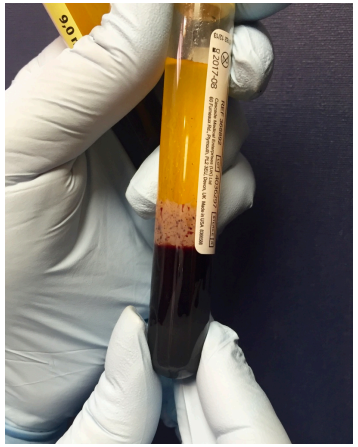
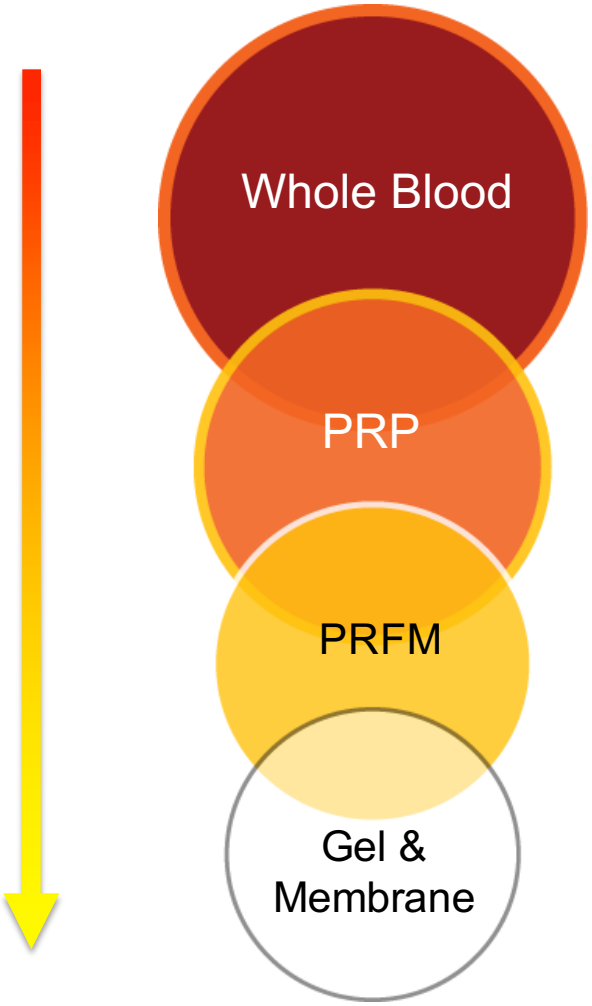
SELPHYL® Overview

SELPHYL®

- FDA Cleared Medical Device with CE Mark (EU)
- Kit allows physician to:
  - Draw a small amount of blood
  - Spin to make PRFM (platelet-rich fibrin matrix)
  - Prepare for injection
- Procedure takes <30 minutes from start to finish
- Best-in-Class Technology in Regenerative Medicine



