms and pathways which are not well characterized in the case of measurements at populations levels. Measurements of single cells however raise issues in terms of achievable throughput and sensitivity. Several approaches have been developed in recent years, such as fluorescence-activated cell sorting (FACS) and single-cell sequencing. These techniques are however invasive in the sense that they require labelling and often involve the destruction of the sample. In particular, FACS is limited to surface receptors when measuring live cells, and requires fixation for the detection of intracellular molecules.

We developed recently a multimodal label-free optical platform that combines quantitative phase microscopy (QPM) and Raman spectroscopy, for which we designed specific procedures that can ensure high-throughput, by relying on QPM imaging and single-cell spectra measurements [1]. This approach provides indicators of both cellular morphology (as extracted from imaging) and intracellular molecular content (from spectroscopic measurements) that can be obtained non-invasively on live cells. Such indicators have been employed separately in different studies and have proven successful to distinguish for instance different cell types such as healthy versus cancerous cells.

We coupled these label-free indicators with machine learning algorithms to detect the fine changes that occur during the immune response of macrophage cells, and could show that our approach can detect the activation state of single cells, and is also sensitive enough to provide a dose-response behavior, and to detect pathway-dependent responses [2]. More recently, we also demonstrated the validity of our approach in the case of primary cells, which display much larger heterogeneity than clonal cell lines. In that context, it was possible to detect both the activation state and the origin of the cells, as *in vivo* immune cells are constituted of populations from different developmental origins [3].

References

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