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[ADVANCED](#)[TOP](#) > [Available Issues](#) > [Table of Contents](#) > [Abstract](#)

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[\[PDF \(1334K\)\]](#) [\[References\]](#)**Effect of heat on synthesis of gelatinases and pro-inflammatory cytokines in equine tendinocytes**Yoshinao HOSAKA¹⁾, Sachiko OZOE¹⁾, Rikio KIRISAWA²⁾, Hiromi UEDA¹⁾, Kazushige TAKEHANA¹⁾ and Mamoru YAMAGUCHI³⁾

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ABSTRACT

The aim of this study was to clarify whether matrix metalloproteinases (MMP-2 and -9: gelatinases) and pro-inflammatory cytokines [tumor necrosis factor (TNF) α and interleukin (IL)-1 β] are induced by heat in tendon tissue *in vitro* and to test the hypothesis that heat exposure causes tendinocytes to synthesize pro-inflammatory cytokines and that synthesis of these cytokines, in turn, leads to up-regulation of synthesis of gelatinases. Isolated tendinocytes from equine superficial digital flexor tendons were cultured and all experiments were performed on cells passaged 3 or 4 times. In the cells exposed to heat (37 to 45°C, 0 to 60 min), the survival rate decreased sharply in a temperature- and time-dependent manner, especially at 42 and 45°C. Cells exposed at 40°C, however, showed little change in survival rate and morphology. Gelatin zymograms revealed that proMMP-2 and -9 were the only two MMPs remaining in the supernatant of the cultured tendinocytes, including that of untreated cells. Addition of TNF α and IL-1 β to the culture medium of tendinocytes accelerated proMMP-9 synthesis considerably. Heating the tendinocytes (40°C) led to a three-fold increase in proMMP-9 synthesis in a short time. Only TNF α was detected in tendinocytes after heat exposure for 30 and 60 min. In contrast, IL-1 β was under the detectable level in ELISA. Cooling of heat-exposed cells from 40°C to 37°C considerably down-regulated cellular proMMP-9 synthesis. Furthermore, proMMP-9 level was greatly reduced in cells treated at lower temperatures, 20°C and 5°C. These findings support our

hypothesis that hyperthermia in the horse tendon induces tendinocytes to synthesize pro-inflammatory cytokines and that the synthesis of these cytokines results in the up-regulation of gelatinases.

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