Thursday, December 12th

Session: NANOSCIENCE FOR CANCER

14h00 – 16h30

Abstracts

The SFNano C'NANO joint meeting 2019

Thematic Session: Nanoparticules & therapeutic targeting
Keywords: Multicellular tumor spheroids; light sheet fluorescent microscopy; confocal laser scanning microscopy; drug penetration;

In quest of a suitable tool to assess drug and nanomedicine penetration into multicellular tumor spheroids

Gianpiero Lazzari[1], Daniele Vinciguerra[1], Anna Balasso[1], Valerie Nicolas[2], Nicolas Goudin[3], Meriem Garfa-Traore[3], Julien Nicolas[1], Patrick Couvreur[1], Simona Mura[1]

1. Institut Galien Paris-Sud, UMR 8612, CNRS, Univ Paris-Sud, Université Paris-Saclay, Faculté de Pharmacie, 5 rue Jean-Baptiste Clément, F-92296 Châtenay-Malabry cedex, France.

2. Institut Paris-Saclay d'Innovation Thérapeutique (IPSIT), UMS IPSIT Université Paris-Sud US 31 INSERM, UMS 3679 CNRS, Microscopy facility, 5 rue Jean-Baptiste Clément, 92296 Châtenay-Malabry cedex, France

3. Structure Fédérative de Recherche (SFR) Necker, Inserm US 24 CNRS UMS 3633, Cell Imaging Platform UMS 24, Hôpital Necker Enfants Malades, Bâtiment Imagine, 24 boulevard du Montparnasse 75015 Paris, France

Over the past 50 years a large number of advanced nanoscale systems for drug delivery (nanomedicines) has been developed as they hold the potential to overcome the limitations of conventional chemotherapy. Although few of them have reached the market, the small number unveils that a huge gap between preclinical results and the clinical performances still exists.
This might be partly ascribed to the methods used in the early stages of nanomedicine preclinical evaluation *in vitro*, mainly based on 2D monocultures of cancer cells. Despite their relative ease of handling, these cultures are devoid of structural architecture and lack the complex physiology of real tumor tissues. Hence, 3D culture methodologies have been proposed to better recreate the tumor complexity and allow a more predictive *in vitro* evaluation.
We have recently constructed a 3D model of pancreatic adenocarcinoma capable to reproduce the heterogeneity of the tumor tissue and the cancer cells/stroma interactions. We demonstrated that the presence of a complex microenvironment reduced the sensitivity of cancer cells to chemotherapy thus mimicking the resistance to treatments often observed in vivo.[1] Then, we used this model to investigate the penetration of doxorubicin (free form and loaded in nanoparticles). We showed that Confocal Laser Scanning Microscopy was not suitable to monitor the penetration through the whole spheroid. Contrarywise a complete 3D tomography was obtained by Light Sheet Fluorescence Microscopy and multi-view image fusion.[2]
These results strongly encourage the use of opportune imaging tools to carry out reliable preclinical *in vitro* screenings.

[1] Lazzari G et al., *Acta Biomat* 2018, 78, 296
[2] Lazzari G et al., *Eur J Pharm Biopharm* 2019, 142, 195

The SFNano C'Nano joint meeting 2019

Thematic Session: Nanoscience for Cancer

Keywords: targeted nanotherapy, magnetic nanoparticles, mechanical forces, tumor microenvironment, cell death

Mechanical destruction of tumor microenvironment through rotating magnetic field-induced torque of nanoparticles

Sara Lopez[1,2], Yoann Lalatone[3], Nicolas Halalli[2], Pascal Clerc[1,2], Arnaud Hillion[2], Joana Antunes[3], Daniel Fourmy[1,2], Laurence Motte[3], Julian Carrey[2], Gigoux Véronique[1,2].

1. INSERM ERL1226, Receptology and Targeted Therapy of Cancers, Toulouse, France.
2. Laboratoire de Physique et Chimie des Nano-Objets, CNRS UMR5215-INSA, Université de Toulouse III, Toulouse, France.
3. Laboratory for Vascular Translational Science, INSERM U1148, University Paris 13, Bobigny, France.