Selphyl Platelet-rich Fibrin Matrix



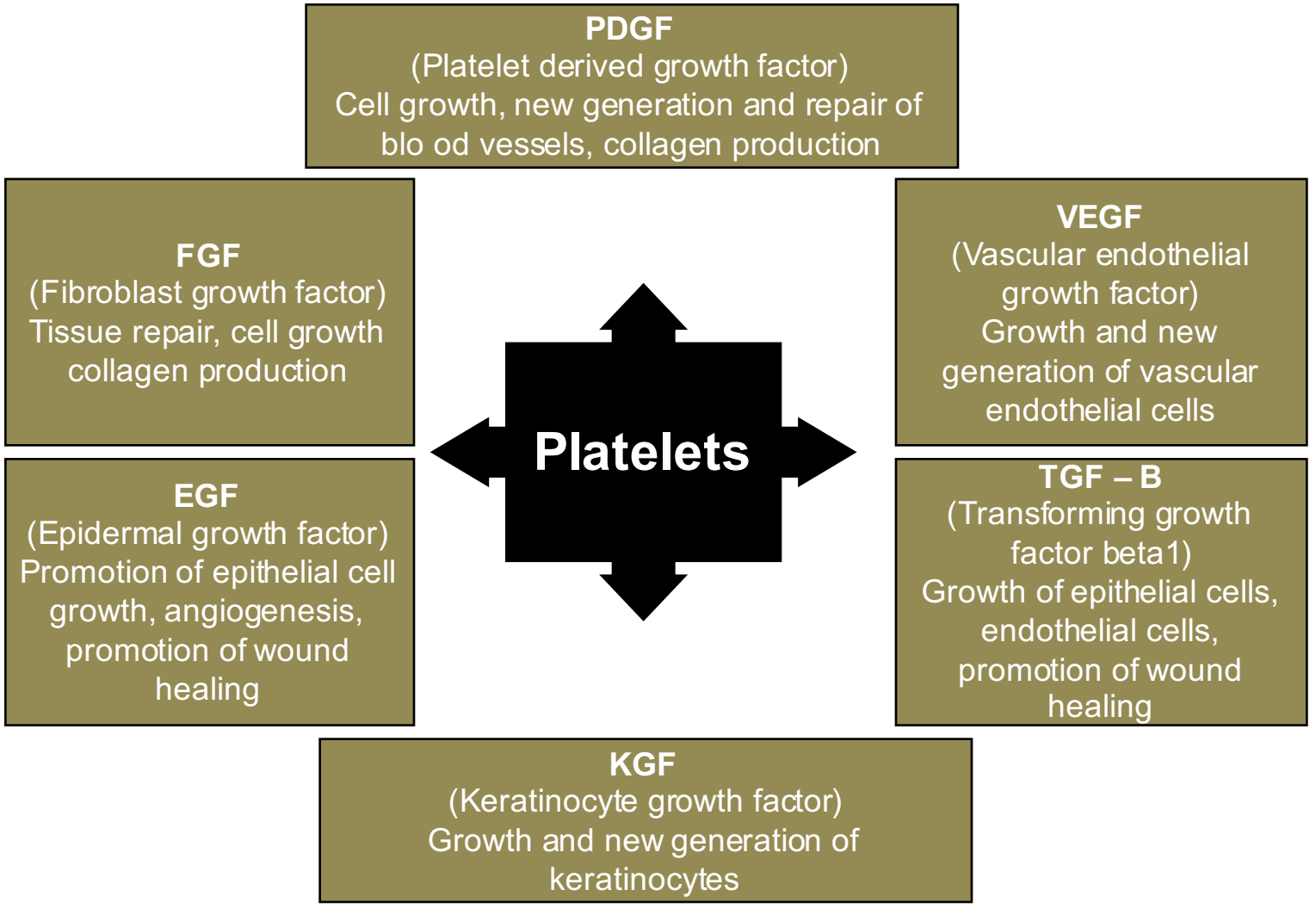
Blood performs numerous functions exquisitely

