Guarigione delle ferite e dei traumi e effetti di Arnica

Phases of wound healing:

اا] Inflammation

(biochemical activation)

[II] Proliferation

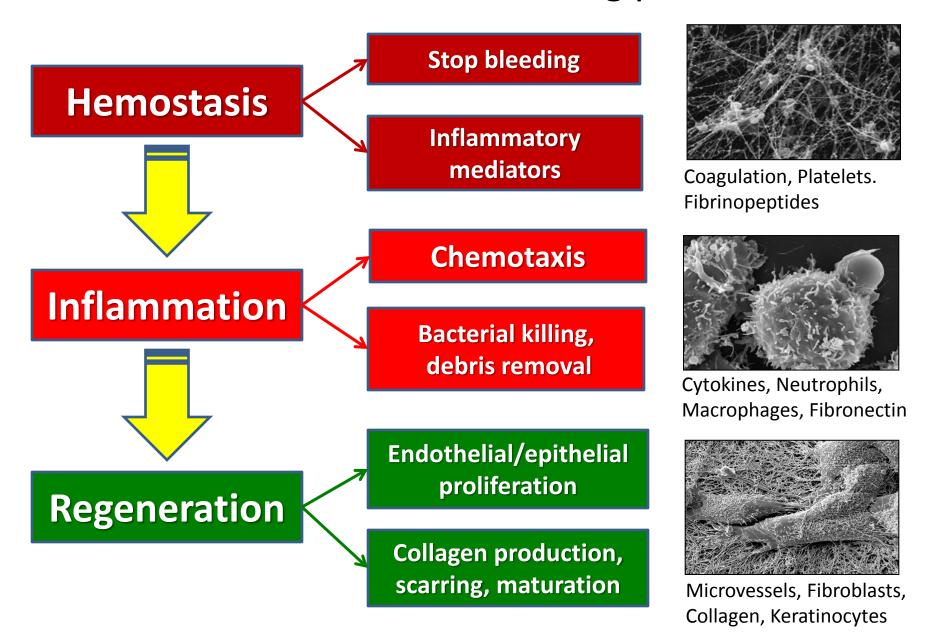
cellular activation)

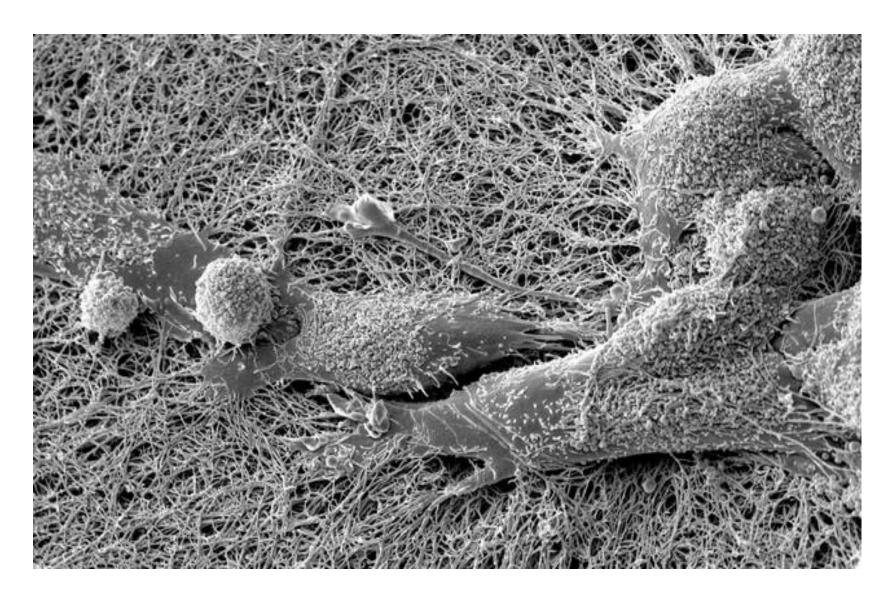
[III]

Remodeling

(maturation & differentiation of scare tissue)

