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HEMATOPORPHYRIN MONOMETHYL ETHER-MEDIATED PHOTODYNAMIC EFFECTS ON MACROPHAGES

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Objectives Photodynamic therapy (PDT) has been shown to attenuate atherosclerotic plaque progression and decrease macrophage-infiltration. The effectiveness of PDT depends strongly on the type of photosensitizers. Hematoporphyrin monomethyl ether (HMME) is a promising second-generation porphyrin-related photosensitizer for PDT. This study is designed to investigate HMME mediated Photodynamic therapy on macrophage and define the cell-death pathway.

Methods Fluorescence of HMME with different incubated time was tested. Use confocal scanning laser microscope to investigate HMME subcellular distribution. THP-1 derived macrophages were cultured with HMME for 2 h and then exposed to 635 nm diode lasers for 1.5 min and 3 min. Six-hours later, cell viability analysis was performed with 3-(4,5)-dimethylthiahiazo (-z-y1)-3,5-di-phenytetrazoliumromide (MTT) assay and annexin V/PI staining by flow cytometer. The activities of caspase-9 and caspase-3 were measured using the fluorescent assay kits.

Results Our data demonstrated that the intensity of laser-induced HMME fluorescence in macrophages steadily increased with the increasing incubation concentration of HMME. The survival rate of macrophages determined by MTT assay decreased with the increasing HMME concentration and irradiation time. HMME-based PDT induced macrophage apoptosis via caspase-9 and caspase-3 activation pathway detected by caspase fluorescent assay kit and flow cytometer. The 1.5 min group increased the number of apoptotic macrophages 5.36±3.24 at 12 h post irradiation (mean ±SD, n=3, $p<0.05$), whereas the 3 min group increased the number of apoptotic macrophages 67.18±5.17 (mean±SD, n=3, $p<0.001$).

Conclusions Our data demonstrated that HMME could accumulate in macrophages and HMME-mediated PDT induced macrophage apoptosis. These results imply that photodynamic therapy with HMME may therefore be a useful clinical treatment for unstable atherosclerotic plaques.