Competitors - rbc and wbc contamination

Selphyl® - removes almost all rbc and wbc; fibrin matrix

Selphyl® Product Enhancements

Platelets Release Growth Factors



Platelets and Fibrin Matrix

Platelets release growth factors

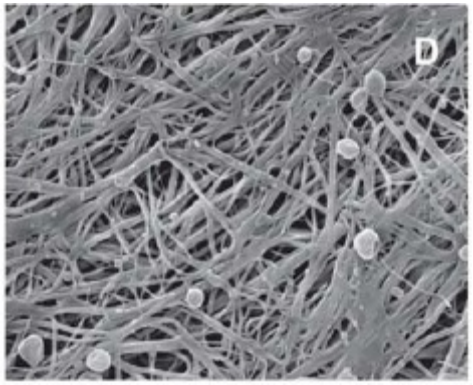
Angiogenesis stimulated

New blood vessels

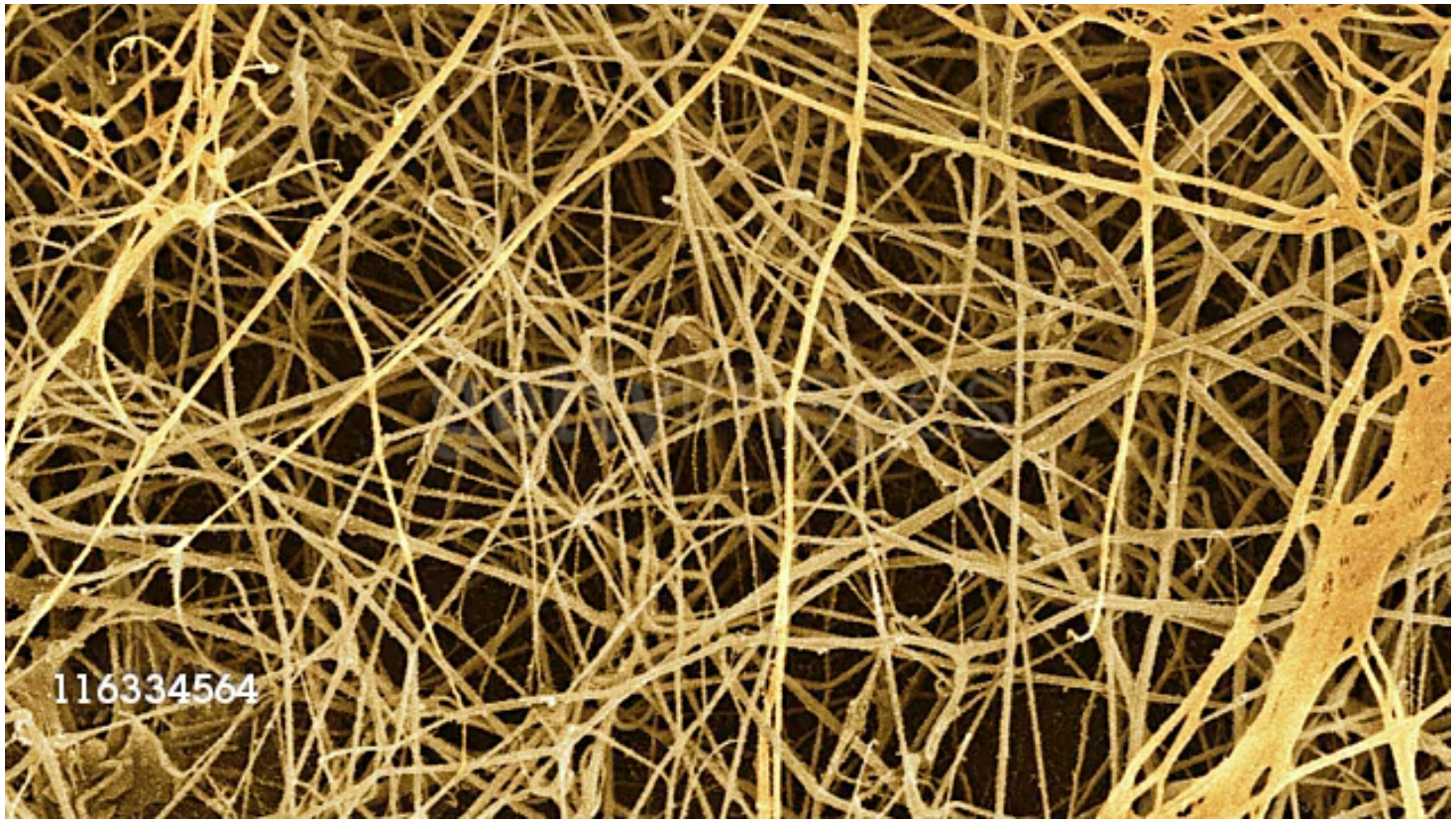
Fibroblast & Stem Cell Migration

Fibrin Matrix

Scaffold to support sustained GF release



Fibrin Matrix Scaffold



PRFM Superior to PRP

Platelet-rich fibrin (PRF): A second-generation platelet concentrate. Part II: Platelet-related biologic features

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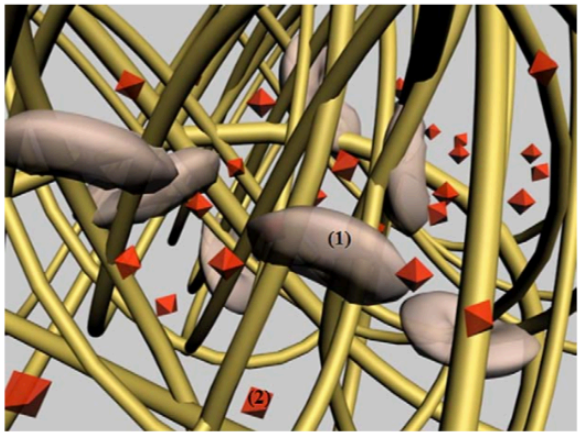
Nice and Paris, France, Los Angeles, Calif, and Göteborg, Sweden
NICE UNIVERSITY, UNIVERSITY OF PARIS V, UNIVERSITY OF PARIS VI, UNIVERSITY OF SOUTHERN CALIFORNIA, AND GÖTEBORG UNIVERSITY

Platelet-rich fibrin (PRF) belongs to a new generation of platelet concentrates, with simplified processing and without biochemical blood handling. In this second article, we investigate the platelet-associated features of this biomaterial. During PRF processing by centrifugation, platelets are activated and their massive degranulation implies a very significant cytokine release. Concentrated platelet-rich plasma platelet cytokines have already been quantified in many technologic configurations. To carry out a comparative study, we therefore undertook to quantify PDGF-BB, TGFβ-1, and IGF-I within PPP (platelet-poor plasma) supernatant and PRF clot exudate serum. These initial analyses revealed that slow fibrin polymerization during PRF processing leads to the intrinsic incorporation of platelet cytokines and glycanic chains in the fibrin meshes. This result would imply that PRF, unlike the other platelet concentrates, would be able to progressively release cytokines during fibrin matrix remodeling; such a mechanism might explain the clinically observed healing properties of PRF. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:E45-50)**

