Modulation of skin collagen metabolism in aged and photoaged human skin in vivo.
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Abstract

To the best of our knowledge, no study has been conducted to date to directly compare the collagen metabolism of photoaged and naturally aged human skin. In this study, we compared collagen synthesis, matrix metalloproteinase-1 levels, and gelatinase activity of sun-exposed and sun-protected skin of both young and old subjects. Using northern blot analysis, immunohistochemical stain, and Western blot analysis, we demonstrated that the levels of procollagen type I mRNA and protein in photoaged and naturally aged human skin in vivo are significantly lower than those of young skin. Furthermore, we demonstrated, by northern blot analysis, that the procollagen alpha1(I) mRNA expression of photoaged skin is much greater than that of sun-protected skin in the same individual. In situ hybridization and immunohistochemical stain were used to show that the expression of type I procollagen mRNA and protein in the fibroblasts of photoaged skin is greater than for naturally aged skin. In addition, it was found, by Western blot analysis using protein extracted from the dermal tissues, that the level of procollagen type I protein in photoaged skin is lower than that of naturally aged skin. The level of matrix metalloproteinase-1 protein and the activity of matrix metalloproteinase-2 were higher in the dermis of photoaged skin than in naturally aged skin. Our results suggest that the natural aging process decreases collagen synthesis and increases the expression of matrix metalloproteinases, whereas photoaging results in an increase of collagen synthesis and greater matrix metalloproteinase expression in human skin in vivo. Thus, the balance between collagen synthesis and degradation leading to collagen deficiency is different in photoaged and naturally aged skin.
Characteristics of the Aging Skin.

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Abstract

SIGNIFICANCE:

Although most researches into the changes in skin with age focus on the unwelcome aesthetic aspects of the aging skin, skin deterioration with age is more than a merely cosmetic problem. Although mortality from skin disease is primarily restricted to melanoma, dermatological disorders are ubiquitous in older people with a significant impact on quality of life. The structural and functional deterioration of the skin that occurs with age has numerous clinical presentations, ranging from benign but potentially excruciating disorders like pruritus to the more threatening carcinomas and melanomas.

RECENT ADVANCES:

The degenerative changes that occur in the aging skin are increasingly understood at both the molecular and cellular level, facilitating a deeper understanding of the structural and functional deterioration that these changes produce.

CRITICAL ISSUES:

A loss of both function and structural stability in skin proceeds unavoidably as individuals age, which is the result of both intrinsic and extrinsic processes, which contribute simultaneously to a progressive loss of skin integrity. Intrinsic aging proceeds at a genetically determined pace, primarily caused by the buildup of damaging products of cellular metabolism as well as an increasing biological aging of the cells. Estrogen levels strongly influence skin integrity in women as well; falling levels in midlife, therefore, produce premature aging as compared with similarly aged men. Extrinsic insults from the environment add to the dermatological signs of aging.

FUTURE DIRECTIONS:

A deeper understanding of the physiological basis of skin aging will facilitate progress in the treatment of the unwelcome sequelae of aging skin, both cosmetic and pathogenic.
Dermatologic and cosmetic concerns of the older woman.

Bolognia JL

Abstract

The cutaneous signs of aging including wrinkles, solar lentigines ("liver spots"), and telangiectasias are primarily the result of repeated exposures to ultraviolet light (photoaging). Chronologic aging, and in women, estrogen withdrawal also exert an effect on the structure and function of the epidermis and dermis. In this article, the relative roles of these three factors are discussed, as are the most common skin lesions found in the older woman. Lastly, the therapeutic options available for the treatment of these age-associated cutaneous disorders are outlined.
Epidermal growth factor immunoreactive material in the central nervous system: location and development.

Fallon JH, Seroogy KB, Loughlin SE, Morrison RS, Bradshaw RA, Knave DJ, Cunningham DD.

