Photodynamic Action to *Combat Pneumonia*: *In Vitro* Studies

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Pneumonia is among the most lethal respiratory infections in the world and considering the alarming increase in the rate of antibiotic-resistant microorganisms, it is extremely urgent to develop new treatments that have a broad spectrum of action and focus on multiple non-specific molecular targets. Antimicrobial Photodynamic Therapy (aPDT) is a potential alternative since its mechanism is based on oxidative stress, with a low risk of developing resistance. Previous studies carried out by our research group demonstrated an excellent reduction of *Streptococcus pneumoniae in vitro* using indocyanine green (ICG) and infrared lighting, in addition to the delivery of these elements having already been well established in animal models. However, for the success of aPDT *in vivo* there are still some challenges to be overcome, due to the presence of pulmonary surfactant (LS), which traps photosensitizers (PS) preventing them from reaching the microbial target. In the present work, different physicochemical approaches (use of perfluorocarbons, oxygen nanobubbles and biopolymers) were employed in order to optimize the antimicrobial response of aPDT using ICG in the presence of LS. The most promising strategy consisted of the combination of ICG (10 µM) with the Gantrez AN-139 biopolymer (0.2% (w/v)), which showed high microbial reduction of *S. pneumoniae* concomitantly with non-toxicity for human lung epithelial cell lines (A549) and fibroblasts (MRC-9). These results point to a way to improve the distribution of PSs across the LS leading to successful pulmonary aPDT.