Image-Activated Cell Sorting

Sorting sensitive cell samples based on high-quality microscopy image analysis

Artistic illustration of image-activated sorting of T cells showing T cell receptor clustering upon activation. Only via spatially-resolved imaging and analysis, the cells with clustered T cell receptors in their membrane can be distinguished from those with homogeneously distributed receptors.

Image-activated sorting of small, valuable cell samples overcomes previous limitations of classical sorting methods and enables working at a completely new level of quality

Problem

Separation of heterogeneous cell populations is a key technology in modern biomedicine. However, conventional sorting methods based on low-dimensional (»low-content«) sorting criteria such as integral fluorescence intensity or whole-cell scattered light are not able to detect spatially-resolved (»high-content«) features such as the subcellular distribution of proteins, the number and localization of cell organelles or their binding to other cells and use them as separation criteria.

To utilize spatially-resolved features for cell sorting, imaging techniques need to be combined with high-precision cell sorting functions. Only then can high-resolution microscopic image data be used together with AI-assisted image analysis to classify and separate cells based on their morphological information.

Feature	Example of application
Nuclear-cytoplasmic ratio	Isolation of malignant cells for personalized medicine
Morphology of cells or organelles	Isolation of special yeast strains for the food industry
(Co-)localization of proteins or organelles	Isolation of activated immune cells
Cell aggregation	Isolation of tumor antigen-specific T cells
Chromosome number / FISH analysis	Isolation of malignant cells
Extracellular vesicles	Isolation of virus-infected cells

Our Approach

In the Fraunhofer-funded IMAGO project, scientists from three different Fraunhofer Institutes (Fraunhofer IIS, IOF and IZI-BB) are working together with researchers from Charité Berlin on a microfluidic method in which the microscopic image information of individual cells flowing through a micro-channel is captured and analyzed automatically. According to the separation criterion previously defined by the user, the system generates a sorting decision and precisely separates the target cells from the remaining cells by electrokinetic forces.

Our microscope-based approach offers high flexibility in the choice of the imaging technique. Transmitted light, phase contrast or (multi-color) fluorescence imaging with a variety of excitation and emission wavelengths can be easily combined with our approach, as well as less common imaging techniques such as polarization microscopy, quantitative phase imaging and many more.

The possibility of image-activated cell sorting in combination with low-loss processing of even small cell numbers overcomes previous limitations of classical sorting methods and opens up new avenues in biomedical research with applications in the fields of immunotherapies and stem cell biology or for the analysis of organoids or small tissue biopsies, and many more.

What we offer

- Sorting as a service: We sort your valuable cell samples on the basis of high-content features.
- Technology or product licensing:
  - Microfluidic sorting technology
  - AI-based image data analysis
  - Optical system design
  - Microfluidic chips

Fast Facts

- High resolution, high quality imaging data (e.g. 60x magnification)
- Multispectral image acquisition with support for 3-4 fluorescent colors or markers
- AI-supported cell classification, customizable by the user to the respective use case
- »Train by example« using cell images instead of cell attributes in classic »gating«
- Processing of low cell numbers of $10^4 - 10^6$ cells
- High yield, high purity
- Low shear forces, high biocompatibility due to microfluidic cell processing
- Aerosol-free cell deposition
- In the future:
  - Single-use microfluidic chips to avoid cross-contamination
  - GMP conformity

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