Efficacy of anti-cancer treatments is limited by low drug concentration at the tumor site and development of resistance to treatments. Cancer progression is not only determined by the genotype of cancer cells, but also by their interactions with tumor microenvironment. Cancer-associated fibroblasts (CAFs) secrete collagen increasing extracellular matrix density, which limits the penetration of chemotherapeutic agents into the tumor, and factors promoting tumor growth and resistance of cancer cells. In this context, the development of nanotherapy targeting CAFs represents an opportunity to destroy tumor microenvironment and inhibit cancer progression. Alternatively to heat release upon a high frequency alternating magnetic field exposure, magnetic nanoparticles (MNPs) generate torque or mechanical forces in response to a rotating low frequency magnetic field (RMF). We elaborated 6-nm MNPs decorated with the agonist gastrin (MNP@Gastrin) to target CAFs that express the CCK2 receptor (CCK2R), chosen as a model. MNP@Gastrin bind to the CCK2R, internalize and accumulate in the lysosomes of CAFs. Based on physics simulations on an assembly of ~4000 MNPs (representing MNPs accumulation in a lysosome), we screened different amplitudes/frequencies of RMF and demonstrated that RMF exposure induces the death of CAFs having accumulated MNP@Gastrin into their lysosomes. 40mT/1Hz RMF generating a 10pN torque was the optimal condition that causes the death of ~40% of CAFs. Finally, we showed that cell death occurs through a lysosomal pathway. This study establish the proof-of-concept that targeted MNPs can induce cell death and disrupt tumor microenvironment through mechanical forces upon RMF exposure and open new opportunities for cancer therapy.

The SFNano C'Nano joint meeting 2019

Thematic Session: (Nanochemistry: synthesis & functionalization of nanosystems for bioapplications, Nano for (bio-)imaging, diagnosis and theranostics, Nanoscience for Cancer)
Keywords: (Synthesis, Gold nanoparticles, Encapsulation, Formulation, Biodistribution, internalization, Personalized cancer therapy, cancer theranostic)

Design of multifunctional gold nanoparticles-loaded PLGA nanocarriers for biomedical applications

Gautier Laurent[a,b], Claudia Flores[a], Yann Pellequer[a], Rana Bazzi[b], Vivek Sudam Thakare[c], Franck Denat[c], Stéphane Roux[b] and Arnaud Béduneau[a]*

[a] PEPITE EA4267, Univ. Bourgogne Franche-Comté, F-25000 Besançon, France

[b] Institut UTINAM, Univ. Bourgogne Franche-Comté, UMR 6213 CNRS-UBFC, 25030 Besançon Cedex, France

[c] Institut de Chimie Moléculaire de l'Université de Bourgogne (ICMUB), Université de Bourgogne Franche-Comté, UMR 6302 CNRS-UBFC, 21078 Dijon Cedex, France
* : Corresponding author: Tel : +33 3 81 666 52 91 ;
E-mail : arnaud.beduneau@univ-fcomte.fr

Due to their imaging and radiosensitizing properties, gadolinium-coated gold nanoparticles (Au@TADOTAGA), represent a promising approach in the treatment of tumors by image guided therapy. However, the short plasma half-life due to a rapid renal clearance limit drastically the tumoral accumulation. A study was initiated for optimizing the pharmacokinetic properties of Au@TADOTAGA while maintaining the renal clearance, which is a prerequisite for *in vivo* application of inorganic nanoparticles. This strategy rests on the encapsulation of Au@TADOTAGA in larger polymeric nanoparticles. An original encapsulation procedure using a polycation, the polyethyleneimine (PEI), was set up to electrostatically entrap gold nanoparticles in biodegradable poly-lactic-co-glycolic acid (PLGA) eventually conjugated to PEG.

Sizes were dependent of the PEI/Au ratio (between 115 and 196 nm). Encapsulation yield was close to 90% whereas no loading was observed without PEI. Electron microscopy demonstrated a high Au@TADOTAGA density in the PLGA nanoparticles (Au@PLGA). Furthermore, DIL fluorochrome, which provide molecular weight and hydrophobic properties similar of common chemotherapeutics like Paclitaxel or Docetaxel, was co-encapsulated with gold nanoparticles showing the potential for this object to achieve both chemotherapy and image guided therapy.

