

## Comparative Evaluation of Agents on Dupuytren's Contracture and Keloid Fibrosis

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**INTRODUCTION:** Neoplasms are the result of abnormal cell proliferation. Dupuytren's contracture and keloid scar are characterized by fibroblast hyperproliferation and collagen deposition resulting in abnormal scar tissue. This similarity has led to investigation of antiproliferative/antimetabolite agents used in the treatment of neoplasms to control/alleviate Dupuytren's contracture and keloid scar. While individual drug treatments show some decrease in contraction, there has not been a reported investigation comparing antiproliferative/antimetabolite substances and their proposed mechanism of action. The purpose of this experimental series is to comparatively evaluate respective levels of TGF- $\beta_1$  and - $\beta_2$ , the rate and extent of contraction of fibroblasts derived from keloid scar and Dupuytren's contracture when treated with antiproliferative/antimetabolite agents.

**METHODS:** Fibroblasts obtained from explants of Dupuytren's contracture and palmar fascia (control) as well as keloids and normal scar (control) were utilized. These fibroblast populated collagen lattices (FPCL) were exposed to 72 hours of non-cytotoxic doses of 5-Fluorouracil, Methotrexate, Paclitaxel, Tamoxifen, Mitomycin-C, and Bleomycin. Standardized photography was utilized to evaluate FPCL contraction. The supernatant of FPCL was analyzed using TGF- $\beta_1$  and - $\beta_2$  immunoassays.

**RESULTS:** Dupuytren's and keloid fibroblasts' FPCLs exhibit increased contraction when compared with controls. These abnormal scar types showed a significant decrease of contraction after exposure to particular antiproliferative agents. TGF- $\beta_1$  secretion did not result in a significant difference between abnormal scars when compared with controls. Various antiproliferative treatment agents on abnormal scar groups decreased the expression of TGF- $\beta_1$  compared to the untreated controls. Abnormal scar types had elevated TGF- $\beta_2$  when compared with controls. Treatment of fibroblasts with all drugs tested resulted in significant down-regulation of TGF- $\beta_2$  expression compared to untreated fibroblasts from these abnormal scar types.

**CONCLUSION:** Non-cytotoxic doses of antiproliferative/antimetabolite agents used in this study decrease fibroblast contraction significantly when compared with untreated fibroblasts. These agents also cause a significant decrease in both TGF- $\beta_1$  and - $\beta_2$ , a likely cause of decreased fibroblast contraction. Antiproliferative and antimetabolite agents, especially Paclitaxel, Methotrexate and Tamoxifen, are effective *in vitro* to limit fibroblast contraction. Further testing is warranted to provide evidence of their efficacy *in vivo*.

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