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In vitro photophysical and photobiological properties of Ce6-based dendrimer nanoparticles

Estelle Bastien[1,2], Raphael Schneider[3], Lina Bezdetnaya[1,2], Beate Röder[4], Steffen Hackbarth[4], Annegret Preuß[4], Jordane Jasniewski[5], Vadzim Reshetov[1], Henri-Pierre Lassalle[1,2]

[1]*Centre de recherché en Automatique de Nancy, Université de Lorraine, CNRS UMR 7039, Vandœuvre-lès-Nancy, France*
[2]*Institut de Cancérologie de Lorraine, Vandœuvre-lès-Nancy, France*
[3]*Laboratoire Réactions et Génie des Procédés, Ecole National Supérieure des Industries Chimiques, Université de Lorraine, Nancy, France*
[4]*Institut of physic, Humboldt University, Berlin, Germany*
[5]*Laboratoire d'ingénierie des biomolécules, Université de Lorraine, Vandœuvre-lès-Nancy, France*

Context: The photosensitizers vectorization enables better tumor localization and therefore a better tumoricidal PDT efficacy. Dendrimers are hyperbranched macromolecules that are considered as an attractive class of biocompatible nanovectors for drug targeting in tissues. In this study we report a novel PDT drug-carrier system, composed of chlorin e6 grafted to the periphery groups of poly(amido amine) dendrimers (PAMAM).

Materials & Methods: The size and zeta potential of our nanoparticles were determined by dynamic light scattering (DLS). The nanoparticle singlet oxygen generation in pharynx carcinoma (FaDu) cells was assessed by luminescence at 1268 nm. Phototoxicity was evaluated by MTT assay. Uptake was assessed by chemical extraction associated with fluorescence spectroscopy measurements. Finally, the uptake mechanism was determined by the use of endocytosis specific inhibitors.

Results: Ce6-dendrimers nanoparticles displayed a 40 times greater uptake along with a 25 fold higher photocytotoxic activity in FaDu cells compared to free Ce6. Also, a much longer singlet oxygen lifetime was demonstrated for Ce6-dendrimers compared to Ce6. Cellular incorporation of nanoparticles was completely inhibited at 4°C, demonstrating that uptake was mediated via endocytosis. Further investigations using specific inhibitors revealed that incorporation was partially mediated by macropinocytosis pathway.

Conclusion: Dendrimeric based nanoparticles showed a good photodynamic efficacy towards cancer cells *in vitro*, suggesting them as a promising vehicle for PDT. In the future we shall test dendrimer-based nanoparticles *in vivo*, in pre-clinical models.