Internalization test (9L) showed Au@TADOTAGA were not internalized contrary to Au@PLGA using a passive mechanism. After injection in healthy rat, Au@TADOTAGA concentration in the blood was tremendously increased within the first hour with Au@PLGA compared with Au@TADOTAGA. The very low gold content in the kidney tissue suggests a postponed renal clearance. T_1-weighted magnetic resonance imaging showed that the PLGA shell did not alter the imaging contrast agent properties of gadolinium.

The SFNano C'NANO joint meeting 2019

Thematic Session: Nanoscience for cancer

Keywords: Photothermal therapy, cholangiocarcinoma, tumor associated fibroblasts, tumor stroma

Targeting tumor-associated fibroblast and modulation of tumor stroma in cholangiocarcinoma with gold decorated iron oxide nanoflower – mediated photothermal therapy.

Alba Nicolas-Boluda[1,2], Javier Vaquero[3], Gautier Laurent[4], Gilles Renault[2], Rana Bazzi[4], Stéphane Roux[4], Emmanuel Donnadieu[2], Laura Fouassier[3]*, Florence Gazeau[1]*

1. Laboratoire Matière et Systèmes Complexes (MSC), CNRS-UMR 7057, Université Paris Diderot, Paris, France
2. Institut Cochin, INSERM U1016/CNRS UMR 8104, Université Paris Descartes, Paris, France
3. Sorbonne Université, INSERM, Saint-Antoine Research Center, Paris, France
4. Institut UTINAM, CNRS UMR 6213, Université Bourgogne Franche-Comté, Besançon, France

Cholangiocarcinoma (CCA) is a very aggressive cancer of the biliary tract, characterized by a desmoplastic stroma with an abundant extracellular matrix. Late diagnosis compromises the effective therapeutic options, which are based on surgical resection only possible in 20% of cases, while chemotherapies are virtually palliative given the marked chemoresistance of this cancer. For this reason, the need of alternative therapies for CCA is of upmost importance. Over the last decades, nanoparticle-mediated photothermal therapy (PTT) is becoming a very promising therapeutic alternative for cancer treatment. Nanoparticle-mediated PTT allows the generation of a localized hyperthermia in a spatiotemporal-controlled manner that affects the tumor microenvironment, including its extracellular matrix. In this study, we report the design of an optimized nanoparticle featuring an iron oxide nanoflower-like multicore nanoparticle conceived for high near-infrared (NIR) absorption coefficient suitable for PTT. The decoration of the iron oxide nanoflowers with gold nanoparticles (Au@DTDTPA) increased the heating efficiency of the nanoparticles compared to the non-decorated ones. In addition, a preferential uptake by cancer associated fibroblasts (CAFs) allowed targeting this cell population. CAF-targeted mild-hyperthermia was performed in a preclinical model of CCA. Tumor stiffness evolution, directly linked to the extracellular matrix accumulation, was mapped non-invasively, using shear wave elastography (SWE). The days following GIONF-mediated PTT, the treated tumors exhibited a significant reduction of tumor stiffness accompanied by regression, directly linked to the decrease of CAFs in the tumor. In conclusion, our study highlights a physical strategy targeting CAFs to normalize the tumor microenvironment stiffness that may apply to CCA treatment.

The SFNano C'NANO joint meeting 2019

Thematic Session: Nano for imaging, diagnosis & theranostics

Keywords: Ouzo, nanoparticle, nanoprecipitation, radiotherapy, glioblastoma

From the Ouzo effect to nanocapsules for radiotherapy enhancement – Application to glioblastoma

Clément GOUBAULT[1a], Flavien SCIORTINO[1a], Ulrich JARRY[1b], Mégane BOSTOEN[1b], Agnès BUREL[1c], Pierre-Antoine ÉLIAT[1c], Stéphanie DUTERTRE[1c], Myrtil L. KAHN[2], Thierry GUILLAUDEAUX[1b, 1c, 1d], Arnaud LE GOFF[1b, 3], Soizic CHEVANCE[1a] & Fabienne GAUFFRE[1a]