Phases of wound healing process

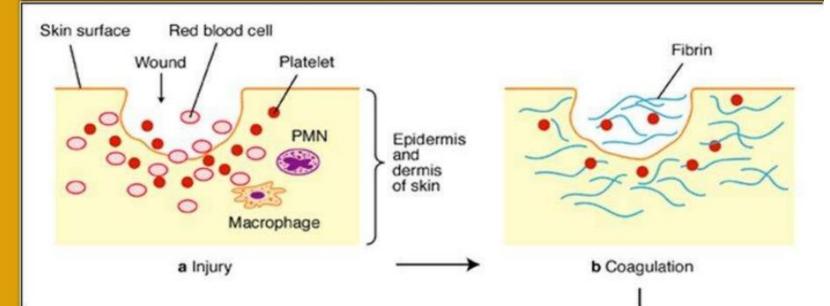




Firoblast on collagen

1ry vascular reaction:

- Activation of clotting factors cascac
- Platelet aggregation
- Clot formation (The scab) which temporarily closes the wound consists mainly of fibrin mesh trapped other blood cells →hemostasis.
- Temporary constricting of small blood vessels (few minutes) → temporary blanching.



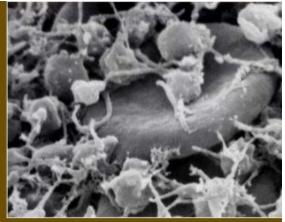
Inflammatory

 Tissue injury & blood vessel damage exposure of subendothelial collagen to platelets and vWF activates the coagulation pathway

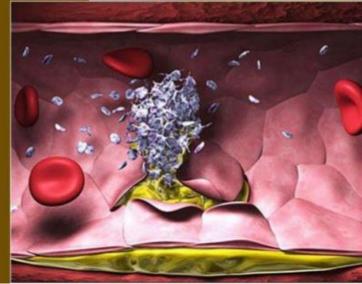


Provisional matrix:
 platelets, fibrin, and fibronectin

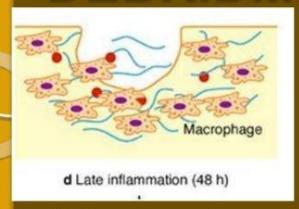
Platelet aggregation:
 Thromboxane (vasoconstrict),
 thrombin, platelet factor 4

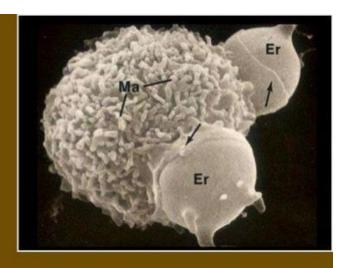






DEBRIDMENT





Macrophages

- are essential for wound healing.
- Macrophages (monocytes) enter the wound from the 2nd after wounding and present until the reparative process is complete.
- Along time macrophages continue
 - phagocytose & cleaning the wound site of bacteria, debris, F.B and necrotic matter.
 - producing the activation growth and chemotactic factors similar to those of platelets (complete the function of platelets).....

Macrophages Necessary

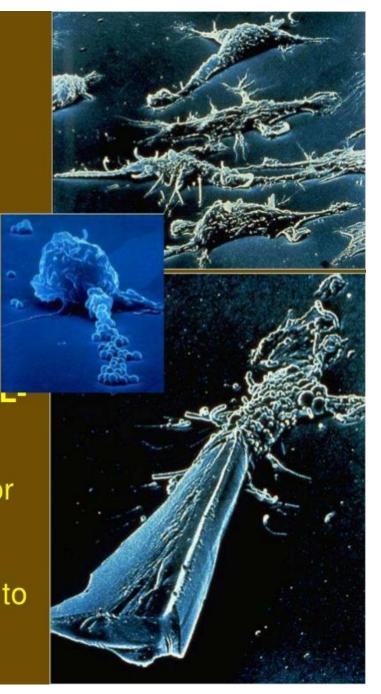
 Monocytes migrate & activate: Macrophages

 Appear when PMN's disappear 24-48 hr

Do the same activities as PMN

 Plus orchestrate release of enzymes (collagenase, elastase), PGE's, cytokines (IL-1, TNF alpha, IFN), growth factors (TGF & PDGF), and fibronectin (scaffold/anchor for fibroblasts)

 Activate Fibroblasts, endothelial and epithelial cells to form Gran.



