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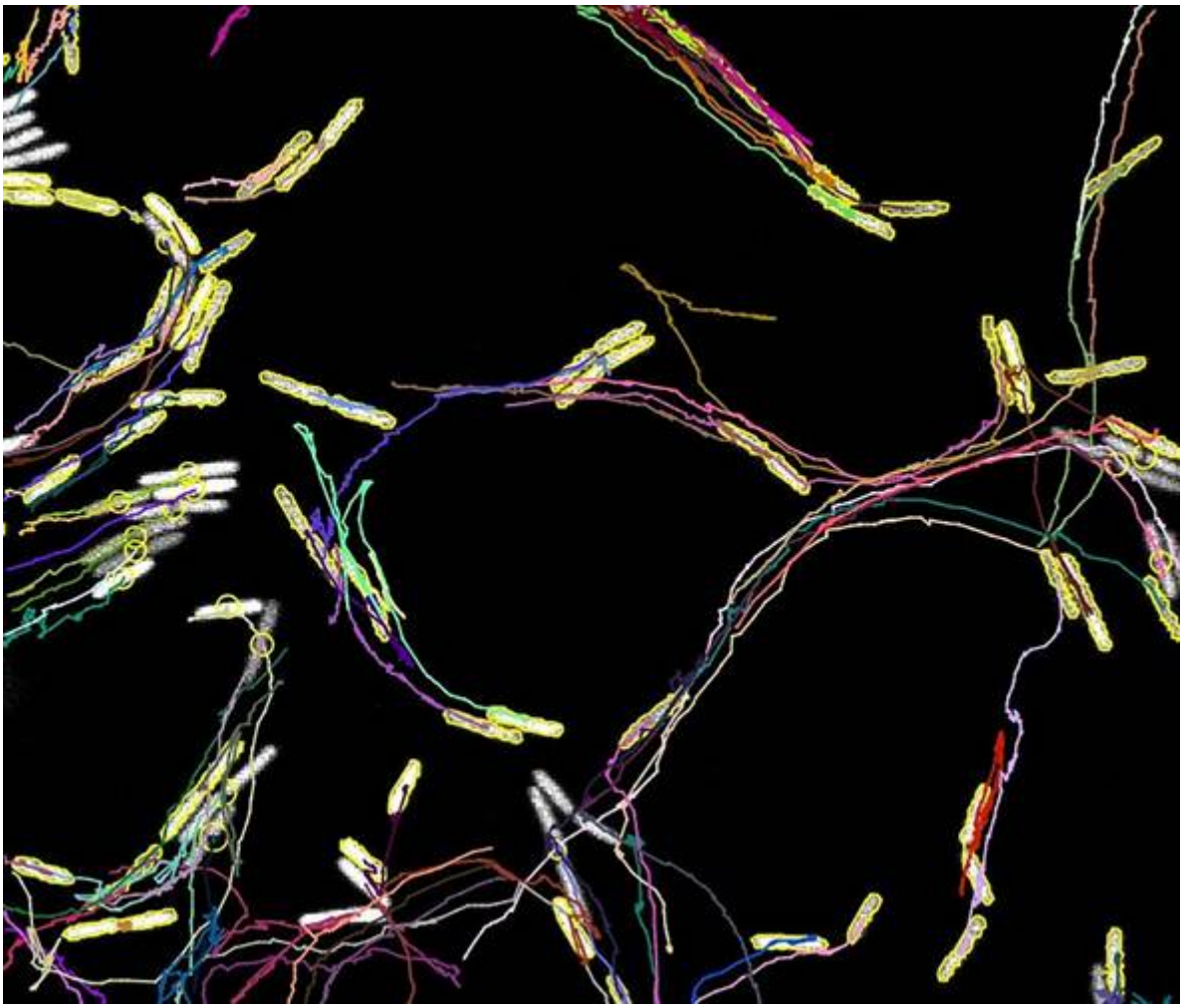

Foto: Se hace camino al andar. Celeste Dea. 1er puesto. Concurso fotográfico SAMIGE 20 años.

DELAYED INTERACTION BETWEEN PHOTOSENSITIZER-LOADED HYDROGELS AND BACTERIAL CELLS DELAYS PHOTOINACTIVATION OF Pseudomonas aeruginosa

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The development of novel, efficient approaches is crucial to address the global challenge of microbial resistance. Antimicrobial photodynamic therapy (aPDT) emerges as a promising alternative, particularly for treating localized infections. One of the main challenges in applying aPDT to infected skin and wounds is the development of suitable photoactive carrier systems that can effectively release therapeutic compounds at the target site. TMPyP, a cationic porphyrin, is a well-studied photosensitizer (PS) known for generating reactive oxygen species upon irradiation with light of an appropriate wavelength, leading to cell inactivation. In our laboratory, we designed carrier systems based on ionic complexes between the bioadhesive anionic polymer Carbomer-974P and TMPyP. The resulting C-TMPyP hydrogels are uniform in appearance, physically stable, and exhibit pH and viscosity levels appropriate for topical application while modulating the release of TMPyP. Preliminary results demonstrated that both transparency and photoinactivation efficiency are dependent on the polymer concentration. This study focuses on characterizing selected C-TMPyP hydrogels, with particular attention to how the hydrogel-based carrier system influences the interaction/association of the photosensitizer with bacterial cells, specifically with an antimicrobial-resistant *Pseudomonas aeruginosa* isolate. Surface electrokinetic potential measurements of cultures exposed to C-TMPyP hydrogels reveal higher negative values compared to controls, attributed to the negative charges contributed by the polymer matrix. Although there is no initial charge interaction between the carrier system and the bacterial surface, the bioadhesive properties of the hydrogel and the modulated release of TMPyP enhance subsequent interactions between the PS and the bacteria. Flow cytometry analyses indicate that alterations in internal bacterial architecture/organization (SSC parameter: granularity), PS association and/or internalization, and partial depolarization of the cytoplasmic membrane are delayed compared to those induced by free PS. Fluorescence microscopy images corroborate the time-dependent effects observed with C-TMPyP hydrogels. This delayed response accounts for the observed lag in the photoinactivation of P.aeruginosa, as evidenced by viable cell counts in cultures exposed to hydrogels under varying irradiation times. Despite the delayed interaction between the photosensitizer in C-TMPyP hydrogels and bacterial cells, complete photoinactivation of the cultures is achieved under exposure times and light doses applicable to in vivo studies. When combined with the

bioadhesive properties, resistance to bacterial or fungal contamination, and the physical stability of these polymer-based hydrogels, already approved for topical delivery systems, they are excellent candidates for aPDT formulations targeting this administration route.

Palabras clave: Porphyrins, TMPyP, Antimicrobial Photodynamic Therapy, Pseudomonas aeruginosa