Abstract

Epidermal growth factor (EGF) is a potent mitogen with hormonal activity in the gastrointestinal tract. Material cross-reacting with EGF was detected in the central nervous system of the developing and adult albino rat by the indirect immunofluorescence technique. High concentrations of EGF-cross-reacting material were identified in forebrain and midbrain structures of pallidal areas of the brain. These include the globus pallidus, ventral pallidum, entopeduncular nucleus, substantia nigra pars reticulata, and the islands of Calleja. Thus, EGF may represent another gut-brain peptide with potential neurotransmitter-neuromodulator functions in pallidal structures of the extrapyramidal motor systems of the brain.
Profiling and metaanalysis of epidermal keratinocytes responses to epidermal growth factor.

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Abstract

BACKGROUND:

One challenge of systems biology is the integration of new data into the preexisting, and then re-interpretation of the integrated data. Here we use readily available metaanalysis computational methods to integrate new data on the transcriptomic effects of EGF in primary human epidermal keratinocytes with preexisting transcriptomics data in keratinocytes and in EGF-treated non-epidermal cell types.

RESULTS:

We find that EGF promotes keratinocyte proliferation, attachment and motility and, surprisingly, induces DUSPs that attenuate the EGF signal. Our metaanalysis identified overlapping effects of EGF with those of IL-1 and IFNγ, activators of keratinocyte in inflammation and wound healing. We also identified the genes and pathways suppressed by EGF but induced by agents promoting epidermal differentiation. Metaanalysis comparison with the EGF effects in other cell types identified extensive similarities between responses in keratinocytes and in other epithelial cell types, but specific differences with the EGF effects in endothelial cells, and in transformed, oncogenic epithelial cell lines.

CONCLUSIONS:

This work defines the specific transcriptional effects of EGF on human epidermal keratinocytes. Our approach can serve as a suitable paradigm for integration of new omics data into preexisting databases and re-analysis of the integrated data sets.
INTRODUCTION:
Wound healing is a complex process involving interactions among a variety of different cell types. The normal wound repair process consists of three phases—inflammation, proliferation, and remodeling that occur in a predictable series of cellular and biochemical events. Wounds are classified according to various criteria: etiology, lasting, morphological characteristics, communications with solid or hollow organs, the degree of contamination. In the last few years many authors use the Color Code Concept, which classifies wounds as red, yellow and black wounds. This paper presents conventional methods of local wound treatment (mechanical cleansing, disinfection with antiseptic solutions, wound debridement—surgical, biological and autolytic; wound closure, topical antibiotic treatment, dressing), as well as general measures (sedation, antitetanus and antibiotic protection, preoperative evaluation and correction of malnutrition, vasoconstriction, hyperglycemia and steroid use, appropriate surgical technique, and postoperative prevention of vasoconstriction through pain relief, warming and adequate volume resuscitation).

THE ROLE OF PHYSIOLOGICAL FACTORS AND ANTIMICROBIAL AGENTS IN WOUND HEALING:
Growth factors play a role in cell division, migration, differentiation, protein expression, enzyme production and have a potential ability to heal wounds by stimulating angiogenesis and cellular proliferation, affecting the production and the degradation of the extracellular matrix, and by being chemotactic for inflammatory cells and fibroblasts. There are seven major families of growth factors: epidermal growth factor (EGF), transforming growth factor-beta (TGF-beta), insulin-like growth factor (IGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), interleukins (ILs), and colony-stimulating factor (CSF). Acute wounds contain many growth factors that play a crucial role in the initial phases of wound healing. The events of early wound healing reflect a finely balanced environment leading to uncomplicated and rapid wound healing. Chronic wounds, for many reasons, have lost this fine balance. Multiple studies have evaluated the effect that exogenously applied growth factors have on the healing of chronic wounds. In the study conducted by Knighton and colleagues, topical application of mixture of various growth factors (PDGF, TGF-beta, PDAF, PF4, PDEGF) demonstrated increased wound healing over controls. Brown and associates demonstrated a decrease in skin graft donor site healing time of 1 day using topically applied EGF. Herndon and ass. used systemic growth hormone in burned children and reduction in healing time made a significant clinical difference by allowing earlier wound coverage and decreasing the duration of hospitalization. The TGF family of growth factors is believed to be primarily responsible for excessive scar formation, especially the beta 1 and beta 2 isoforms. TGF-beta 3 isoform has recently been described and may have an inhibitory function on scar formation by being a natural antagonist to the TGF-beta 1 and TGF-beta 2 isoforms. Cytokines, especially interferon-alpha (INF-alpha), INF-alpha, and INF-alpha 2b, may also reduce scar formation. These cytokines decrease the proliferation rate of fibroblasts and reduce the rate of collagen and fibronectin synthesis by reducing the production of mRNA. Expression of nitric oxide synthase (NOS) and heat shock proteins (HSP) have an important role in wound healing, as well as trace elements (zinc, copper, manganese). Applications of some drugs (antioxidants—asiaticoside, vitamin E and ascorbic acid; calcium D-pantothenate, exogenous fibronectin; antileprosy drugs—oil of hydnocarpus; alcoholic extract of yeast) accelerate wound healing. Thymic peptide thymosin beta 4 (T beta 4R) topically applied, increases collagen deposition and angiogenesis and stimulates keratinocyte migration. Thymosin alpha 1 (T alpha 1R), peptide isolated from the thymus, is a potent chemoattractant which accelerates angiogenesis and wound healing. On the contrary, steroid drugs, hemorrhage and denervation of wounds have negative effect on the healing process.
Improved texture and appearance of human facial skin after daily topical application of barley produced, synthetic, human-like epidermal growth factor (EGF) serum.