1. Univ Rennes – 1a) CNRS, ISCR - UMR6226 ; 1b) Laboratoire Commun Oncotrial, UMS 3480 CNRS/US018 INSERM Biosit, Université Rennes 1 ; 1c) CNRS, Inserm, BIOSIT - UMS 3480, US_S 018 ; 1d) CLCC Eugène Marquis, INSERM COSS 1242
2. Laboratoire de Chimie de Coordination - UPR8241, CNRS, 205 rte de Narbonne, Toulouse
3. Biotrial Pharmacology, Unité de Pharmacologie Préclinique, Rennes

The "Ouzo effect" has attracted much attention since its first description in 2003 [1]. It is characterized by the spontaneous formation of a metastable and monodisperse emulsion, without using surfactant or external energy input. Typically, upon mixing a water-miscible solvent containing a hydrophobic impurity with a large amount of water, the supersaturation of the hydrophobic compound spontaneously leads to the formation of solvent-rich droplets. This phenomenon has been used mostly for the formation of polymeric nanoparticles and nanocapsules [2].

The originality of this work is the implementation of the "Ouzo effect" in presence of inorganic nanoparticles into a fast and simple process for the preparation of nanocarriers (D_H ~100 nm): "Hybridosomes®" [3]. These nano-objects show an innovative design, with a porous and elastic hybrid shell made of inorganic nanoparticles (iron oxide, gold, quantum dots…) and polymer. Interestingly, it is possible to encapsulate hydrophobic compounds in the aqueous inner cavity of the capsules under a nanoprecipitated form, very efficiently with an outstanding encapsulation yield. The delivery and release of a hydrophobic dye has been studied *in vitro* and *in vivo*. The core/shell complementary properties present a real potential for biomedical applications such as diagnosis (MRI, fluorescence imaging…) and therapy (radiotherapy, chemotherapy…). We therefore investigated the effectiveness of such nano-objects in a mouse glioblastoma tumor model with MRI diagnosis (iron oxide nanoparticles) and radiotherapy enhancement (gold nanoparticles). Further developments include the encapsulation and intratumoral release of an anti-cancer drug.

[1] S. A. Vitale et al., *Langmuir* **2003**, 19, 4105-4110.
[2] a) F. Ganachaud et al., *ChemPhysChem* **2005**, 6, 209-216 ; b) E. Lepeltier et al., *Adv. Drug Delivery Rev.* **2014**, 71, 86-97 ; c) C. Solans et al., *Curr. Opin. Colloid Interface Sci.* **2016**, 22, 88.93.
[3] a) F. Sciortino et al., ChemNanoMat 2016, 2, 796-799 ; b) Patent WO2017103534 (FR1562860 / 2015-12-18) F. Gauffre, F. Sciortino, S. Chevance, M. Kahn, G. Casterou ; c) F. Sciortino et al., Soft Matter 2017, 13, 4393-4400.

The SFNano C'NANO joint meeting 2019

Thematic Session: Nanoscience for cancer.

Keywords: Glioblastoma; peptide; toxicity; tolerated dose; tumour volume.

Preclinical studies of the anti-glioblastoma NFL-TBS.40-63 peptide following intra venous administrations in adult rats

Claire Lépinoux-Chambaud[1], Marie-Christine Rousselet[2], Valérie Moal[3], Franck Geneviève[4], Joël Eyer[1]

1. Micro et Nanomedecines Translationnelles, MINT, UNIV Angers, UMR INSERM 1066, UMR CNRS 6021, Angers, France.
2. Département Pathologie Cellulaire & Tissulaire, Centre Hospitalier Universitaire, IBS, 49033 Angers, France.
3. Département Biochimie et Génétique, Plateau Technique Automatisé - Biochimie, Centre Hospitalier Universitaire, IBS, 49033 Angers, France.
4. Hematology Laboratory, Angers University Hospital, Angers, F-49000, France; Fédération Hospitalo-Universitaire, 'Grand Ouest Against Leukemia' (FHU) GOAL, France.

