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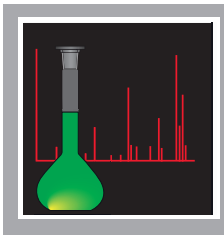

Highlights of Analytical Chemistry in Switzerland

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Lighting-up Cancerous Cells and Tissues with Lanthanide Luminescence

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Time-resolved luminescence immunoassays as well as cell and tissue imaging are showcase applications of lanthanides. Novel assays are inspired by the unique emissive properties of trivalent lanthanide ions (Ln^{III}): easy-to-recognize narrow emission bands, large Stokes' shifts making facile wavelength discrimination, long excited state lifetimes allowing time-resolved detection, henceforth resulting in highly sensitive analyses, and little or no photobleaching.

New and targeted therapies for cancer treatment need rapid, specific and reliable tools to identify treatment targets on cancer cells and tissues as well as other relevant biomarkers. Lanthanide luminescent bioprobes are ideal for this type of analyses. During the past five years, we have teamed up with pathology at the University Hospital to develop practical microfluidic devices for the detection of cancerous cells *via* the biomarkers expressed by them. The lanthanide luminescent probes used are binuclear helicates, self-assembled in water under physiological conditions. The designed ligand framework yields thermodynamically stable and kinetically inert molecular entities with adequate photophysical properties and low cytotoxicity. They can be conveniently bioconjugated to avidin or monoclonal antibodies. The microfluidic device is 2.5 cm long and has a meandering 100-μm microchannel. Reactant flows are controlled by precision micropumps.

Cells such as MCF-7 breast cancer cell line can be grown in the microchannels and, after fixation, specifically be detected *via* the 5D10 antibody – which recognizes a mucin-like antigen on the cell membrane – using time-resolved luminescence microscopy. It yields bright, background-free signals, allowing high performance screening on breast cancer cells and tissues.

Two receptors expressed by these cells are relevant for treatment decisions: human epidermal growth factor receptor (Her2/*neu*) expressed on the cell membrane and estrogen receptors (ER) expressed in the nucleus. We have placed 4-μm sections of well-characterized, formalin-fixed breast carcinomas in the microchannel and visualized the two markers by dual indirect immunohistochemical luminescent assays under time-resolved conditions. Our first device allowed this test to be completed within 20 minutes versus more than 2 hours in a hospital laboratory and using 1/5 of the expensive reagents. **We are currently validating this protocol for routine diagnostic application. Test times are now down to only five minutes.**

References

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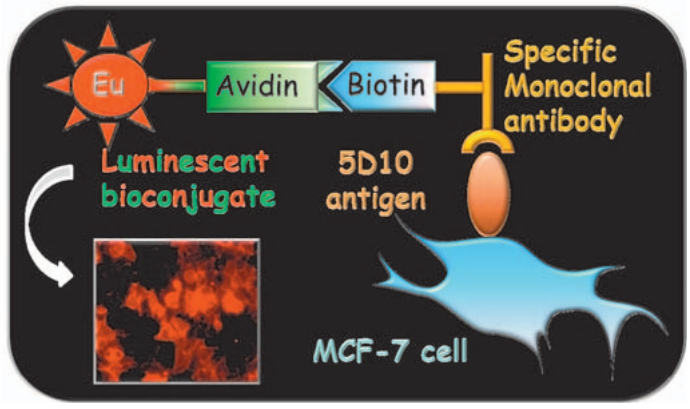
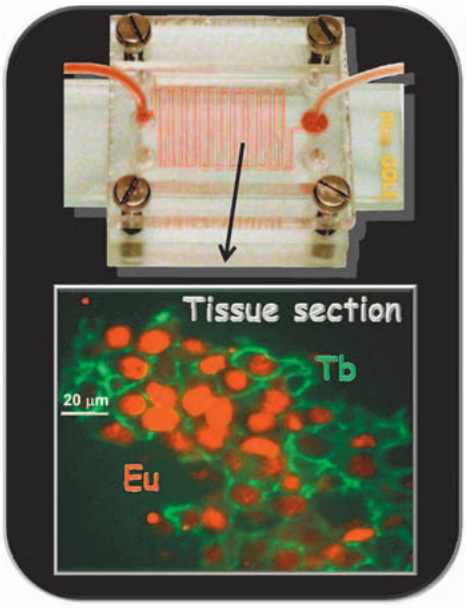


Principle of detection of MCF-7 breast cancer cells combining biochemical recognition of the 5D10 antigen they express with time-resolved luminescence microscopy of a Eu-labelled avidin and a biotinylated 5D10 antibody, taking advantage of the strong avidin-biotin interaction.



Microfluidic device and its potential for dual assays: ER (red) and Her2/*neu* (green) receptors evidenced by time-resolved luminescence microscopy. Her2/*neu* receptors: polyclonal rabbit anti-human c-erbB-2 oncoprotein antibody / Tb-labelled goat anti-rabbit IgG antibody. ER receptors: anti-human ER mouse mAb / Eu-labelled goat anti-mouse IgG Ab.

Can you show us your analytical highlight?
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