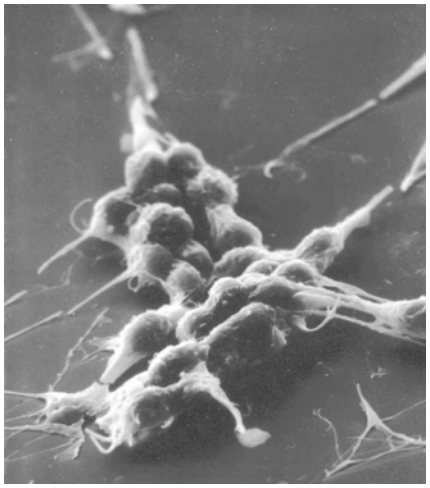


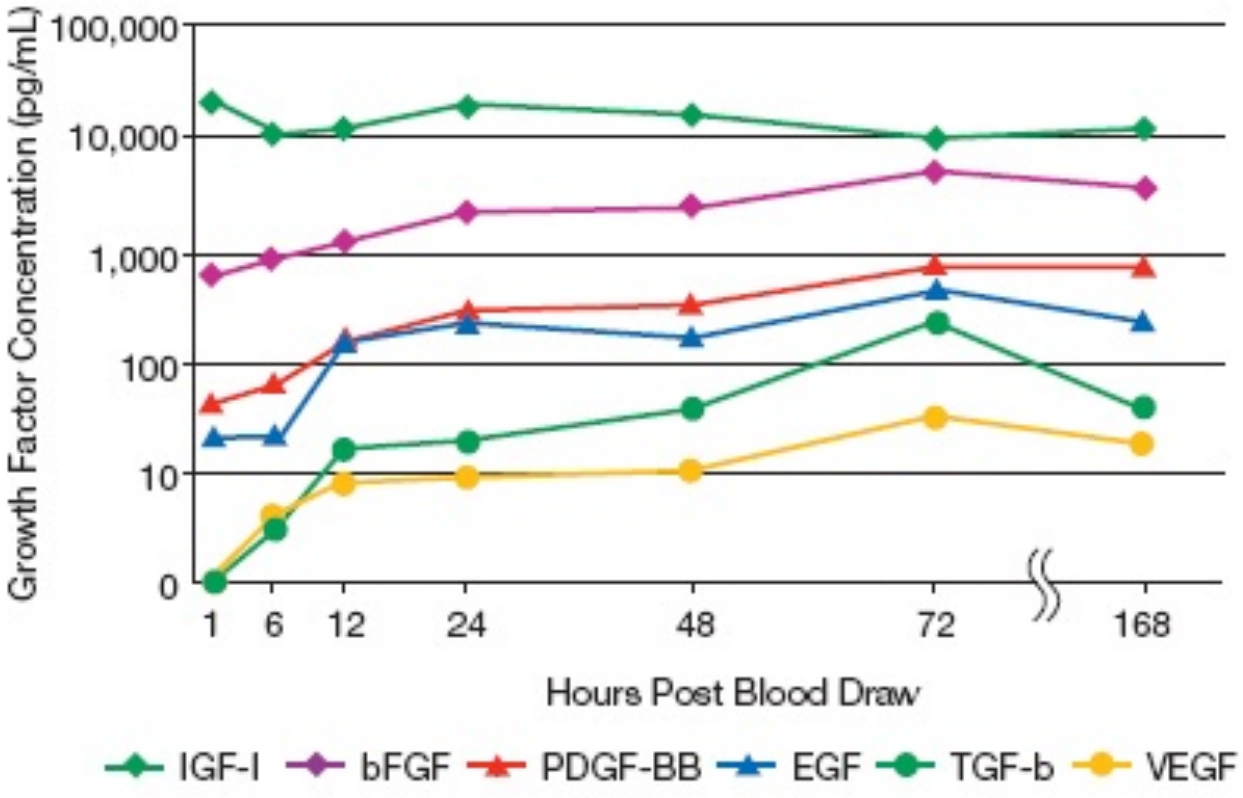
Platelets (1) release significant amounts of growth factors (2) while retained in fibrin matrix

Fibrin Matrix is Key:

- Calcium chloride allows for controlled fibrin polymerization
- Scaffold is a biologic connector that supports stem cell migration
- Platelet remain viable and localized
- Sustained cytokine/growth factor release

Sustained Growth Factor Release





Optimal Platelet Concentration
2-3X Baseline

In Vitro, Animal and Human Studies

Physiologic Range is Better Than Pharmacologic Range [Wound Healing, Bone, Spinal Cord Injury]

"Those methods with lower concentrations of platelets – 1 to 3 times baseline – showed more robust healing rates than those with higher concentrations 3 to 8 times baseline."
Rappl LM et al., Int Wound J 2011; 8:187-195

