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Fraunhofer-Institut für Toxikologie und Experimentelle Medizin ITEM
Dr. Cathrin Nastevska

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Chip cytometry: a promising tool for analysis of induced sputum and BAL in multi-center clinical trials

In a clinical proof-of-concept study, Fraunhofer ITEM researchers were able to demonstrate that chip cytometry can also be used to analyze bronchoalveolar lavage (BAL) fluid or induced sputum. This method enables quantitative and even multiple repeated analyses also of the small amounts of morphologically heterogeneous cell populations that are typical of these biological samples.

Analysis of the cellular composition of BAL fluid and induced sputum plays an important role in research on bronchial and pulmonary diseases and in their diagnosis. Cell analysis allows conclusions to be drawn about the stage or progression of a respiratory disease. In addition, it can be used to evaluate drug response and to monitor and analyze a particular treatment in clinical trials.

Established methods of cell analysis have certain drawbacks – especially in multi-center clinical trials – which is why Fraunhofer researchers are pioneering new approaches. They have optimized chip cytometry for analyses of BAL fluid and induced sputum. Normally, this method is used to analyze blood samples, which contain larger quantities of the different cell types and in which case the samples themselves are free of contaminants. In contrast, analyzing biological samples such as BAL fluid and induced sputum is not that easy. The reason is that these types of samples include morphologically more heterogeneous cell populations in small quantities and frequently also a considerable amount of cell debris and large squamous cells from the oral mucosa, making it difficult to identify and differentiate cells. “We evaluated the performance of chip cytometry in a proof-of-concept study using endotoxin challenge of healthy subjects. We demonstrated that the method is a very good alternative to characterize and quantify cellular changes in the major cell populations in BAL fluid and sputum. And, above all, it can be used in multi-center clinical trials,” explains Fraunhofer ITEM scientist Saskia Carstensen.

Chip cytometry is opening up new possibilities in clinical research
Chip cytometry is a novel tool that combines the analytical capabilities of cell differentiation by microscopy and flow cytometry. The cells are transferred to specific microfluidic chambers, referred to as chips, and fixed. This allows a temporal separation of sample preparation and cytometric measurement without compromising sample quality. By means of fluorescence-stained biomarkers, these chips can be used to investigate cell morphology, expression of surface markers, and intracellular functions. A special advantage is that the measurement does not cause the cells to be lost and that they can thus be re-analyzed repeatedly for comprehensive immunological and functional characterizations. Depending on the cell population, analyses at the single-cell level and also storage of the chips are possible over prolonged periods of time. Furthermore, the method facilitates sample transportation. This is particularly important for sample analyses in multi-center trials, when samples from different clinical sites, which are usually located far away from each other, are to be centrally analyzed in a core facility.

Differential cell count by microscopy and flow cytometry are less appropriate methods of analysis in multi-center clinical trials

Chip cytometry excels over other methods of analysis that are commonly used: it combines direct optical analysis of cells with the possibility to repeatedly label single cells with antibodies and analyze them, while preserving the sample material after the measurement. Among the other methods of analysis are differential cell count by microscopy and flow cytometry. The first one is fast, simple, inexpensive, and available in many clinical laboratories. It allows adequate analysis of changes in the cellular inflammatory response of the major cell populations. A differentiation of monocytes and small macrophages, however, is difficult due to their overlapping morphological features. Moreover, analysis of rare cell populations is inaccurate and the amount of information that can be obtained is limited. Flow cytometry, in contrast, allows more detailed cellular characterization and is able to distinguish between monocytes and macrophages. In addition, it detects rarer cell populations more accurately. However, this technology requires comprehensive expertise and professional equipment. In multi-center clinical trials, lack of instrumentation, extensive requirements for technical harmonization or known inter‑laboratory variability hamper the use of flow cytometry. Alternatively, samples could be measured and analyzed in a central laboratory, but this is difficult because preservation, storage, and shipment of cells can affect cell viability and the activation status of cells and thus sample quality.

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URL zur Pressemitteilung: https://www.item.fraunhofer.de/en/crc-hannover/chipcytometry.html Chip cytometry at Fraunhofer ITEM

URL zur Pressemitteilung: https://www.youtube.com/watch?v=dh-ajUW7FsQ About chip cytometry

Chip cytometry is an appropriate method of analysis for bronchoalveolar lavage fluid and induced sputum – in particular in multi-center clinical trials.
Till Holland
Fraunhofer ITEM