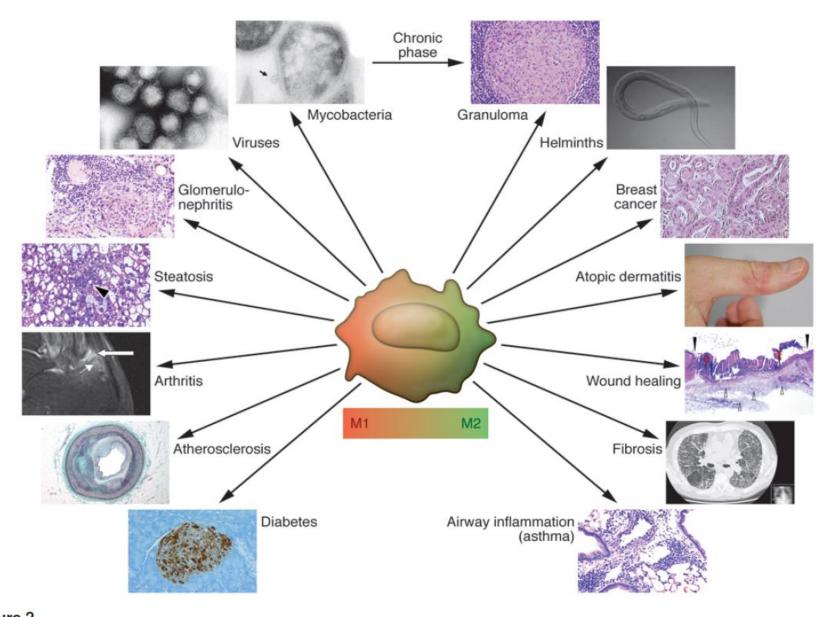


Figure 2
Schematic representation of macrophage plasticity and polarization in pathology. Dynamic changes occur over time with evolution of pathology: for instance, a switch from M1 to M2 macrophage polarization characterizes the transition from early to chronic phases of infection. Moreover, mixed phenotypes or populations with different phenotypes can coexist. For pathologies not discussed in the text, see Supplemental References. Images adapted from refs. 141–144.

Proliferative

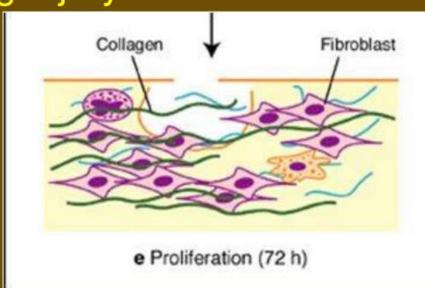
 Regenerative or Reparative (granulation & cellular activation) starts after 3-5 days takes 5-20 c

INCLUDES:

- Granulation tissue formation
- Epithelization
- Contraction
- Angiogenesis: endothelial cells activate & degrade Basement membrane, migrate, and divide to form more tubules
- Granulation Tissue: capillary ingrowth, collagen, Macrophages, Fibroblasts, Hyaluroni c acid (GAG)

Granulation tissue

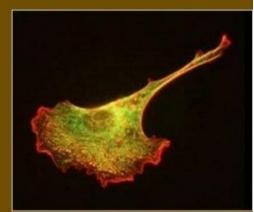
 Granulation tissue formation occurs 3-5 days following injury



 Includes: Inflammatory cells, Fibroblasts and collagen, ground substance and Vascular and lymphatic proliferation

Fibroblast

 The fibroblast is a critical component of granulation tissue.

