

Tissue Regeneration

Dr Alain Gondinet of ReGen Lab reviews cell therapies using platelet rich plasma autologous cellular regeneration

This article describes the potential for doctors to use platelet rich plasma in their daily practice in the aesthetic fields of mesotherapy, nappage and fillers.

A MULTIDISCIPLINARY PROGRAMME FOR SKIN REJUVENATION

From the centrifuged blood of the patient, we can obtain, in a specific tube, a plasma, with platelets and white cells separated from the red cells by a gel. Once we have this plasma, we can inject it into the patient's skin in different ways: nappage, mesotherapy and/or fillers. But before starting the protocol for aesthetics injections, we have to understand what autologous cell regeneration (ACR) means, and what the components of the PRP are.

WHAT IS AUTOLOGOUS CELL REGENERATION?

Autologous cell regeneration is the bio-stimulation of the cells of the dermis using an injection technique which utilises the patient's own bio-active platelet rich plasma (PRP), including leucocytes. The aim of these injections is to stimulate and regenerate aged and damaged skin and hypodermal tissues, and to produce a new dermis.

WHAT IS PLATELET RICH PLASMA?

Platelet rich plasma is an autologous concentration of human platelets in a small volume of plasma measured as 1,000,000 platelets per mm³ or two to three times the native concentration of whole blood at a pH of 6.5-6.7 (whole blood pH is 7.0-7.2).

It is also referred to as autologous platelet gel, plasma rich growth factors (PRGFs) or autologous platelet concentrate. PRP is a concentration of the fundamental protein growth factors which have been proved to

Figure 1: Growth factors acting on 'healing cascade'

Factor	Name	Principal source	Effects
PDGF aa PDGF bb PDGF ab	Platelet derived growth factors	Activated thrombocytes	Mitogenes of mesenchymal stem cells promote the synthesis of the extracellular matrix
TGF-alpha TGF-beta	Transforming growth factors	Activated thrombocytes	Stimulation of DNA synthesis, proliferation of various types of cells. Favours the synthesis of collagen
IGF-I IGF-II	Insulin-like growth factors	Activated thrombocytes	Stimulates proliferation and differentiation of osteoblasts
EGF	Epidermal growth factor	Activated thrombocytes	Stimulates proliferation and differentiation of epidermis cells, co-stimulating angiogenesis
VEGF	Vascular endothelial growth factor	Leucocytes and endothelial cells	Stimulates angiogenesis and chemo-attraction of osteoblasts

In addition, the activated thrombocytes have on their surface a multitude of signalisation molecules, for example: CD9, CD-W17, CD31, CD41, CD42a-d, CD51, CD-W60, CD61, CD62P, CD63

Figure 2: Benefits of PRP reported in the 'healing cascade'

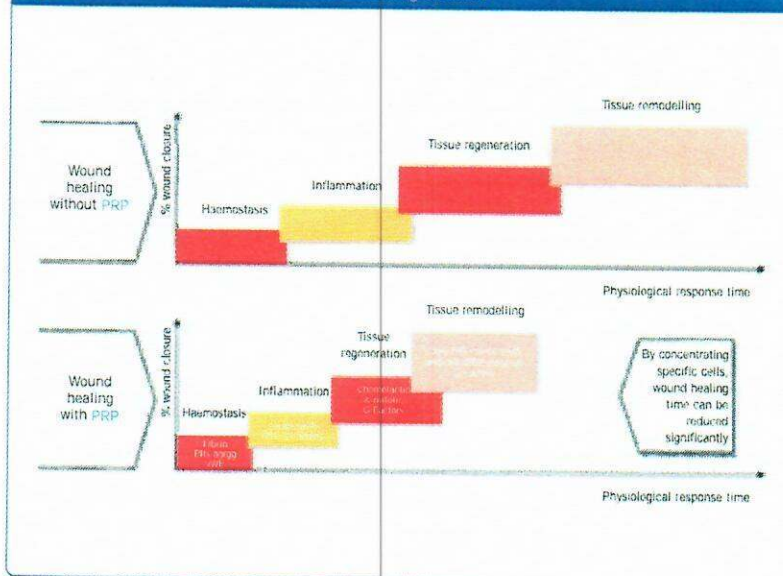


Figure 3: Visible effect in time on healing and discomfort (randomised study US)

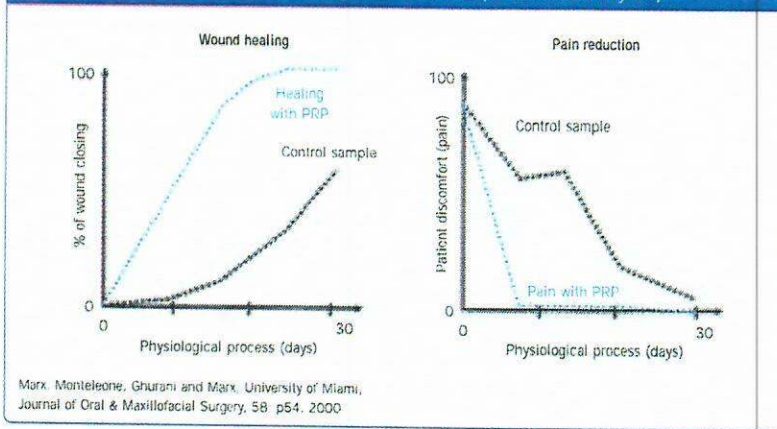
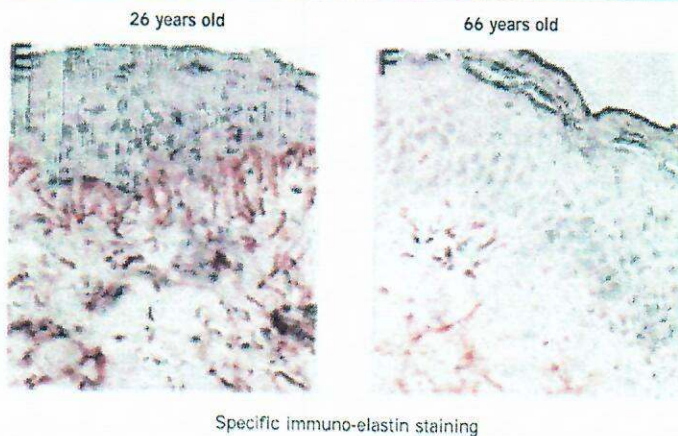


