Thursday, December 12th

Session: NANO FOR IMAGING, DIAGNOSIS AND THERANOSTICS

9h30 – 12h15

Keynote speaker: Hatice ALTUG

Nanophotonics: enabling technology for biosensing and imaging

Keynote speaker: Kevin BRAECKMANS

Light-triggered delivery of functional macromolecules in cells and antibacterial agents in biofilms

Abstracts

The SFNano C'Nano joint meeting 2019

Thematic Session: Nano for imaging, diagnosis & theranostics

Keywords: gold nanoclusters; infrared photoluminescence; optical imaging; theranostic agents

Investigation of gold quantum clusters for non-invasive *in vivo* optical imaging in the wide infrared window 700-1700 nm

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Gold quantum clusters (Au NCs) are ultra-small particles with metal core smaller than 3 nm exhibiting molecular-like properties and a discretization of the energy levels. These species have shown a high interest as contrast agents for bioimaging due to their photoluminescence in the first near-infrared window (NIR: 700-900 nm)[1] and recently by us in the second infrared window called "shortwave infrared" (SWIR: 900-1700 nm)[2]. The photoluminescence of Au NCs in these spectral windows is strongly influenced by the nature of the ligands and how it stabilized the metal core.

We develop gold quantum clusters stabilized by short thiol organic molecules to tailor their photoluminescence emission and intensity notably in the SWIR region reaching a quantum yield up to 6.1% in water[3]. After a full characterization of these particles by spectroscopic and optical techniques, investigation was conducted in mice to visualize non-invasively the vascular network and to study their biodistribution. It demonstrates two important findings: i) a pharmacokinetic of Au NCs in mice highly driven by the nature and the density of the ligands protecting the gold core, and ii) the benefit moving from NIR to SWIR optical windows for bioimaging leading to higher spatial resolution deeper in tissue mainly due to the strong decrease of scattering at longer wavelengths.

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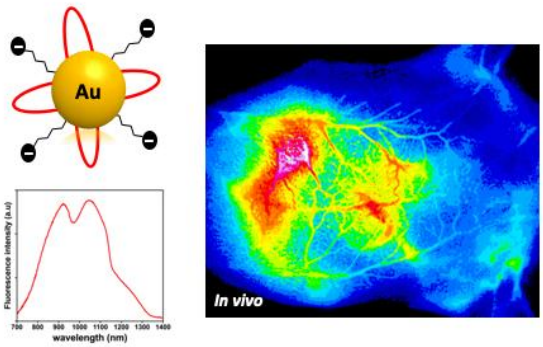
[2] Chen, Y.et. al., *Nanoletters* **2017,** *17*, 6330.
[3] Musnier, B. et al., *Nanoscale* **2019,** *11*, 12092.



The SFNano C'Nano joint meeting 2019

Thematic Session: Nano for imaging, diagnosis & theranostics
Keywords: *In vitro* and *in vivo* imaging, detection, instrumentation

Probing intraneuronal transport *in vivo* with optically active photostable nanocrystals

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Neurodegenerative disorders such as Alzheimer's disease involve a large network of genes displaying subtle changes in their expression. Abnormalities in intraneuronal transport have been linked to genetic risk factors found in patients, suggesting the relevance of measuring this key biological process. However, current techniques are not sensitive enough to detect minor abnormalities.

In 2017, we reported a method able to measure changes in intraneuronal endosomal transport induced by brain disease-related genetic risk factors mimicked in transgenic mice (*1*). It relied on tracking fluorescent nanodiamonds (FNDs) after their spontaneous endocytosis by hippocampal neuron in culture, and takes advantage of FND.

Here we report the extension of this nanoparticle tracking based-approach to multiphoton microscopy (MPM), opening the possibility of intracellular transport measurement *in vivo* thanks to tissue transparency in MPM excitation wavelength range. To this aim we have tracked sized≈100 nm $KTiOPO_4$ (KTP) nonlinear nanocrystals endocytosed in axons of the periventricular neurons after microinjection in the optical tectum of living zebrafish larvae. NanoKTP large nonlinear second order optical response (*2*) allowed us to maintain the same 20 frames/s rate as in widefield imaging with FND, despite the need for raster-scanning. We showed that we can detect slight endosomal transport impairment due either to very low concentration drug-induced cytoskeleton destabilization or to knock-out of molecular motor-related genes.

1. S. Haziza *et al.*, *Nat. Nanotechnol.* **12**, 322–328 (2017).
2. L. Mayer *et al.*, *Nanoscale*. **5**, 8466–71 (2013).

