

News Release

Title

Plasma-activated medium suppresses choroidal neovascularization in mice: a new therapeutic concept for age-related macular degeneration

Key Points

○Plasma-activated medium (PAM) reduced choroidal neovascularization (CNV) *in vivo*.

○PAM injection had no effect on regular retinal vessels, nor did it show retinal toxicity *in vivo*.

Summary

Professor Hiroko (Department of Ophthalmology), Assistant professor. Hiroki Kaneko (Department of Ophthalmology), Professor. Fumitaka Kikkawa (Department of Obstetrics and Gynecology) in Nagoya University Graduate School of Medicine (Dean:Masahide Takahashi,MD.PhD), Professor Masaru Hori (Director of Plasma Medical Science Global Innovation Center, Institute of Innovation for Future Society) in Nagoya University, Professor Masaaki Mizuno (Center for Advanced Medicine and Clinical Research) in Nagoya University Hospital and their collaborators investigated the therapeutic ability of plasma-activated medium (PAM) to suppress CNV.

The effect of PAM on vascularization was assessed on the basis of human retinal endothelial cell (HREC) tube formation. In mice, laser photocoagulation was performed to induce CNV (laser-CNV), followed by intravitreal injection of PAM. N-Acetylcysteine was used to examine the role of reactive oxygen species in PAM-induced CNV suppression. Fundus imaging, retinal histology examination, and electroretinography (ERG) were also performed to evaluate PAM-induced retinal toxicity. Interestingly, HREC tube formation and laser-CNV were both reduced by treatment with PAM. N-acetylcysteine only partly neutralized the PAM-induced reduction in laser-CNV. In addition, PAM injection had no effect on regular retinal vessels, nor did it show retinal toxicity *in vivo*. These findings indicate the potential of PAM as a novel therapeutic agent for suppressing CNV.

These findings was published (online) in an English journal *Scientific Reports* on January 9th 2015.

Research Background

Choroidal neovascularization (CNV) is the main pathogenesis of age-related macular degeneration (AMD), which leads to severe vision loss in many aged patients in most advanced country. CNV compromises vision via hemorrhage and retinal detachment on account of pathological neovascularization penetrating the retina. Plasma medicine represents the medical application of ionized gas “plasma” that is typically studied in the field of physical science.

Research Results

Here we examined the therapeutic ability of plasma-activated medium (PAM) to suppress CNV. The effect of PAM on vascularization was assessed on the basis of human retinal endothelial cell (HREC) tube formation. In mice, laser photocoagulation was performed to induce CNV (laser-CNV), followed by intravitreal injection of PAM. N-Acetylcysteine was used to examine the role of reactive oxygen species in PAM-induced CNV suppression. Fundus imaging, retinal histology examination, and electroretinography (ERG) were also performed to evaluate PAM-induced retinal toxicity. Interestingly, HREC tube formation and laser-CNV were both reduced by treatment with PAM (Figure 1). N-acetylcysteine only partly neutralized the PAM-induced reduction in laser-CNV. In addition, PAM injection had no effect on regular retinal vessels, nor did it show retinal toxicity *in vivo*. Our findings indicate the potential of PAM as a novel therapeutic agent for suppressing CNV.

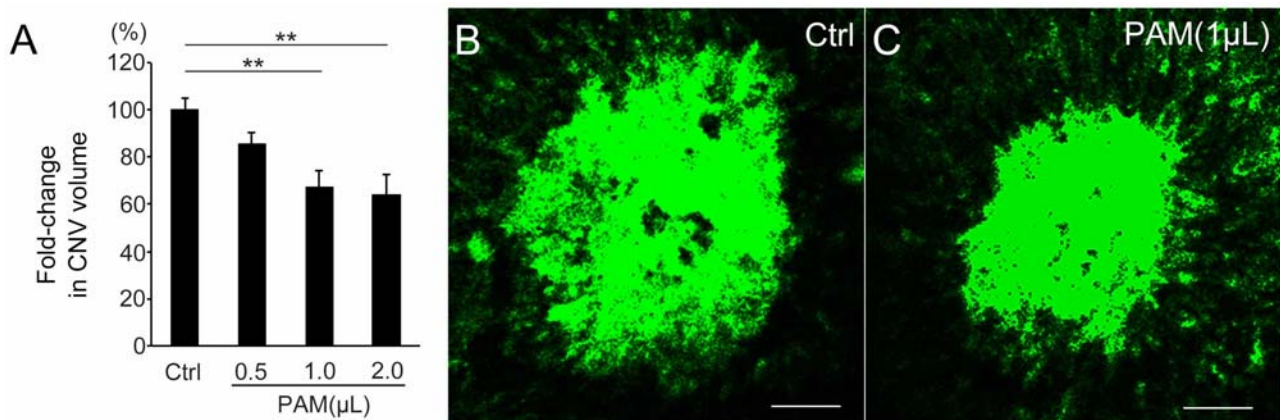


Figure 1: PAM reduced CNV volume *in vivo*.

Research Summary and Future Perspective

PAM has great therapeutic potential for use in human, further studies are needed to address several important problems. First, the precise mechanism by which PAM suppresses CNV, beyond ROS induction, must be elucidated. Second, more thorough evaluations of the retinal toxicity of PAM are needed. Clinically, the use of PAM for treating ocular conditions is relatively easier compared with its application in other tissues, because ophthalmologists can deliver specific drugs and media via topical delivery modes such as intravitreal injections. Although our results showed that retinal function was not altered by intravitreal injection of PAM, further assessments of the side effects of PAM administration are necessary, and the conditions for PAM treatment must be optimized to avoid side effects. Finally, a specific scale for PAM dosing is required to standardize PAM treatments.

The authors and title of the paper

Ye F, Kaneko H, Nagasaka Y, Iijima R, Nakamura K, Nagaya M, Takayama K, Kajiyama H, Senga T, Tanaka H, Mizuno M, Kikkawa F, Hori M, Terasaki H. Plasma-activated medium suppresses choroidal neovascularization in mice: a new therapeutic concept for age-related macular degeneration. *Scientific Reports* 2015; 5:7705: srep07705

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