

## Influence of Single Nucleotide Polymorphisms on the Efficacy of Platelet-Rich Plasma in the Treatment of Injuries

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### Single Nucleotide Polymorphisms in Platelet-Rich Plasma

Tissue repair in musculoskeletal injuries is often a slow and sometimes incomplete process. Musculoskeletal injuries have a great impact on athletes' especially elite athletes – and a rapid recovery of full efficiency and return to competition is of primary importance. The search for a minimally invasive treatment of these injuries is of great importance, especially in the world of sports.

The use of growth factors is thought to be useful in clinical practice because it promotes rapid healing with a high-quality tissue and allows a nearly and safe return to unrestricted activity. Platelet-rich plasma (PRP) is a simple and minimally invasive way to obtain a natural concentration of autologous growth factors, including IGF, EGF, TGFb1, and FGF2.

PRP is currently being widely experimented in different fields of medicine due to its ability to help in the regeneration of tissue with low healing potential. Since PRP was first introduced as topical adjuvant therapy to treat chronic ulcers in the late 1980s [1], its use has been extended to many fields of medicine, such as dermatology, ophthalmology [2], dentistry [3] and maxillofacial surgery [3]. Recently, PRP injections have emerged as a fashionable non-invasive treatment also in sports medicine [4], where they are used to treat acute or chronic tendinopathy [5-8] and muscle [9,10] and ligament [11,12] injuries, because PRP provides numerous growth factors needed to promote the healing process and an analysis of the literature reveals a lack of solid evidence supporting the use of PRP [13].

The analysis of the literature shows promising preclinical results but contradictory clinical findings in individual response to treatment in sports injuries.

These contradictions could be due to inter individual differences in the presence of single nucleotide polymorphisms (SNPs) in genes related to PRP and/or their receptors. These SNPs can determine a greater or lesser response to treatment and consequently a shorter or longer recovery time.

In recent years there has been increasing research into genes related to the healing of soft tissue. SNPs in genes that codify for these growth factors could influence treatment effectiveness and explain differences observed in recovery times.

Future studies have to focus on examine the maximum possible number of SNPs in PRP-related genes (or their receptors) in order to identify a gene signature that promotes tissue healing and in order to determine an objective measurement of an individual's predisposition to recovery after this kind of treatment (Table 1).

Candidate Growth Factors
Insulin-like growth Factor (IGF-1)
Transforming growth factor b1 (TGFb1)
Endothelial growth factor (EGF)
Fibroblast growth factor (FGF)
Platelet -derived growth factor (PDGF)

Table 1: Best genes linked to PRP or their receptors.

Nowadays, the use of PRP treatment has increased in a somewhat random manner without real knowledge of its effectiveness, since contradictory results have been reported.

Some growth factors (BMP-2, TGF and FGF) have been proven to enhance the tendon-bone healing process related to ACL injuries, *in vitro* [14] and graft remodelling and moderation may be accelerated by actions of PDGF, TGF-b1 and IGF-1 [15]. The addition of platelet concentrates to ACL reconstruction may have a beneficial effect on graft maturation and could improve it by 20-30% on average, but with substantial variability, despite there is currently insufficient evidence to support the routine use of PRP for treating ACL injuries [16].

The addition of PRP to a collagen hydrogel resulted in a significant increased cellular metabolic activity, reduced apoptotic rate and stimulation of collagen production in the cells from the immature and adolescent animals ( $p < 0.05$ ) but had less of an effect on adult cells. Maturity may influence the response to PRP [17].

Scientists should provide a tool to identify the individuals and injuries most likely to benefit from PRP treatment and thus improve not only recovery time but also *restitutio ad integrum* by reducing the risk of re-injury.

Further studies of these SNPs may shed light on the tendency of certain individuals to recover more rapidly and more completely from injuries and may help identify individuals with an enhanced injury repair system.

That is the cornerstone to classify patients within "good or bad responders".

Despite the wide use of PRP injections, research into their clinical efficiency is still in its infancy, and more studies are required to confirm preliminary results and provide stronger scientific evidence [18].

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