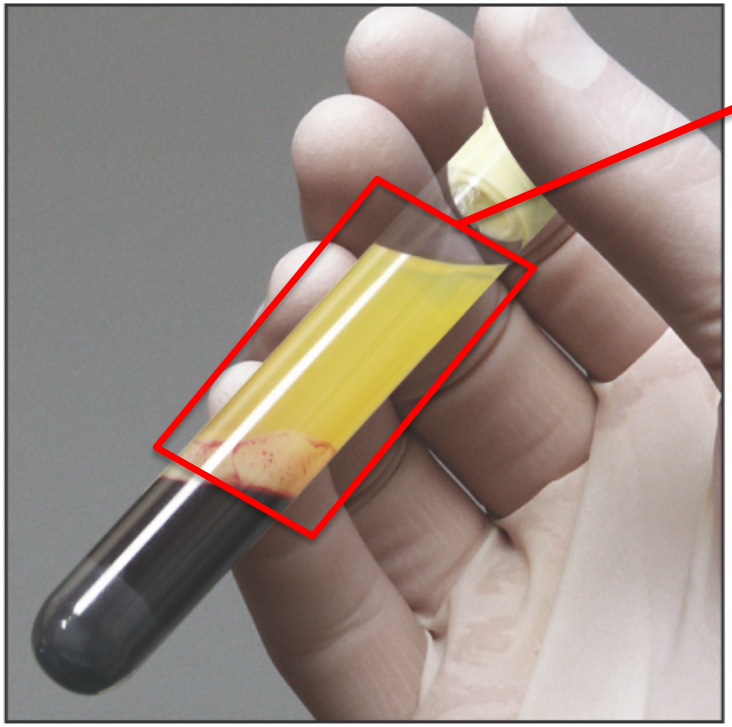
"the use of highly concentrated platelet preparations appeared to have an inhibitory influence…reasons could be unwanted inhibitory and cytotoxic effects of growth factors at such high concentrations."
Weibrich G et al., Bone 2004; 34:665-671

"PRP might exert positive effects…in a dose-dependent manner up to a certain level, but adverse effects occur when it is highly concentrated."
Yamaguchi R et al., J Surg Res 2012; 173(2): 258-266

"Optimal results were observed at a platelet concentration of 2.5 X…increased concentrations resulted in a reduction in proliferation and a suboptimal effect on osteoblast function."
Graziani F et al., Clin Oral Impl Res 2006; 17: 212-219

Best-in-Class Technology

Platelet-rich Fibrin Matrix for Tissue Regeneration



- Superior Technology
- “Golden” visual guide to quality
- Purest PRP
- Closed-System
- Fibrin Matrix scaffold
- Viable platelets
- Sustained growth factor release

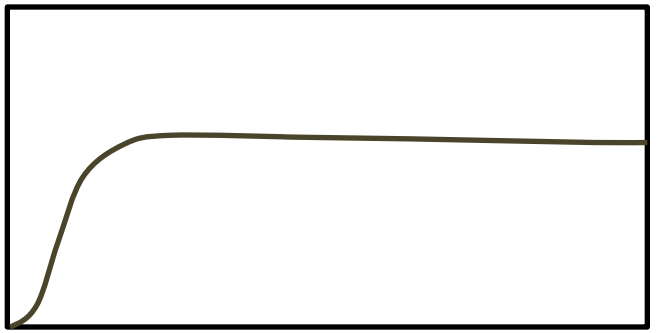
PRFM - Next Generation PRP

PRP

- Platelets in plasma
- Activation is immediate
- Alpha granules release growth factors quickly (bolus)
- Short-term tissue signaling
- Minutes - hours

PRFM

- Platelets in fibrin matrix
- $CaCl_2$ binds to Na Citrate 1:1
- Clotting cascade resumes (Fibrinogen - Fibrin)
- Platelets remain viable with controlled GF release
- hours - days



Wound Repair and Regeneration

Platelet-rich fibrin matrix improves wound angiogenesis via inducing endothelial cell proliferation

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Comprehensive Wound Center, Department of Surgery, Davis Heart and Lung Research Institute, The Ohio State University Medical Center, Columbus, Ohio