Glioblastoma represent the most frequent and aggressive brain tumours with a poor median survival (14-16 months) despite neurosurgery, radiotherapy and chemotherapy. The NFL-TBS.40-63 peptide (NeuroFilament Low subunit-Tubulin Binding Site 40-63) is a novel and specific anti-glioblastoma candidate, inducing a reduction of tumour volume in rats bearing glioblastoma after its local administration (Berges et al. 2012). When nanocapsules are functionalized with the peptide, they are targeted *in vitro* and *in vivo* to glioblastoma cells (Balzeau et al. 2013). Here, its innocuity, pharmacokinetic, biodistribution and efficacy after intravenous administrations were characterized to further evaluate the possibilities to develop it as an anti-cancer drug for clinical trials. We reported its short-term toxicity in healthy adult rats following single or repeated intravenous administrations, and measured its pharmacokinetic parameters. Finally, we analysed its biodistribution and efficacy in rats bearing intra-cranial glioblastoma following intravenous administrations. The results indicate that after repeated intravenous administrations the anti-glioblastoma activity of this peptide is similar to the standard treatment (Temozolomide). These results suggest the ability of the peptide to cross the blood-brain-barrier to target glioblastoma and confirm the promising potential of this peptide for the treatment of glioblastoma.

This work was supported by AFM (Association Française contre les Myopathies), ARC (Association pour la Recherche sur le Cancer), Ligue contre le Cancer, MATWIN (Maturation & Accelerating Translation With Industry), UNAM (Université Nantes, Angers, Le Mans), and "Région Pays de la Loire" to J. Eyer, and by the "Société d'Accélération du Transfert de Technologie (SATT) Ouest Valorisation" to C. Lépinoux-Chambaud.

The SFNano C'Nano joint meeting 2019

Thematic Session: Nanoscience for Cancer

Keywords: poloxamer, peritoneal carcinomatosis, drug release, thermogel

Poloxamer-based thermogel combined with 5FU and oxaliplatin for prevention of recurrence after cytoreductive surgery

Johanne SEGUIN[1], Cynthia PIMPIE[2], Chantal AL SABBAGH[1], Marc POCARD[2], Vincent BOUDY[1] Nathalie MIGNET[1]

1. *Unité des Technologies Chimiques et Biologiques pour la Santé (UTCBS), Université Paris Descartes, Université de Paris, CNRS UMR8258, INSERM U1267, 75006 Paris, France*
2. *Carcinomatosis Peritoneum Paris Technology, Université Paris 7, Université de Paris, INSERM U965, Department of Oncologic and Digestive Surgery, AP-HP Hospital Lariboisière, 75010 Paris, France.*

Colorectal cancer is the third most common cancer in the word in terms of incidence (1.2M new case, both sexes) and the fourth in terms of mortality with 690 000 estimated deaths in 2012 [1].the main problem of this cancer type is not the treatment of primitive tumor but the metastasis recurrence. One way of metastatic spread is the invasion of the peritoneal cavity which leads to peritoneal carcinomatosis (PC). The PC is not ease to cure and actually the cytoreductive surgery (CS) and hypertermic intraperitoneal preoperative chemotherapy (HIPEC) were combined and shown to be the more promising therapeutic procedures. Nevertheless, this protocol was still associated with a significant poor prognosis [2]. In this context, we proposed to replace HIPEC by an anti-adhesive thermogel containing chemotherapeutics to increase the life span of the drugs and to limit the adhesion of tumor cells. The bioavailability of the thermogel was tested intraperitoneally in mice and no toxicity was observed in terms of change in body weight, anatomopathology and blood biomarkers. In vitro experiment, proved that the thermogel reduced the adhesion of the tumor cells. Finally, the evaluation of thermogel in combination with 5-Fluoruacile and oxaliplatin significantly decreased the peritoneal carcinomatosis index (PCI) and ascites in a model of colorectal peritoneal carcinomatosis CT26 in mice as comparison with the control group. These preclinical results confirmed that the thermogel associated with standard chemotherapy 5FU and oxaliplatin could be a good candidate for the replacement of the HIPEC protocol.

[1]. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int. J. Cancer. 2015;136:E359–86.
[2]. Lemoine L, Sugarbaker P, Van Der Speeten K. Pathophysiology of colorectal peritoneal carcinomatosis: Role of the peritoneum. World J. Gastroenterol. 2016;22:7692–707.

