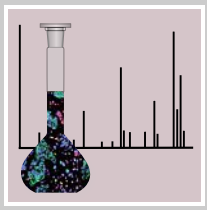
doi:10.2533/chimia.2015.637



Highlights of Analytical Sciences in Switzerland

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Laser Ablation ICP-MS for Single-Cell-based Tissue Imaging

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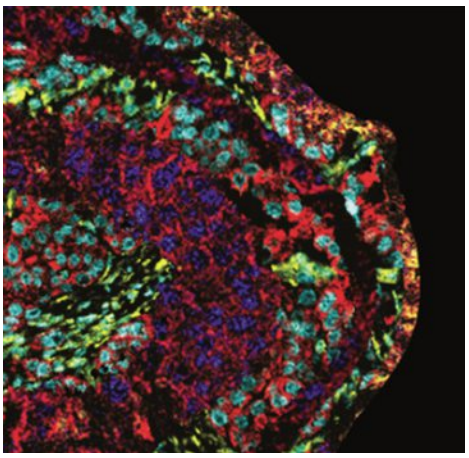
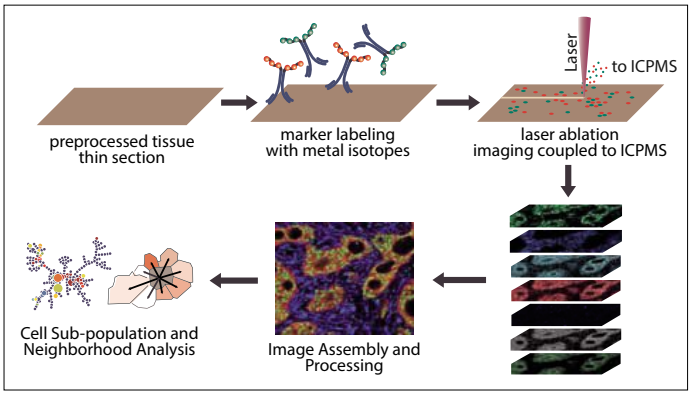
Keywords: Imaging mass cytometry · Laser ablation ICPMS · Multiplexed tissue analysis · Subcellular resolution · Tumor cell heterogeneity

The cell heterogeneity of tumor tissues drives tumor pathogenesis and progression and is currently of particular interest in biomedical research. Adapting and combining mass cytometry workflows with laser ablation techniques brings with it the opportunity to visualize this tumor cell heterogeneity, and cell-to-cell interactions in the so-called microenvironment, on the single-cell level in tissue thin sections. Similar to immunohistochemistry, tissue sections are treated with distinct rare earth isotope-tagged antibodies. Subsequently, the tissue is analyzed by scanning using a high-energy pulsed laser across the surface and transfer of the so generated aerosol into an inductively coupled plasma mass spectrometer (ICPMS) for detection of the metal labels. In addition to a novel ICP-TOFMS, a dedicated laser ablation system was developed, facilitating high spatial resolution, fast image acquisition, high sensitivity and multiplexed elemental analyses. A laser spot size of 1 µm diameter enables recognition and distinction of features at subcellular resolution. Specific markers can be employed to enable the detection of individual cells for automated, software-based data evaluation. The imaging mass cytometry approach allows labeling of potentially more than 100 different markers for highly multiplexed tissue analyses.



The tumor microenvironment in breast cancer tissues can be investigated by the combination of laser ablation imaging and mass cytometry (artistic design and copyright Nicole Seidel).

In a pilot study, 32 different protein markers and protein modifications could successfully be localized in tissue samples from 20 patients in an automated and high throughput manner at a limit of detection of approx. 500 marker molecules per pixel. The analysis revealed a variety of cancer cell subtypes in groups of patients, which had been classified as similar using classical histology schemes.



Workflow for imaging mass cytometry, based on mass cytometry and laser ablation ICPMS imaging.

The laser ablation ICPMS imaging and in combination with element labels is now routinely used for imaging mass cytometry studies at the University of Zurich. Of special interest is the interplay of particular cells, their regulatory circuits and how processes in the tumor microenvironment are induced and maintained.

Received: August 21, 2015

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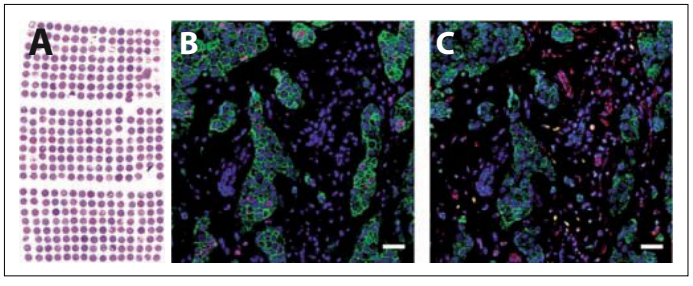

(A) On a typical tissue microarray each sample has a diameter of about 0.7 mm. (B and C) Mass cytometry images of breast cancer tissue. (B) Overlay of markers Ki-67 (red), H3 (blue) and HER2 (green). (C) Overlay of cytokeratin 8/18 (green), H3 (blue), vimentin (red), and CD68 (yellow). The white size bars indicate 25 µm.

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