Wound Rep Reg (2011) 19 753–766

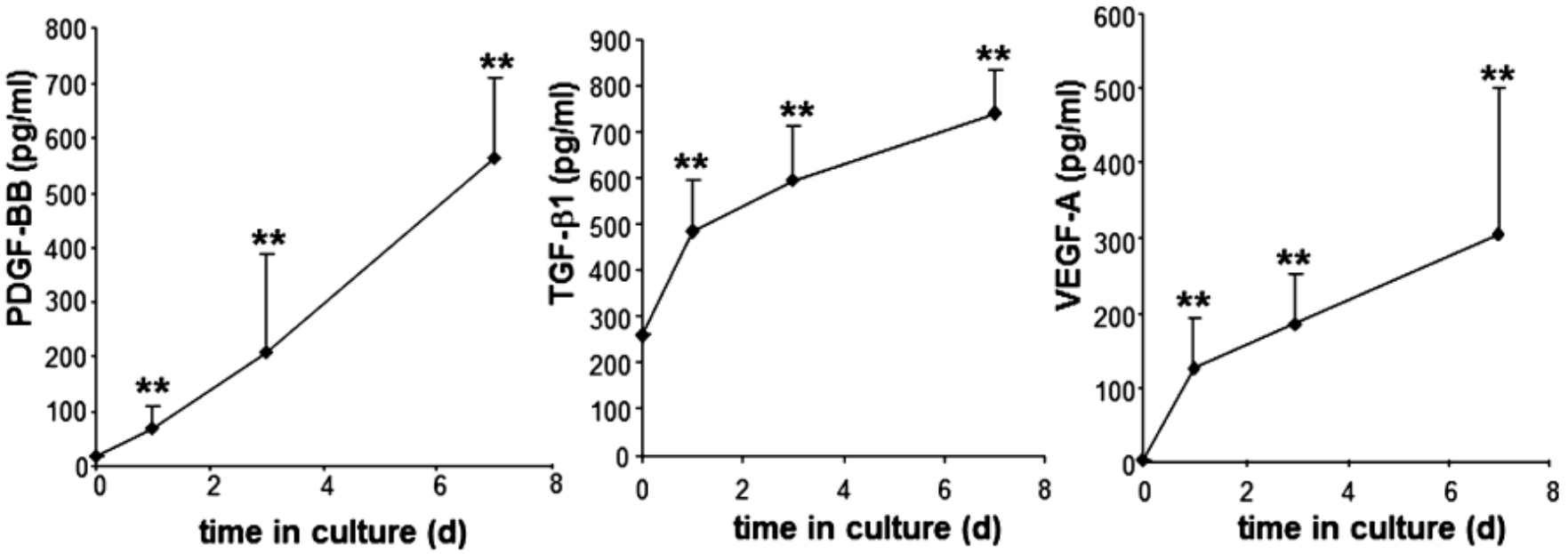

Figure 2. Release of growth factors from platelet-rich fibrin matrix (PRFM) in culture. PRFM was prepared and placed in 6-well culture plates with RPMI 1640 media. Growth factors (platelet-derived growth factor [PDGF-BB], transforming growth factor [TGF]-β1, and vascular endothelial growth factor [VEGF-A]) released in media were measured using enzyme-linked immunosorbent assay. Data shown are actual growth factor levels (ng/mL) in media bathing PRFM. Data are mean ± standard deviation ($n = 10$ for PDGF and $n = 5$ for VEGF and TGF-β1); $^{**}p < 0.01$ compared to 0 hour (baseline) sample.