The SFNano C'Nano joint meeting 2019

Thematic Session: Nanoscience for cancer

Keywords: Glioblastoma, Hydrogel, Lipid nanocapsules, Cancer stem cells, Combination therapy

Long-term treatment of glioblastoma through a multi-drug nanomedicine hydrogel

Bozzato E.[1], Bastiancich C.[2], Tsakiris N.[1], Petay M.[3], Bastiat G.[4], Preat V.[1]

1. Advanced Drug Delivery and Biomaterials, Louvain Drug Research Institute, Université Catholique de Louvain, Brussels, Belgium
2. Institut de NeuroPhysiopathologie - CNRS, UMR 7051, Aix-Marseille Université, Marseille, France
3. ENS Paris-Saclay, Université Paris-Sud, Paris, France
4. Micro et Nanomedecines Translationnelles, Université Angers, INSERM 1066, CNRS 6021, Angers, France

Even with the current standard of care therapies, glioblastoma patients cannot reach an acceptable overall survival due to the onset of recurrence, mainly caused by the presence of glioma stem cells (GSCs), a self-renewing and tumorigenic subpopulation of cells[1].
Our aim is to develop a dual-drug hydrogel that can be injected in the resection cavity, allowing the release of an anticancer drug and an anti-GSCs drug. The brain implantable Lauroyl-Gemcitabine ($GemC_{12}$) hydrogel[2] delays the onset of recurrences in preclinical studies and can be a nanodelivery platform for other drugs, to obtain a combined long-term local therapeutic treatment for glioblastoma[3].
An *in vitro* screening was performed on U87-MG glioma cells to find the best anti-GSCs molecules, showing that Salinomycin and Curcumin were interacting synergistically with $GemC_{12}$. These molecules were encapsulated in the lipid nanocapsules composing the hydrogel, obtaining a size of about 60 nm, an encapsulation efficiency around 95% and a drug release lasting for 30 days.
Ongoing *in vitro* data on cell spheroids show that the combination between $GemC_{12}$ and Salinomycin is the most effective to decrease the size of the spheroids and the percentage of GSCs markers. Moreover, *in vivo* ongoing experiments on 9L (rat) and GL261 Red-FLuc (mouse) orthotopic models seem to confirm the anticancer activity after tumor resection and local administration of this dual-drug hydrogel.
In conclusion, the dual-drug nanomedicine hydrogel $GemC_{12}$-Sal-LNC has displayed good physico-chemical characteristics and promising features for the elimination of glioblastoma cells and GSCs, thus potentially leading to the eradication of this disease.

References:

1. Reya, Tannishtha, et al. nature 414.6859 (2001): 105.;
2. Bastiancich, Chiara, et al. Journal of Controlled Release 225 (2016): 283-293.;
3. Bastiancich*, Chiara, Bozzato*, Elia, et al. International journal of pharmaceutics 559 (2019): 220-227.

The SFNano C'Nano joint meeting 2019

Thematic Session: Nanoscience for cancer

Keywords: photodynamic therapy; lipid nanoparticles, ovarian cancer, drug delivery system, verteporfin

Verteporfin-loaded lipid nanoparticles improve ovarian cancer photodynamic therapy *in vitro* and *in vivo*

Thierry Michy[1,2], Thibault Massias[1], Claire Bernard[1,2], Laetitia Vanwonterghem[1], Maxime Henry[1], Mélanie Guidetti[1], Guy Royal[3], Jean-Luc Coll[1], Isabelle Texier[4], Véronique Josserand[1,*], and Amandine Hurbin[1,*]

1. Institut pour l'Avancée des Biosciences, INSERM U1209, CNRS UMR5309, Université Grenoble Alpes, Grenoble, France
2. CHU Grenoble Alpes, Université Grenoble Alpes, Grenoble, France
3. Département de Chimie Moléculaire, CNRS UMR5250, Université Grenoble Alpes, Grenoble, France
4. CEA, LETI-DTBS, Université Grenoble Alpes, Grenoble, France

