16-months post-doctoral position

Light-triggered delivery of therapeutic oligonucleotides with plasmonic gold nanoparticles

Location: CentraleSupélec and ENS Paris-Saclay, Gif s/Yvette Campus, Université Paris-Saclay	
Laboratories: Light, Matter and Interfaces (LuMIn) Biology and Applied Pharmacology lab. (LBPA)	**Web sites:** http://www.lumin.universite-paris-saclay.fr/en https://lbpa.ens-paris-saclay.fr/
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Scientific project

Most cellular dysfunctions in many diseases result from the expression of mutated or deregulated genes that overexpress proteins. Gene therapy revolutionizes the treatment of these diseases by turning off a defective gene using an oligonucleotide (DNA, RNA). In addition, gold nanoparticles under illumination at their plasmon resonance behave like miniature converters of light into heat. When illumination is achieved by ultra-short laser pulses, the heating is brief, intense and very localized. Our project makes it possible to perform, quantify and optimize the intracellular delivery of oligonucleotides for gene therapy. The DNA is grafted onto nano-cargoes consisting of gold nanorods coated with a silica layer. The delivery is controlled by laser-induced local photothermal conversion, using precise thermal management at the nanoscale, and quantitatively assessed by *in vitro* and *in vivo* analyses. This project, lead together with the *Laboratory of Biology and Applied Pharmacology* (LBPA, CNRS-ENS Paris-Saclay), has been awarded financial supports from *Institut d'Alembert* in Ecole Normale Supérieure Paris-Saclay and *labex Nano-Saclay*.

Description of the post-doctoral work

AuNPs covered with a thin layer of silica (AuNR@SiO_2) are synthesized by our partners in the *Surface Reactivity Laboratory* (LRS, CNRS, Sorbonne University, Paris).

1. **Biofunctionalization and ssDNA grafting.** The AuNR@SiO_2 surface will be prepared as to optimize DNA grafting. We will graft a nucleic acid onto the AuNP surface and characterize this biofunctionalization by appropriate techniques available in our lab.
2. **Photo-induced oligonucleotide release: analysis and optimization.** She/he will quantify the laser-induced release of fluorescence-labeled DNA from duplex dsDNA grafted onto AuNPs, *in vitro* and then *in cellulo*, by fluorescence imaging.
3. **Optimization of the irradiation for *in vivo* gene delivery.** The efficiency of the light-induced oligonucleotide release will be demonstrated and improved in a murine model with our partners in Avicenne Hospital (INSERM-APHP-Univ. Sorbonne Paris-Nord).

Requested profile

The candidate has a background in physics (optics, condensed matter, nanoscience) or physical chemistry. Additional training or experience in fluorescence microscopy or/and cell biology will be appreciated. He/she has a strong taste for multidisciplinary research.

Duration: 16 months

References:

1. *Coating gold nanorods with silica prevents the generation of reactive oxygen species under laser light irradiation for safe biomedical applications*, S. Mitiche, S. Gueffrache, S. Marguet, J.-F. Audibert, R. B. Pansu, B. Palpant *J. Mater. Chem. B* **10**, 589 - 597 (2022). DOI
2. *Influence of the sequestration effect of CTAB on the bio-functionalization of gold nanorods*, H. J. Łaszewski, B. Palpant, M. Buckle, C. Nogues, *ACS Appl. Bio. Mater.* **4**, 4753–4759 (2021). DOI
3. *Interplay between cellular uptake, intracellular localization and the cell death mechanism in triphenylamine-mediated photoinduced cell death*, R. Chennoufi *et al.*, *Sci. Rep.* **10**, 1-14 (2020). DOI
4. *Pulsed-laser irradiation of multifunctional gold nanoshells to overcome trastuzumab resistance in HER2-overexpressing breast cancer*, T. Nunes *et al.*, *J. Exp. Clinic. Canc. Res.* **38**, 306 (2019). DOI
5. *Absorption of ultrashort laser pulses by plasmonic nanoparticles: not necessarily what you might think*, X. Hou, N. Djellali and B. Palpant, *ACS Photonics* **5** (9), 3856–3863 (2018). DOI
6. *High-resolution AFM structure of DNA G-wires in aqueous solution*, K. Bose, C. J. Lech, B. Heddi, A. T. Phan, *Nature Commun.* **9**, 1959 (2018). DOI