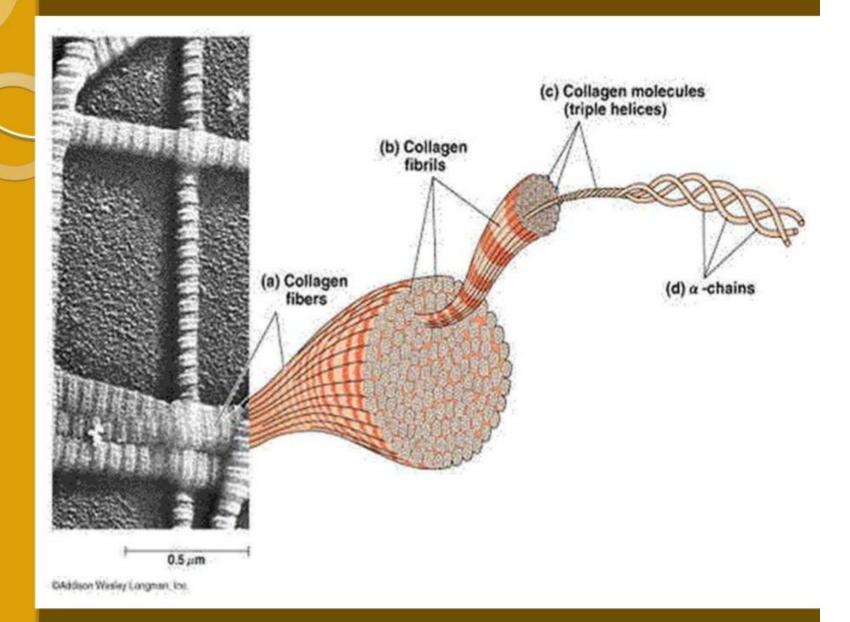


- Fibroplasia begins from surrounding mesenchymal cells 3-5 days after injury and may last as long as 14 days.
- Fibroblasts migrate and proliferate in response to platelets growth factors.
- Fibroblasts are responsible for the production of collagen, elastin, ground substance



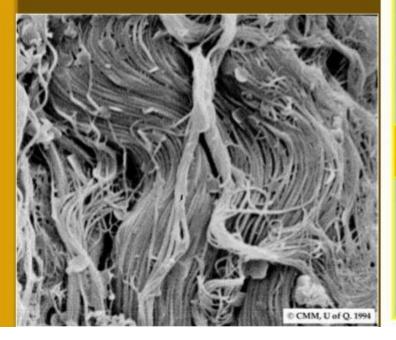
Collagen synthesis

- The collagen fibers which is essential for:
 - bridging the wound gap
 - supporting the growing vessels and
 - wound strength.
- Fibroblasts → Collagen III → held together by weak electrostatic forces and is soluble in weak salt solution. It is laid down irregularly and haphazardly
- then → polymerization occurs by cross linked to the collagen molecules → Thick strong less soluble collagen [I] become more regular and perpendicular on the plane of wound.
- The process of collagen synthesis:
 - Starts on the 3rd day
 - The peak reaches by the 5-7 days



Collagen

Type III predominant collagen synthesis days 1-2
Type I days 3-4
Type III replaced by Type I in 3 weeks



I (80% skin)	Most Common: skin, bone, tendon. Primary type in wound healing.
II	Cartilage
111 (20 % skin)	Increased Ratio in healing wound, also blood vessels and skin
IV	Basement Membrane
V	Widespread, particularly in the cornea

Ground substance

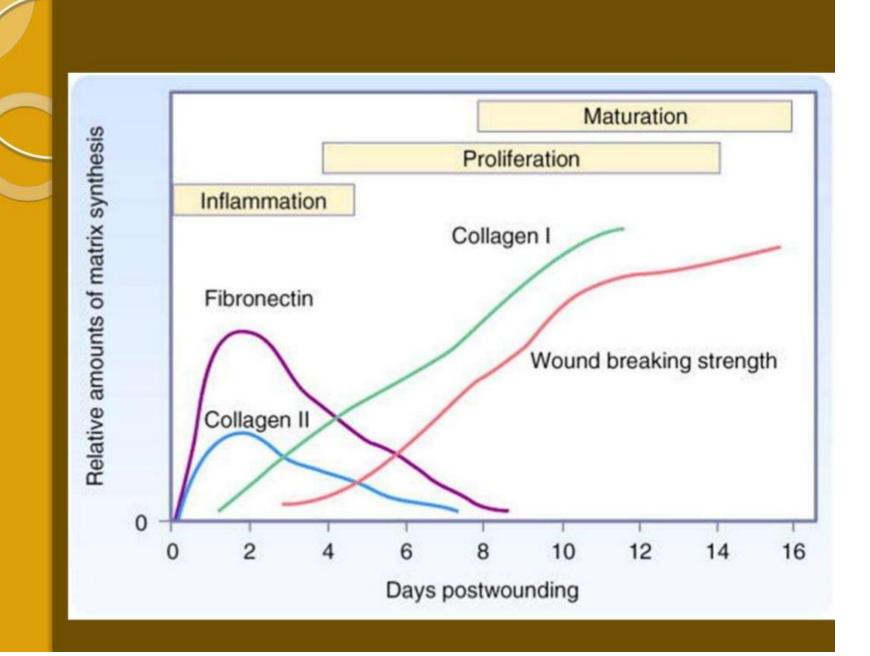
 Produced by fibroblasts (water – electrolytes – mucopolysaccharides (proteoglycans) – fibronectins – glycoproteins).