Figure 4: What happens when we get older?



Figure 5: Elastolysis: degeneration of elastic fibres



be actively secreted by platelets to initiate all wound healing. PRP includes three blood proteins known for acting as cell adhesion molecules: fibrin, fibronectin and vitronectin. Because all constituents retrieved in PRP are autologous in origin, the risk of a local immunological reaction is ruled out.

The preparation of the PRP required for treatments is simple, rapid and

advantageous. When we inject the PRP into the skin, we increase the rate of healing and tissue restructuring. Let's have a look at the physiology of the healing process:

- During the ageing process, the body reacts with a series of repairing steps. The healing cascade that we can see during any injury of the skin shows that there are specific

components of blood plasma, such as thrombocytes and leukocytes, which play an important role in every phase of tissue regeneration

- The leukocytes and the activated platelets begin to release signalisation proteins (chemiokines), which promote the migration of the macrophages from the conjunctive tissue
- The macrophages have to clean up to start tissue regeneration

The alpha granules of the activated thrombocytes release more and more growth factors, inducing the migration and the proliferation of non-differentiated mesenchymal cells. These stem cells become cells with specific functions. The leukocytes also release a growth factor (VEGF), which induces the creation of new blood vessels (angiogenesis).

Adhesion molecules, polypeptides, enzymes, vitamins and oligo-elements retrieved in the plasma, show a crucial role in the recruitment and the differentiation of stem cells. These molecules are necessary to support the high level of metabolism associated with these activated cells.

In Figure 3 we can see how the wound healing process has been shortened thanks to the PRP, and the pain reduction with PRP treatment.

In Figures 4 and 5, we can see the differences of structure in the papillary dermis, and specifically the degeneration and the lack of the elastic fibres responsible for elastolysis. At the same time, we have degradation via metalloproteinase-1, which is induced by UV light and smoking.

FIVE MAJOR STEPS IN THE ACR REGENERATION PROCESS

Intra dermal and hypodermal injections of autologous cellular rich plasma acts as a bio-scaffold which comprises a 'structure and signals' process including:

- Formation of a tri-dimensional fibrin network

- Release of growth factors by thrombocytes and leucocytes in their biologically determined ratios
- Chemo-attraction of macrophages and stem cells
- Stem cell proliferation (mitosis)
- Stem cell differentiation

THE ADVANTAGES OF THE AUTOLOGOUS CELL REGENERATION THERAPIES

There are distinct advantages of ACR therapies today for patients and doctors:

- Autology: no allogenic (donor) treatment
- Tissue regeneration and rejuvenation
- Safety: non-allergenic and free from concerns over transmissible diseases such as HIV, Hepatitis B & C, CJD and so on

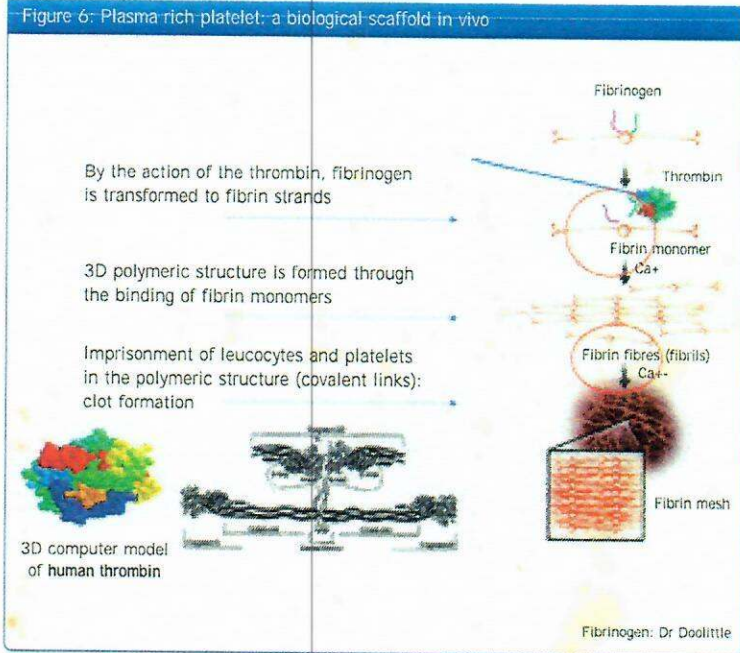


Figure 7: Ultra micro photo of a mesh

Dr Susan Lim



Figure 8: *In vivo* biologic scaffold – 'structure and signals' (1)