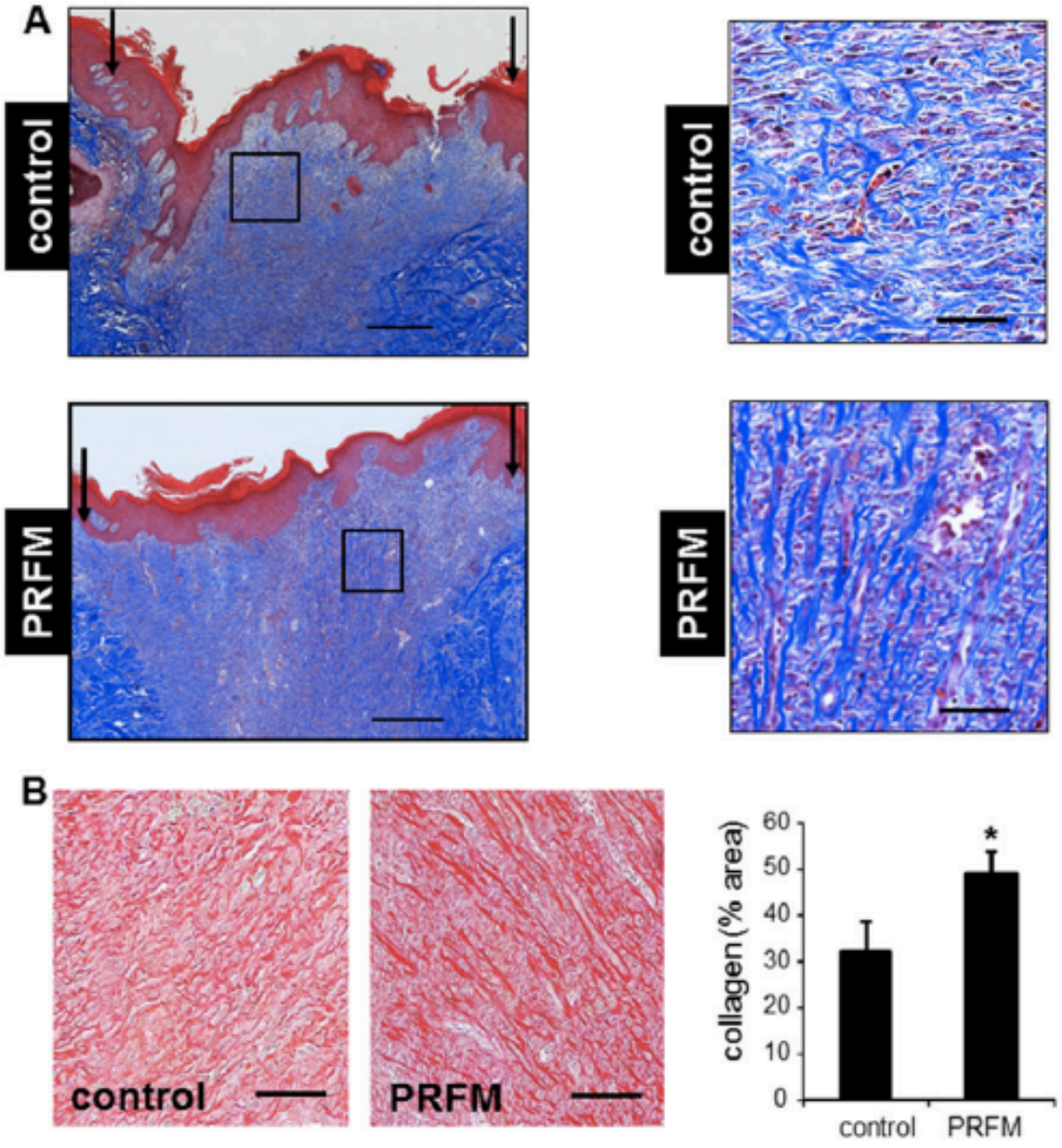

Figure 7. Ischemic wound histology following treatment with platelet-rich fibrin matrix (PRFM) membranes. Wound-edge tissues were collected on 14 days post-wounding. Formalin-fixed paraffin-embedded biopsy tissues were sectioned (5 µm) and stained using (A) Masson's trichrome staining. This staining results in blue-black nuclei, blue collagen, and cytoplasm. Epidermal cells appear reddish. The arrows indicate the start and the end of wound. Scale bar = 500 µm. Right panels are the zoom of boxed area of images shown in left panel. Scale bar = 50 µm. (B) Picrosirius red staining. The red staining is the birefringence of collagen fibers, which is largely due to co-aligned molecules of type I collagen. Bar graph shows quantitation of the collagen fibers in PRFM-treated or -untreated wounds. Scale bar = 50 µm. Data are mean ± standard deviation ($n = 3$); $^*p < 0.05$ compared to untreated wounds.

Growth Factor-Rich Plasma Increases Tendon Cell Proliferation and Matrix Synthesis on a Synthetic Scaffold: An *In Vitro* Study

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Andreas Kern, Ph.D.,[2] Anthony Ratcliffe, Ph.D.,[2] and Keri L. Gardner, M.S.[1]

TISSUE ENGINEERING: Part A
Volume 16, Number 3, 2010

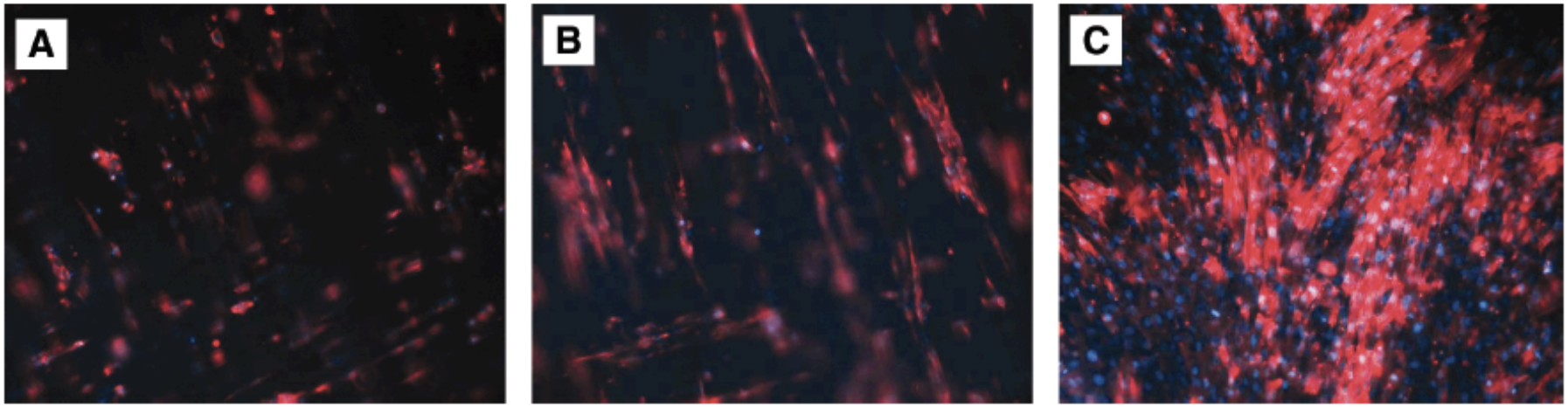

FIG. 3. Representative photomicrographs of the cell-seeded surface of a control (**A**) serum-enriched (**B**) and GFRP-enriched (**C**) scaffold stained with rhodamine phalloidin and DAPI after 24 h in culture. Note the dramatic increase in cell density of the GFRP-enriched scaffold compared with the other groups. Color images available online at www.liebertonline.com/ten.

