High-Throughput Selection of Therapeutic ADC Candidates Using Imaging Flow Cytometry

Ziv Porat
Weizmann Institute of Science, Rehovot, Israel

Abstract:

Antibody-drug conjugates (ADCs) represent a rapidly expanding class of targeted oncology therapeutics that merge antibody specificity with cytotoxic payloads. A critical bottleneck in ADC development is verifying lysosomal internalization, the essential mechanism for intracellular drug release. While traditional confocal microscopy offers high-resolution visual confirmation, it lacks the statistical throughput required for robust candidate screening. This study demonstrates how imaging flow cytometry (IFC) bridges this gap by providing high-content, automated quantification of intracellular trafficking at a single-cell level.

By leveraging IFC, we established a robust screening pipeline using the Bright Detail Intensity (BDI) and Bright Detail Similarity (BDS) features. These specific morphometric parameters enabled automated, objective tracking of antibody localization and lysosomal co-localization across thousands of cells. Our data show that relying on BDS and BDI features provides superior statistical power to identify and select the optimal ADC candidates compared to traditional methods. Furthermore, we discuss how combining the spatial precision of confocal microscopy with the high-throughput statistical depth of IFC creates a synergistic validation workflow, ultimately streamlining the selection of highly effective ADC candidates.