The SFNano C'NANO joint meeting 2019

Thematic Session: nanomaterials

Keywords: (self-assembling, radioimaging, fluorinated dendrimer, biodistribution)

Supramolecular dendrimer nanosystem for bioimaging

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Abstract

Nanotechnology-based imaging for cancer diagnosis is endowed with unique advantages of improved imaging sensitivity and specificity.[1] Dendrimers are ideal nanocarriers for imaging agents by virtue of their well-defined dendritic structure and multivalent cooperativity.[2] Recently, we have successfully constructed self-assembling supramolecular dendrimer nanosystems for tumor imaging using various imaging modalities such as optic imaging[3], positron emission tomography (PET) [4] and single photon emission computed tomography (SPECT).[5] Interestingly, by introducing a fluorinated component into the dendrimer, the uptake of imaging agent in the liver can be significantly reduced, offering an extremely benefit for reducing non-specific imaging and eventual imaging guided internal radiotherapy. The possibility of closely controlling the chemistry, the size and the hydrophobicity-hydrophilicity balance of dendrimers provides us with a unique opportunity to create tailor-made supramolecular dendrimer nanosystems for various biomedical applications in general.

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The SFNano C'Nano joint meeting 2019

Thematic Session: Nano for imaging, diagnosis and theranostics

Keywords: Metal-bis(dithiolene) complexes, Organic nanoparticles, Photothermal therapy, Photo-controlled drug delivery, Photoacoustic

ORGANIC NANOPARTICLES CONTAINING NICKEL-BIS(DITHIOLENE) COMPLEXES FOR PHOTOTHERMAL THERANOSTICS

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Metal-bis(dithiolene) complexes are known as strong NIR absorbers in a wide range of NIR wavelengths and have been widely used in laser technologies. However, we have recently demonstrated that nickel-bis(dithiolene) complexes also display strong photothermal activities under laser irradiation in the near infrared region which is of great interest in material science and in biotechnologies.[1]

Recent investigations have demonstrated that NIR irradiation of thermally sensitive liposomes and PEG-*b*-PMLABe block-copolymer nanoparticles containing nickel-bis(dithiolene) allows the fine control of the release of their drug contents in solution under NIR-laser irradiation.[2] It has also been demonstrated that the photothermal activity can be used to induce cell death under NIR-laser irradiation, highlighting that such metal-bis(dithiolene) containing organic nanoparticles can be good candidates for photothermal therapies (PTT).[3] Finally, more recently, it has been found that these metal complexes also exhibit remarkable photoacoustic properties. The photoacoustic signal is easily detected and its intensity is directly proportional to the concentration of complexes and to the laser energy, showing that metal-bis(dithiolene) complexes can also be used as exogenous contrast agents for photoacoustic bioimaging.[4]

All these results highlight that this class of metal-bis(dithiolene) complexes containing organic nanoparticles can allow developing new multipotent nanoparticles for theranostics.

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The SFNano C'Nano joint meeting 2019

Thematic Session: Nanoscience for Cancer

Keywords: Elemental imaging, LA-ICP-MS, metal-nanoparticles, Biodistribution, Tumor Kinetics

Studying the preclinical ex-vivo distribution of metal nanoparticles: label-free direct elemental quantitative imaging with LA-ICP-MS

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Abstract

Introduction

Nanoparticles' labeling is most of the time required to follow and characterize their distribution in vivo or ex vivo. However, this labeling might alter the physico-chemical properties of the particles such as their size/weight, hydrophobicity or fine distribution. To perform label-free ex-vivo imaging of different metal nanoparticles (**Au, Ag, Pt**) in murine organs, we used laser ablation-inductively coupled plasma-mass spectrometry (**LA-ICP-MS**) which allows the direct quantitative imaging of the chemical elements in a tissue sample with high sensitivity.

Methods

The nanoparticles (NPs) were administered IV to mice bearing TS/A tumors. Organs were sampled either 1 or 24 hours after injection. Ion intensities of 31P+, 107Ag+, 197Au+ and 195Pt+ in tumor, liver, kidney and spleen were measured by ICP-MS. HDIP (HDF-based Image Processing) software was dedicated to process the mass-spectroscopy data together with the laser ablation position data to obtain the image data of their distributions.

Results

All the elements of interest were observed in the tissue sections. The results show that in the tumor, the smallest NPs may have the best uptake and distribution. The 30 nm size NPs are mainly observed in the spleen and the liver, while they accumulate less in the kidneys.

Conclusion

This elemental imaging method allowed to successfully image and quantify the bio-distribution and elimination processes of metal-based nanoparticles dedicated to theranostic approaches (*i.e.*, for both tumor diagnosis and therapy), **achieving 20 µm resolution and sub-ppm level detection limits**, on entire organs. Being complementary with standard optical microscopy, LA-ICP-MS offers new insights for nanosciences.