WOUND HEALING PROPERTIES OF TRANSFORMING GROWTH FACTOR β (TGF-β)-INDUCIBLE EARLY GENE (TIEG) KNOCKOUT MICE

INTRODUCTION:

Wound healing is a complex and highly regulated process that relies heavily on a large number and variety of molecules. Recently, growth factors have been shown to play an important role in these processes. Of the many cytokines that have been implicated in wound healing, transforming growth factor-β (TGF-β) has the broadest effects on soft tissue healing, such as cell proliferation, migration and extracellular matrix deposition.1,2 The effect of TGF-β is primarily exerted through the TGF-β/Smad signaling pathway.3,4 Over-expression of TIEG has been shown to mimic TGF-β activity in many cell types.3,5

We hypothesized that loss of TIEG would have an effect on cutaneous wound healing. However, to our knowledge, no studies have been published that investigated the effects of TGF-β/Smad pathway in the TIEG -/- mice. The purpose of this study was to investigate the role of TGF-β Inducible Early Gene (TIEG) in wound healing using TIEG knockout mice.

MATERIALS AND METHODS:

Specimen preparation: Thirty C57Black/129 mice, consisting of 15 TIEG knockout mice (TIEG -/-) and 15 wild type controls (TIEG +/+), were used in this study. A 2-cm transverse, linear, full-thickness incision was made below the inferior edge of the scapula. The incision was then closed using five 5-0 Prolene interrupted sutures (Ethicon, Inc., Somerville, NJ). Both TIEG -/- mice and controls were assigned into three subgroups for the evaluation of the time course of wound healing (postoperative day 3, 7 and 14, five mice for each subgroup).

Wound breaking strength measurements: The wound breaking strength was measured using the central portion of the wound (1cm wide) in 5 mice per group at each time point. The skin specimen was fixed in clamps with interdigitating grooves in a mechanical testing machine (MTS, Minneapolis, MN), and distracted at a rate of 20mm/min. Maximum forces required to break the wound at the sutured sites were recorded. The data obtained from the wound breaking strength were analyzed statistically by one factor ANOVA.

Histology: The lateral part of the wound were fixed in 10% formalin for 2 hours before being processed and embedded in paraffin wax. Sections were then cut at a thickness of 5 µm longitudinally. Hematoxylin and eosin (HE) staining was performed.

Results:

DISCUSSION:
The results from this study demonstrated that the wound breaking strength in TIEG knockout mice was significantly decreased at post operation day 14, but not at day 3 and 7, compared with controls, and the re-epithelialization of wound in both TIEG -/- mice and controls were similarly complete at post operation day 7. These findings indicate that loss of TIEG affects the function of TGF-β and TGF-β/Smad pathway in vivo, possibly by decreased stimulation of fibroblast and induction of the ECM deposition, resulting in decreased wound breaking strength. Altered function of TGF-β/Smad pathway in the TIEG -/- mice may induce the increased expression of TGF-β during wound healing.

REFERENCES:

ACKNOWLEDGEMENT:
Funding for this study was from Mayo Foundation.