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NATIONAL PRESS RELEASE I PARIS I 7 OCTOBER 2013

NB: Embargoed until 09:00 pm, 7 October 2013

Observing the living in real time and in a new light

Fluorescence imaging, a very important technique in biology and medicine, makes it possible to observe the living while in movement. However, the labels used in this domain are very often in competition with the natural fluorescence of the biological medium. In fact, this autofluorescence can seriously hinder observation under visible light. On the other hand, under near-infrared light it is virtually zero. The first stable, non-toxic labels that are sufficiently efficient under near-infrared light to be used in fluorescence imaging have been developed by a team led by Inserm researcher Stéphane Petoud at the Centre de Biophysique Moléculaire of CNRS in Orleans (CBM) and Nathaniel Rosi at the University of Pittsburgh (USA). A new tool for exploring the living world in real time is now available to biologists—and probably to clinicians in the future. This work is published online w/c October 7, 2013, in the journal *PNAS*.

Fluorescence imaging is an emerging technique in the field of biomedical applications, allowing a specific target (cell constituents, a pathogenic agent, an active ingredient, etc.) to be observed and monitored in real time and in a non-invasive manner, not only in a single cell but also in a whole body. This is done by using labels, i.e. fluorescent molecules that target the areas to be observed and highlight them during observation.

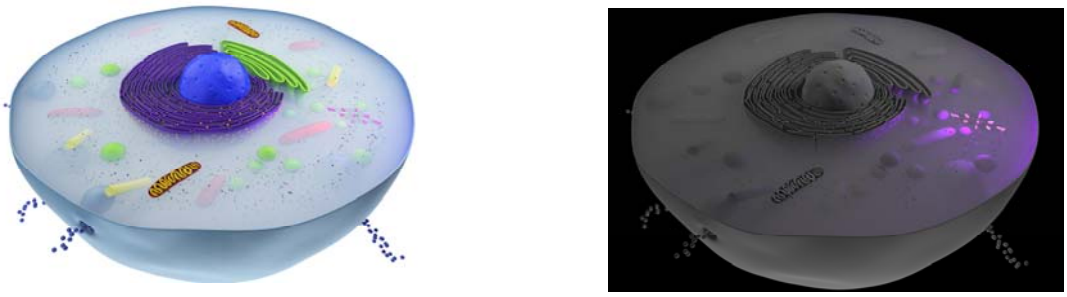
These observations are limited by the natural fluorescence of biological components, which interferes with the signal emitted by imaging agents. Using near-infrared light makes it possible to overcome this phenomenon. In fact, this type of light interacts less with tissue components, allowing image quality to be improved and detection sensitivity to be enhanced. At present, very few efficient fluorescent labels exist for biological imaging in the near-infrared. The few commercially available agents are often highly sensitive to light and degrade very quickly, leading to the disappearance of their fluorescence (photobleaching). They can also be relatively toxic.

Lanthanide based molecules emit a very weak fluorescence signal in the near-infrared, which prevents their use for imaging purposes. The challenge taken up here by the Orleans-based researchers was to develop a compound whose structure allows the number of lanthanides per unit of volume to be multiplied in order to significantly increase detection sensitivity. Using porous materials known as MOFs (metal-organic frameworks)[1], the CMB scientists have been able to obtain significant fluorescence of these compounds in the near-infrared. It has been demonstrated that these compounds, based on luminescent

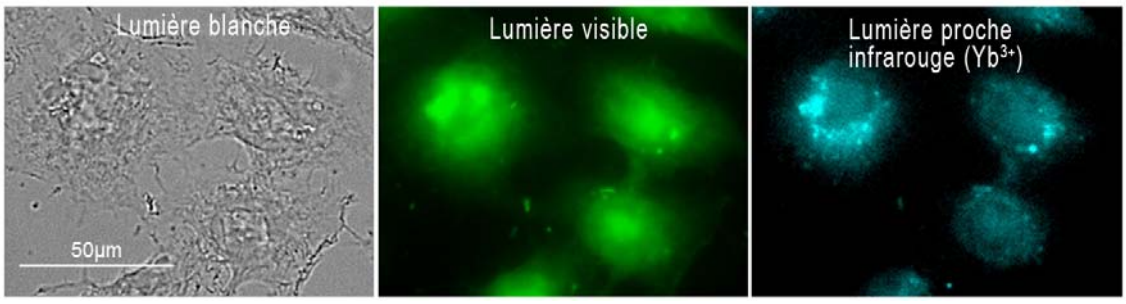
[1] MOFs are rigid, porous nanoparticles already used in applications such as gas storage, fuel cells, catalysis and, much more recently, the delivery of therapeutic molecules and imaging (mainly MRI).

lanthanides, have low toxicity and good resistance in water, which is essential for biology applications. The strategy developed has made it possible to obtain the first microscopy images with compounds based on luminescent lanthanides emitting in the near-infrared in living cells.

This work stems from multidisciplinary research at the interface between chemistry, biology and physics. These initial results are very promising for the development of imaging agents in the near-infrared that can be used in biological research and, in the longer term, in medical establishments.



In the visible domain (image on the left), the cellular components have natural fluorescence that is difficult to distinguish from the fluorescence signal emitted by a specific label. Since autofluorescence is lower or even non-existent in the near-infrared domain, it means the fluorescence signal emitted by the new lanthanide-based labels can be distinguished and localized unambiguously (image on the right). Illustration: Thomas Jullien. © CBM



White light | Visible light | NIR light (Yb^{3+})

"HeLa" cells after incubation with nano-MOF-Yb-PVDC-3. Near-infrared imaging allows the fluorescence signal emitted by the nano-MOFs to be located more precisely without parasitic autofluorescence light in the visible domain. © CBM

Bibliography

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