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#### **ANTIMICROBIAL PHOTODYNAMIC THERAPY (PDT) IN MULTIDRUG RESISTANT PATHOGENS (MDRP)**

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#### **Introduction:**

Infectious diseases caused by multidrug resistant pathogens (MDRP) are emerging in Hong Kong and worldwide. The major concern of bacteria that confer multidrug resistance is the presence of the membrane transport proteins - multidrug efflux pumps. Efflux mechanisms have been recognized as major components of microbial resistance to many classes of antibiotics. The relentless increase of multi-drug resistant pathogens (MDRP) together with the limited development of novel antibiotics makes it imperative to discover new antimicrobial strategies to combat diseases caused by MDRP.

#### **Antimicrobial:**

Antimicrobial Photodynamic Therapy (PDT) can be one of the target therapies to MDRP by employing visible light irradiation on non toxic photosensitizer (PS), with the generation of reactive oxygen species (ROS) to eradicate the MDRP. This pilot study aimed to determine the anti-microbial efficacy of Toluidine Blue O (TBO) mediated PDT in the MDRP.

#### **Objective:**

To evaluate the killing efficacy of TBO mediated PDT on wild type strain, MDR-deficient mutant stain and multidrug resistant strain of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

#### **Methodology:**

Killing efficacy of Toluidine Blue (TBO) mediated PDT on selected bacteria stains were determined by minimum bactericidal concentration and colony count. A wild type strain, a MDR-deficient mutant (gene knockout stain) and a MDR efflux pump over-expressed strain of *Staphylococcus aureus* and *Pseudomonas aeruginosa* were included. The over-expressed MDR efflux pump in *S. aureus* and *P. aeruginosa* were NorA and MexAB-OprM respectively.

#### **Result:**

TBO mediated PDT is unaffected by MDR phenotype in *S. aureus* stains. All three tested stains gave 4.8 log killing at 20 $\mu$ M/2Jcm<sup>-2</sup> and reached 5 log killing at 20 $\mu$ M/5Jcm<sup>-2</sup>. However, the MexAB-OprM expression protects against TBO phototoxicity in *P. aeruginosa* strains. Only 0.4 log killing was obtained in *P. aeruginosa* (MexAB-OprM) at 50 $\mu$ M / 5Jcm<sup>-2</sup> while 3.9 log killing at 50 $\mu$ M/5 Jcm<sup>-2</sup> and 5 log killing at 50 $\mu$ M/10 Jcm<sup>-2</sup> was obtained in both wild type and MDR-

deficient mutant strain. Comparatively, the *S. aureus* (NorA) was more susceptible to TBO mediated PDT than the *P. aeruginosa* (MexAB-OprM).

**Conclusion:**

TBO mediated PDT is effective on both tested wild type and MDR strains bacteria. This study offered new insights of TBO mediated photoinactivation on MDRP. Further studies in the modulation of MDR efflux pumps by TBO mediated photoinactivation in MDR strains deserve investigation. (This study was supported by PolyU grant (G-U422))