Angiogenesis (Vascular and lymphatic proliferation):

- The macrophage growth factors ->stimulates angiogenesis
- New capillaries bud from endothelial cells in capillary near the wound edges appear →proliferation → a new network of capillaries is formed inside the granulation tissues →red granulations.

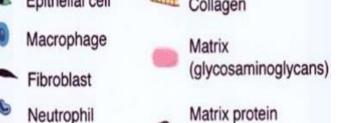
Epithelization

- Stats within hours by mitosis of the basal cell layer.
- The epidermal cells advanced from the edges and creep across the wound surface in a favorable plane dissecting the wound between the living and dead tissue. Migration stops when it meets the opposite advanced epithelium.
- The new epithelium is thin non-pigmented.
- Incisional wounds are epithelized within 24-48 hours after injury (distance of less than 1 mm). This epithelial layer provides a seal



Summary

- Inflammatory phase:
 - A clot forms stop bleeding
 - Vasodilatation → of WBCs
 - cells of inflammation → defending and debridment of injured tissue.
- Proliferative phase
 - Epithelization,
 - Fibroplasia (fibroblasts and collagen), and
 - Angiogenesis occur during the; additionally,
 - Granulation tissue forms and
 - The wound begins to contract.
- Remodeling (maturation) phase
 - Collagen forms tight cross-links to other collagen and with protein molecules,
 Epithelial cell
 Collagen
 - Increasing the tensile streng





Arnica montana subsp. montana Caption: Dipartimento di Scienze della Vita, Università di Trieste -

 L'Arnica (Arnica montana L.) è un'erba medicinale della famiglia delle Asteraceae, ghiandolosa, perenne, a fusto eretto e mediamente robusto, alta 20 – 60 cm, dai grandi capolini di colore giallo aranciato con caratteristici petali "spettinati" e dal gradevole odore aromatico.

Un médicament natural



Iannitti T, Morales-Medina JC, Bellavite P, Rottigni V, Palmieri B.

Effectiveness and Safety of Arnica montana in Post-Surgical Setting, Pain and Inflammation.

Am J Ther. 2016 Jan-Feb;23(1):e184-97

Marzotto M, Bonafini C, Olioso D, Baruzzi A, Bettinetti L, Di LF, Galbiati E, Bellavite P.

Arnica montana Stimulates Extracellular Matrix Gene Expression in a Macrophage Cell Line Differentiated to Wound-Healing Phenotype PLoS ONE 2016;11:e0166340.





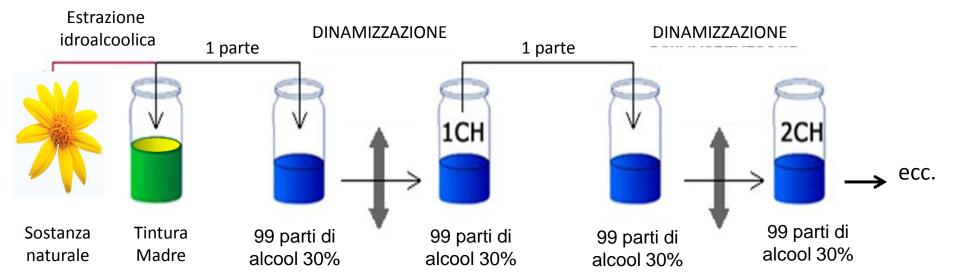
http://www.webmd.com/osteoarthritis/ss/slideshow-osteoarthritis-overview

