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Application of Yoda1 Reduces Lymphedema in a Mouse Tail Model

Michael Cooper

mnc1991@gmail.com

Purpose: Piezo1 is a mechanosensitive ion channel protein that has been implicated in fluid stasis, lymphangiogenesis, and regulation of the lymphatic system. Loss of function studies have been linked to congenital lymphedema as well as defective and deficient lymphatic valves. Yoda1 is an agonist of Piezo1 that has not yet been studied in a secondary lymphedema model. We hypothesized that Yoda1 administration in a mouse tail model would cause a decrease in tail volume lymphedema.

Methods: A secondary lymphedema model was created by excising five millimeters of skin circumferentially. Remaining lymphatics were identified and obliterated utilizing methylene blue and the operative microscope. Eleven strain-matched female mice aged two to six months were split into three groups, control (n=5), low-dose Yoda1 (n=3), and high-dose Yoda1 (n=3). Each group underwent tail lymphedema surgery, and then received 200 microliters of PBS intraperitoneally every other day for the duration of the experiment. Low-dose Yoda1 mice received 71 ug/kg Yoda1 and high-dose mice received 213 ug/kg. The mice were then photographed and weighed every week for five weeks. The tails were analyzed with ImageJ software and tail volumes were calculated and plotted. Results: The control group tail volume increase peaked at 62.268% on post
-operative day (POD) 28. Low-dose Yoda1 peaked on POD 21 at 70.704%. High-dose Yoda1 peaked at 47.500% on POD 14. A significant difference was found in tail volumes between high-dose Yoda1 and both low-dose Yoda1 and control groups at post-operative day 35 ($p < .05$). There was no significant difference in weights for any groups at any time point.

Conclusion: Treatment with Yoda1 improves secondary lymphedema in a mouse tail model. This finding has implications for patients suffering from this condition as it offers a new therapeutic pathway that may provide additional benefit via the novel mechanism of activating Piezo1.