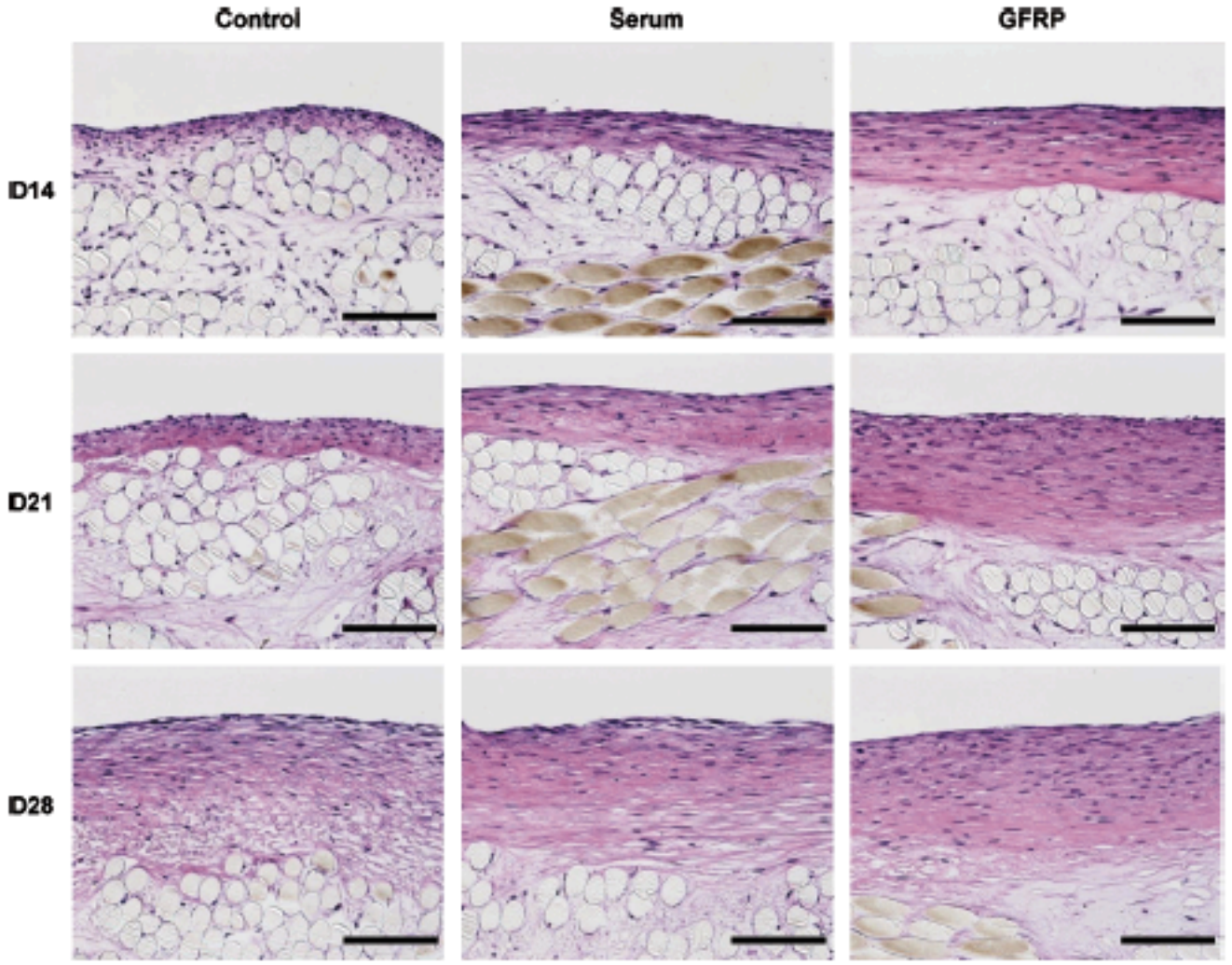

FIG. 5. Photomicrographs of representative transected scaffolds stained with hematoxylin and eosin from each group after 14, 21, and 28 days in culture. Note the relative differences in the surface tissue thickness at each time point. Scale bar = 100 μm. Color images available online at www.liebertonline.com/ten.

New Look & Product Photos