* These authors contributed equally

Advanced ovarian cancer is the most lethal gynecological cancer, with a high rate of chemoresistance and relapse. Photodynamic therapy offers new prospects for ovarian cancer treatment, but current photosensitizers lack tumor specificity, resulting in low efficacy and significant side-effects. In the present work, the clinically approved photosensitizer verteporfin was encapsulated within nanostructured lipid carriers (NLC) for targeted photodynamic therapy of ovarian cancer. Cellular uptake and phototoxicity of free verteporfin and NLC-verteporfin were studied *in vitro* in human ovarian cancer cell lines cultured in 2D and 3D-spheroids, and biodistribution and photodynamic therapy were evaluated *in vivo* in mice. Both molecules were internalized in ovarian cancer cells and strongly inhibited tumor cells viability when exposed to laser light only. *In vivo* biodistribution and pharmacokinetic studies evidenced a long circulation time of NLC associated with efficient tumor uptake. Administration of 2 $mg.kg^{-1}$ free verteporfin induced severe phototoxic adverse effects leading to the death of 5 out of 8 mice. In contrast, laser light exposure of tumors after intravenous administration of NLC-verteporfin (8 $mg.kg^{-1}$) significantly inhibited tumor growth without visible toxicity. NLC-verteporfin thus led to efficient verteporfin vectorization to the tumor site and protection from side-effects, providing promising therapeutic prospects for photodynamic therapy of cancer.

The SFNano C'Nano joint meeting 2019

Thematic Session: Nanochemistry: synthesis & functionalization of nanosystems for bioapplications

Keywords: Phthalocyanine, Photodynamic therapy, Nanoparticle, Encapsulation

Phthalos into Nanos: Improving NIR Photodynamic Efficiency

Fabienne Dumoulin[1]

1. Gebze Technical University, Chemistry Department, Gebze, 41400 Kocaeli, Turkey
fdumoulin@gtu.edu.tr / dumoulin.fabienne@gmail.com

Photodynamic therapy has moved from molecular photosensitisers to nano-photosensitisers in the last decade.[1] Thanks to their strong absorption centered at 700 nm allowing excitation at NIR wavelengths, phthalocyanines are among the most promising molecular bases to produce photosensitisers. Incorporating phthalocyanines into nanoparticles is hence a judicious way to improve their NIR photodynamic efficiency.

Several methods, either covalent (grafting) and non-covalent (encapsulation), have been used to incorporate photosensitising phthalocyanines into nanoparticles

Micellar formulation[2], polyacrylamide[3], phthalocyanine-poly-L-glutamic acid conjugates[4,5] and silsesquioxane[6,7] nanoparticles have been produced and each of them revealed specific advantages that will be discussed.

1. A. Srivatsan, J. R. Missert, S. K. Upadhyay and R. K. Pandey, *J. Porphyrins Phthalocyanines*, **2015**, *19*, 109-134
2. B. Pucelik, I. Gürol, V. Ahsen, F. Dumoulin, J. M. Dabrowski, *Eur. J. Med. Chem.* **2016**, *124*, 284-298.
3. F. Giuntini, F. Dumoulin, R. Daly, V. Ahsen, E. M. Scanlan, A. S. P. Lavado, J. W. Aylott, G. A. Rosser, A. Beebye and R. W. Boyle, *Nanoscale* **2012**, *4*, 2034-2045.
4. L.V. Kiew, H. Y. Cheah, S. H. Voon, E. Gallon, J. Movellan, K. H. Ng, S. Alpugan, H. B. Lee, F. Dumoulin, M. J. Vicent, Lip Yong Chung, *Nanomedicine: NBM*, **2017**, *13*, 1447-1458.
5.H. Y. Cheah, E. Gallon, F. Dumoulin, S. Z. Hoe, N. Japundžić-Žigon, S. Glumac, H. B. Lee, P. Anand, L. Y. Chung, M. J. Vicent, L. V. Kiew, *Mol. Pharmaceutics* **2018**, *15*, 2594-2605.
6. C. Mauriello-Jimenez, M. Henry, D. Aggad, L. Raehm, C. Charnay, X. Cattoen, M. Wong Chi Man, S. Alpugan, V. Ahsen, D. K. Tarakcı, P. Maillard, M. Maynadier, M. Garcia, F. Dumoulin, M. Gary-Bobo, J.-L. Coll, V. Josserand and J.-O. Durand, *Nanoscale,* **2017**, *9*, 16622-16626.
7. G. Ekineker, C. Nguyen, S. Bayir, S. Dominguez-gil, U. Isci, M. Daurat, A. Godefroy, L. Raehm, C. Charnay, E. Oliviero, V. Ahsen, M. Gary-Bobo, J.-O. Durand and F. Dumoulin, *Chem. Commun.* **2019**, *55*, 11619-11622.