Διαλέξεις

ΠΕΜΠΤΗ 15 ΜΑΡΤΙΟΥ 2007

ΑΙΘΟΥΣΑ: «ΑΜΦΙΘΕΑΤΡΟ»
ΩΡΑ: 11.30-12.00
ΣΥΝΤΟΝΙΣΤΗΣ: ΚΑΣΤΑΝΑ ΟΥΡΑΝΙΑ

NEW APPROACHES FOR COMPLEX WOUNDS: THE VIEW OF A SURGEON

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Complex wounds have for a long period of time been given to surgeons, as there was no toher issue than surgery. In many cases, surgery failed and the patient was more or less abandoned to medical doctors.
One of the key element is to have a multidisciplinary approach of complex wounds. The surgeon alone cannot solve the numerous difficulties as:
- The nutritional status: under a level of serum albumin of 25, chances to heal wathever be the solution proposed are minimal. This is the moment of renutrition program, not for surgery.
- The infection status: local infection can be evident, but there is a number of cases when an infection is latent and difficult to manage. This critical colonization situation should be assessed and treated with adapted dressings, prior to any surgical procedure
- The vascularization of the tissues involved in the surgical procedure. Many surgeons consider there is a few places for surgery in devitalized tissues. However, since the emergence of distal bypasses and the technical cacpities of specialists to redilate vessels, surgery can be anticipated, with solutions lmess aggressive than the amputations proposed before. Distal and economic resection of bone, join,ts or segments of foot are now common, when combining vascular bypass surgery, the use of adapted antimicrobiula dressings, the use of negative pressure therapy and the use of limited covering procedure, like skin grafts or limited flaps.
This new combination of techniques , including new modes of debridement less aggressive on the tissues, can help in managing complex wounds using limited surgery, a good strategy of debridement of necrotic tissues followed by an adpated use of covering techniques **.**

ΑΙΘΟΥΣΑ: «ΑΜΦΙΘΕΑΤΡΟ»
ΩΡΑ: 12.00-12.30
ΣΥΝΤΟΝΙΣΤΗΣ: ΔΙΑΜΑΝΤΗ ΣΟΦΙΑ

1. "SIGNALING EVENTS REGULATING FIBROBLAST FUNCTIONS IMPORTANT FOR WOUND HEALING: ROLE OF GROWTH FACTORS – IMPLICATIONS FOR PHARMACOLOGIC INTERVENTION"

ALAIN MAUVIEL - INSERM U697, Paris, France

The JNK group of MAP kinases, also known as stress-activated kinases, are activated upon exposure of cells to cytokines, growth factors, and environmental stresses such as UV irradiation or heat shock. In the nucleus, JNKs phosphorylate transcription factors such as c-Jun, a process that leads to maximal transcriptional activity of the latter. We used both a gene knockout approach and pharmacologic modulation to to elucidate the specific roles played by the Jun-N-terminal kinase (JNK) and NF-κB pathways downstream of TNF-α in the context of α(2) type I collagen gene (COL1A2) expression. In jnk1-/--jnk2-/- double-knockout fibroblasts (jnk-/-), TNF-α inhibited basal COL1A2 expression but had no effect on TGF-β-driven Smad-dependent gene transactivation unless jnk1 was introduced ectopically. Conversely, in NEMO- (NF-κB essential modulator knockout) fibroblasts, lack of NF-□B activation did not influence the antagonism exerted by TNF-α against TGF-β but prevented repression of basal COL1A2 gene expression by TNF-α. Similar regulatory mechanisms take place in dermal fibroblasts, as evidenced using transfected dominant-negative forms of MKK4 and IKK-α, critical kinases upstream of the JNK and NF-κB pathways, respectively. Mechanistically, we identified JNK activation by TNF-β as favouring protein-protein interactions between Jun and Smad3 proteins, critical transcriptional mediators of TGF-β. Jun-Smad3 interactions preventing Smad3 binding to its cognate DNA cis-element(s) in target gene promoters, resulting in the interruption of Smad3-dependent transcription. These results represent a key demonstration of an alternate usage of distinct signaling pathways by TNF-α (NF-κB or JNK) to inhibit the expression of a given gene, COL1A2, depending on its activation state: JNK allows TNF-α to antagonize Smad-dependent COL1A2 gene expression while NF-κB represses basal COL1A2 expression.
Interestingly, we have then been able to identify the JNK pathway as essential to provide anti-fibrotic activities to a variety of pharmacologic drugs/compounds, including 5-fluoro-uracyl at non toxic concentrations, the immunosuppressive drug rapamycin, and the anticoccidial alkaloid halofuginone. Specifically, these drugs are able to both repress collagen gene expression and to activate that of metalloproteinases. Together, our work demonstrates that activators of the JNK pathway may represent interesting candidates for therapeutic intervention in conditions requiring accelerated extracellular matrix turnover and degradation, while JNK inhibitors may accelate tissue repair.

2. "IMPLICATION OF THE JNK PATHWAY IN CELL MIGRATION AND WOUND REPAIR"

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During wound healing the fibroblasts migrate throughout the wound and synthesize extracellular matrix, restoring skin integrity. Multiple cytokines, growth factors and their downstream signaling mechanisms control these events, one of which is transforming growth factor beta (TGF-β). Extracellular stimuli, including TGF-β, transduce their cellular signals through activation of the