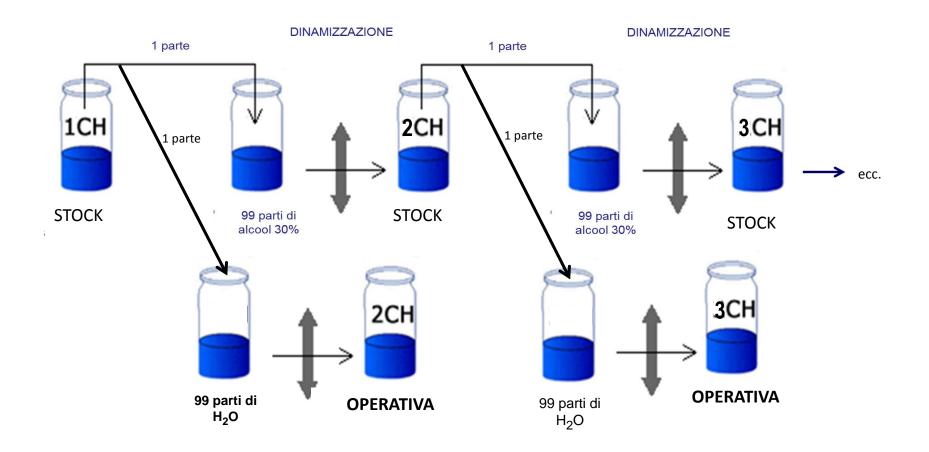
Osteoarthritis



 Osteoarthritis (OA) is the progressive breakdown of the joints' natural shock absorbers. This can cause discomfort when you use the affected joints -- perhaps an ache when you bend at the hips or knees, or sore fingers when you type. Most people over 60 have some degree of OA

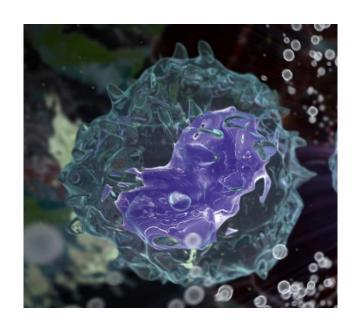
http://www.webmd.com/osteoarthritis/ss/slideshow-osteoarthritis-overview

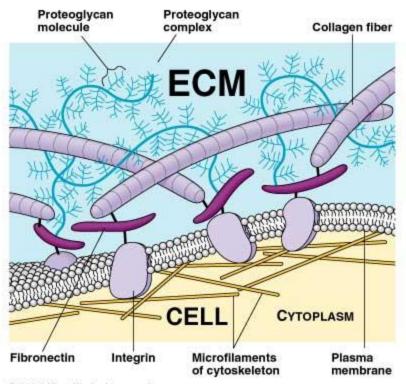




Evaluation of Arnica montana dilutions on the expression of inflammatory genes by a human macrophage cell line







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Integrins connect the cell to it's extracellular matrix. The extracellular matrix (ECM) is the living environment of your cells. The ECM is a complex structural tissue surrounding and supporting cells. The ECM is often referred to as connective tissue and has many key functions, including:

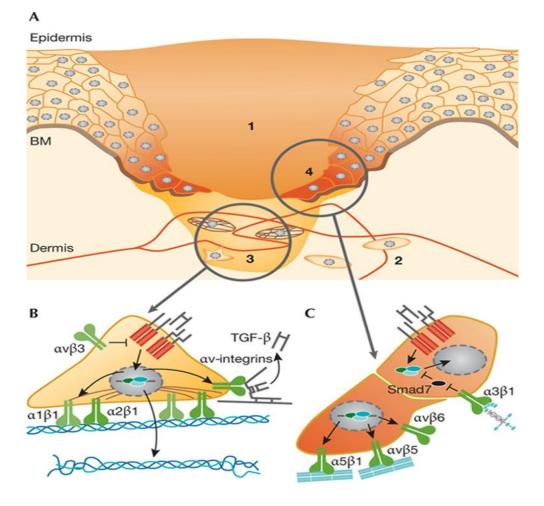
- 1) Mechanical support for cells and tissues.
- Influences cell shape, cell movement, cell development and cell differentiation.
- Coordinates cellular functions through signalling with cellular adhesion receptors (integrins).
- 4) Reservoir for extracellular signaling molecules.

