In Vitro Study of Photodynamic Inactivation against *Fonsecaea monophora* and the Application of ALA-APDT on Chromoblastomycosis

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**Introduction**

As a chronic cutaneous and subcutaneous infection, thousands of cases of chromoblastomycosis (CBM) have been reported worldwide. During the past centuries, several therapeutic regimens have been proposed including systemic antifungals, as monotherapy or combined, physical methods and immune adjuvants. Antifungal Photodynamic Therapy (APDT) has been successfully employed in combination with or without antifungals recently.

**Objectives**

- To evaluate the photodynamic inactivation of 3 different photosensitizers against *F. monophora* in vitro and investigate their mechanisms.
- To review available data regarding the APDT for CBM, discuss their application, advantages and shortages in clinic.

**Methods**

1. The photodynamic inactivation efficacy of TMPyP4, MB, 5-ALA against *F. monophora* were compared;
2. The ROS species involved in the cytotoxicity of 3 PSs were investigated with DCFH-DA probe;
3. The effect of 5-ALA-PDI treated *F. monophora* conidia on macrophage was tested;
4. Clinical APDT treated CBM cases were reviewed and analyzed.

**Results**

Fig.1 CFU of *F. monohora* conidia after PDT mediated by 3 PSs. These 3 PSs can all inactivate *F. monophora* conidia directly with corresponding-wavelength light illumination in a PS concentration-dependent and light dose-dependent manner.

Fig.2 ROS measurement of *F. monohora* conidia after ALA-PDT under different conditions. ALA-PDT increase intracellular ROS levels inside *F. monophora* in a ALA concentration-dependent and light dose-dependent manner.

Fig.3 The effects of ROS on regulating apoptosis of macrophage co-infected with *F. monophora* conidia under different ALA-PDT conditions. ROS generated by photodynamic treated *F. monophora* conidia is associated with mitochondrial-related apoptosis in macrophage.

**Conclusion**

- APDT could be used as promising physical approaches to decrease CBM severity and duration while enhancing the life quality of patients.
- The use of different photosensitizers shows different antifungal efficacy. It is significant to choose a suitable photosensitizer for a specific pathogen. Yet the mechanism is still not clear which merits further investigation.

Fig.4 APDT treated CBM cases. Advantages: No antibiotic resistance; Disadvantage: Relapse, pain.