Schouest JM, Luu TK, Moy RL.

Abstract
A three month, open-label, single center study was conducted to determine whether a uniquely derived serum containing barley bioengineered, human-like epidermal growth factor protein could improve visible signs of photodamage and aging in facial skin. Twenty-nine females, aged 39 to 75 years, with mild to severe, fine and course rhytids, photodamage, and pigmentation were enrolled. Subjects then applied the treatment serum per the prescribed protocol twice-daily for 3 months, in addition to the use of a basic sunscreen and facial cleanser. In-person clinical evaluations and subject self-assessment questionnaires were administered at each follow up visit. In addition, clinical photography was completed at baseline, and each subsequent visit. Clinical evaluations showed statistically significant improvement in the appearance of fine lines and rhytids, skin texture, pore size, and various dyschromatic conditions apparent within the first month of use, and continuing improvement trends for the duration of the study. The treatment serum was well tolerated with minimal treatment-related complications reported throughout. Efficacy of this novel serum and treatment protocol resulted in meaningful improvements in photodamage and visible signs of aging.
The anti-scar effects of basic fibroblast growth factor on the wound repair in vitro and in vivo.


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Abstract

Hypertrophic scars (HTS) and keloids are challenging problems. Their pathogenesis results from an overproduction of fibroblasts and excessive deposition of collagen. Studies suggest a possible anti-scarring effect of basic fibroblast growth factor (bFGF) during wound healing, but the precise mechanisms of bFGF are still unclear. In view of this, we investigated the therapeutic effects of bFGF on HTS animal model as well as human scar fibroblasts (HSF) model. We show that bFGF promoted wound healing and reduced the area of flattened non-pathological scars in rat skin wounds and HTS in the rabbit ear. We provide evidence of a new therapeutic strategy: bFGF administration for the treatment of HTS. The scar elevation index (SEI) and epidermal thickness index (ETI) was also significantly reduced. Histological reveal that bFGF exhibited significant amelioration of the collagen tissue. bFGF regulated extracellular matrix (ECM) synthesis and degradation via interference in the collagen distribution, the α-smooth muscle actin (α-SMA) and transforming growth factor-1 (TGF-β1) expression. In addition, bFGF reduced scarring and promoted wound healing by inhibiting TGFβ1/SMAD-dependent pathway. The levels of fibronectin (FN), tissue inhibitor of metalloproteinase-1 (TIMP-1) collagen I, and collagen III were evidently decreased, and matrix metalloproteinase-1 (MMP-1) and apoptosis cells were markedly increased. These results suggest that bFGF possesses favorable therapeutic effects on hypertrophic scars in vitro and in vivo, which may be an effective cure for human hypertrophic scars.