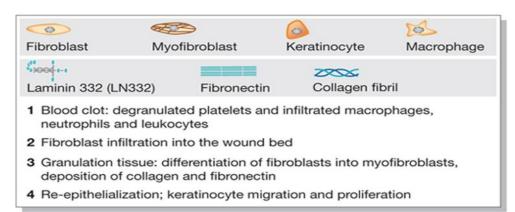
Fibronectins attach cells to a variety of extracellular matrices. Cell to ECM adhesion is regulated by specific cell surface cellular adhesion molecules (CAM) known as integrins. The integrins transmit mechanical stimuli from the ECM to the intracellular cytoskeleton.

COOH Cell Surface Collagen binding domains Fibrin binding fibrin binding domains Fibrin binding fibrin bindi

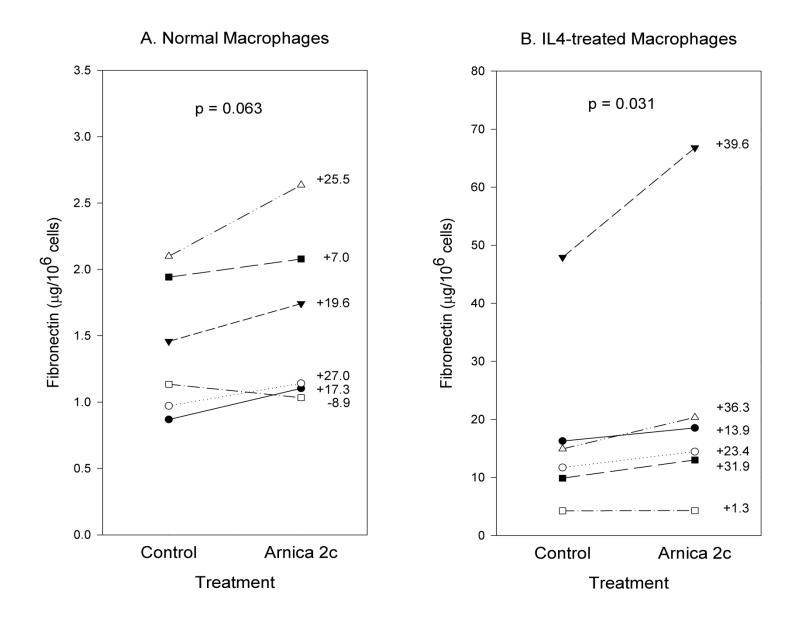
Il ruolo della fibronectina

- La fibronectina è uno dei componenti del coagulo ma è anche presente normalmente nel connettivo (ECM).
- Agisce come fattore chemotattico per i monociti, che sono attratti dai frammenti di fibronectina che contengono il dominio in grado di legarsi alle proteine della superficie cellulare.
- Per la sua capacità di legarsi, la fibronectina probabilmente ricopre i debris presenti nella ferita, le molecole di collagene denaturate, di DNA, di fibrina e di actina, nonché i batteri, e consente la fagocitosi da parte dei macrofagi.
- Interagendo contemporaneamente con la superficie delle cellule e con i
 componenti della matrice extracellulare (ad esempio con il collagene, l'eparina e la
 fibrina), la fibronectina promuove la migrazione ai margini della ferita delle cellule
 dell'epidermide, e la crescita dei fibroblasti e dei capillari.
- Infine si ritiene che la fibronectina costituisca un ordito per la formazione della matrice, ed un indispensabile supporto all'attività dei miofibroblasti che determinano la contrazione della ferita.





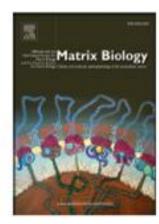
Fibronectin detected in supernatants of cell cultures in the



Fibronectin

MATBIO-1277

Matrix Biol. Aug. 2016. doi: 10.1016/j.matbio.2016.07.011.



Fibronectin, the extracellular glue

Alicia J. Zollinger and Michael L. Smith

Department of Biomedical Engineering, Boston University, Boston, MA 12215, U.

Fibronectin is an extracellular matrix protein that is present during periods of change within tissues.

It is upregulated and necessary in a number of developmental contexts, and it is also present during wound healing.

