INTRODUCTION
The clinical outcome of repaired flexor tendon lacerations in the hand has markedly improved during last three decades. This improvement is partially the result of a better understanding of the mechanisms of tendon healing from animal studies. Although several species, such as dog, rabbit and chicken, have been used for tendon research, there are few studies using rats as the experimental animal. It is true that rat flexor tendons are small (approximately 1 mm. width) compared to the human tendon; however, the rat has been used and well examined as an experimental animal for a long time in a variety of fields. Most important, different types of reagents to the rat are available and the rat genome sequence has been elucidated, which provides a clear advantage to using the rat model to investigate the molecular mechanisms of the tendon healing process. In the present study, the rat tendon injury model, which was developed in our laboratory, was introduced and macroscopic and microscopic findings during first 28 days after surgery were presented. Gene expression levels of several types of collagens and matrix metalloproteases (MMPs) were also examined using reverse transcription polymerase chain reaction (RT-PCR).

METHODS
Surgical procedure: Male Lewis rats aging 7-10 weeks old were anesthetized with ketamine (75.0 mg/kg) and medetomidine hydrochloride (0.5 mg/kg). Under sterile conditions, surgery was performed on the second to fifth toes of both hind feet. A mid-line incision was used to expose the flexor digitorum longus tendon. A complete transverse laceration was made in the flexor tendon in zone II, and immediately repaired with one simple 9-0 nylon stitch. A second transverse laceration was made in the tendon 3.0 mm proximal to the repaired laceration to reduce tensile forces across the repair site. The skin was closed with a running 9-0 nylon suture. Rats were allowed to walk freely after surgery in cages without restriction. On day 3, 7, 14, 21 and 28 after surgery, tendon specimens were harvested. Another uninjured tendon specimen was collected as the control (day 0).

Histological evaluation: Tendon specimens were fixed in 10% buffered formalin, embedded in paraffin, sectioned longitudinally and stained with hematoxylin and eosin (HE).

RT-PCR: At least 30 tendon specimens from 4 rats were pooled in the liquid nitrogen at each harvest time. RNA extracted from harvested tendons was used for RT-PCR using specific primer sets of collagens (types III, V, XII) and MMPs (MMP-1, 2, 9 and MT-MMP).

RESULTS
Macroscopic findings: Lacerated tendons gradually healed through the 28 days after surgery without any obvious gap formation (Fig. 1). The surface of the tendon specimens was smooth and showed a glistening appearance throughout the time course. Hypertrophic changes at the repair site and adhesion formations between the tendon and surrounding tissue were first observed on day 7, peaked at day 21 and decreased by day 28. Adhesion formation was more severe at the proximal free tendon stump than at the repair site. Tendons were easily dissected at each harvest time. No necrotic change was observed in the free tendon segment between the 2 lacerations in all rats.

Microscopic findings: Day 3-7: Epitenocyte like cells gathered in the surface layer of the repair site on day 7 (Fig. 2b). The repaired tendon stumps were superficially joined. No gap formation or cell migration into the repair site were observed. Day 14-21: The lacerated collagen fibers in the repair site were dramatically degenerated and replaced by large and round cells on day 14 (Fig. 2c). These cells gradually proliferated and randomly arranged on day 21. Day 28: Mature collagen fibers crossed in the repair site and cells were aligned in linear fashion (Fig. 2d).

RT-PCR: Expression levels of types III, V, XII collagen genes gradually increased after surgery and peaked at day 14. Expression levels of all 4 MMP genes also increased after surgery. The expression levels of MMP-1 and 9 were greatly up regulated on day 7 and 14, those of MMP-2 and MT-MMP maintained high levels until day 28. The Results of the RT-PCR are shown in Fig. 3.

DISCUSSION
The rat tendon injury model provides a well-healed tendon without gap or severe adhesions at the repair site. This model presents the entire tendon healing process, which includes superficial repair and collagen remodeling. Macroscopic findings revealed that repair of the surface layer was almost completed on day 7, collagen remodeling started during day 7-14, gradually matured to day 28. The origin of the large round cells, which is appeared on day 14 at the repair site, was not clear. The results of RT-PCR showed that expression levels of collagen genes (types III, V, XII) and MMPs (MMP-1, 2, 9 and MT-MMP) were up regulated after tendon repair. Two differential gene expression patterns of MMPs were seen during tendon healing process. The rat tendon injury model described in the present study provides an additional option for investigating the mechanisms of the tendon healing process.

ACKNOWLEDGEMENT
This work was supported by Shriners Hospital grant #8510.

![Fig. 1 Macroscopic appearance of rat tendon healing process (left to right: days 0, 3, 21, 28)](image)

![Fig. 2 Microscopic appearance (HE stain)](image)

![Fig. 3 Agarose gel images of the RT-PCR products visualized UV light](image)