Young Plasma vs PRP

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PRP is defined as an autologous preparation of platelets in a small volume of plasma. Using the plasma of older patients to provide their healing is suboptimal as opposed to injecting young plasma with young growth factors.

Mechanism

Following aggregation and activation in response to vascular injury, platelets aid in tissue healing and regeneration by releasing GFs and other proteins that are stored in a-granules of platelets.

Growth Factors released by platelets that are thought to participate in healing processes:

Category	Proteins	Function
Adhesive proteins	Von Willebrand factor, fibrinogen, fibronectin, vitronectin, lamminin-8	Cell interaction, hemostasis, composition of extracellular matrix
Coagulation factor and associated proteins	Factor V/Va, multimerin, protein S, high-molecular weight kininogen, antithrombin III, tissue factor pathway inhibitor	Thrombin production and regulation
Fibrinolytic factors and associated proteins	Plasminogen, α-2 antiplasmin, histidine-rich glycoprotein, α-2 macroglobulin	Plasmin production and vascular remodeling
Proteases and antiproteases	Ttissue inhibitors of metalloproteases 1-4 (TIMP 1-4), metalloproteases 1, 2, 4, 9, C1 inhibitor, α-1 antitrypsin	Angiogenesis, vascular modeling, coagulation regulation
Growth factors	PDGF, TGF-β 1 and 2, EGF, IGF-1, VEGF, bFGF, HGF, BMP-2, 4, 6, CTGF	Chemotaxis, cell proliferation and differentiation, angiogenesis
Chemokines, cytokines, and others	IL8, FasL, endostatins, osteonectin, bone sialoprotein	Regulation of angiogenesis, vascular modeling, cell interactions, bone formation
Antimicrobial proteins	Thrombocidins	Bactericidal and fungicidal properties
Membrane glycoproteins	Most of the components of the plasma membrane	Platelet aggregation and adhesion, protein endocytosis, inflammation, thrombin generation, platelet-leukocyte interactions
Others	Chondroitin 4 sulfate, albumin, immunoglobulins, semaphoring	Promote angiogenesis, cartilage regeneration, fibrin production, and platelet adhesion

https://www.sciencedirect.com/science/article/pii/S1578219014003357

Data indicates that that cell proliferation and migration of the oxidative stress-induced senescent vascular smooth muscle cells are desensitized to stimulation by platelet-derived growth factor (PDGF)-BB. These findings indicate that the milieu or the “exposome”(what completely bathes the vascular tissues) are of extreme importance if musculoskeletal damage is going to be reversed and healed.

Endothelial Cells from the brain, liver, and visceral fat illustrated an accelerated ageing cell types suggesting that continuous and direct exposure to the aged circulatory system induces strong transcriptomic changes. Endothelial Cells across all tissues seem susceptible to blood-borne influences and young plasma reversed aspects of ageing, especially in capillary endothelial cells. (1).

Using "Older" plasma to heal injuries has had inconsistent results since the necessary growth factors decrease with statistical significance in aging. The study below illustrates a significant drop in the number of growth factors important in the joint healing process.

TABLE IV. Growth Factor Concentrations as a Function of Age. *t*-Test was Carried Out for ≤25 Years Old Versus >25 Years Old Concentrations of EGF, HGF, PDGF-AB, PDGF-BB, and TGFβ-1. Mann–Whitney Rank-Sum Test was Carried Out for ≤25 Years Old Versus >25 Years Old Concentrations of IGF-1 and VEGF

Growth Factor	Age[a]	Mean	SD	*T* Value	*p*	Effect Size	Power
EGF pg/mL	≤25 (*N* = 64)	187.6	60.3	2.31	<0.05*	0.46	0.61
	>25 (*N* = 38)	159.2	59.8				
HGF pg/mL	≤25 (*N* = 64)	136.3	50.4	0.75	>0.05	0.15	0.11
	>25 (*N* = 37)	128.1	56.8				
IGF-1 pg/mL	≤25 (*N* = 60)	85065.0	22993.5	317[b]	<0.001*	0.61	
	>25 (*N* = 38)	56787.8	12225.7				
PDGF-AB pg/mL	≤25 (*N* = 64)	7657.1	2637.5	3.69	<0.001*	0.77	0.96
	>25 (*N* = 38)	5767.0	2246.7				
PDGF-BB pg/mL	≤25 (*N* = 62)	1970.6	773.2	2.00	<0.05*	0.41	0.51
	>25 (*N* = 38)	1652.3	769.3				
TGFβ-1 pg/mL	≤25 (*N* = 64)	8715.5	2901.1	2.32	<0.05*	0.44	0.57
	>25 (*N* = 38)	7483.2	2682.9				
VEGF pg/mL	≤25 (*N* = 63)	76.6	55.9	892[b]	>0.05	0.19	
	>25 (*N* = 37)	54.1	45.9				

*$p < 0.05$. [a]Mean age (SD) for ≤25 group is 20.5 (2.1); for >25 group is 36.0 (8.6); *N* = 64, 38, respectively. [b]Mann–Whitney rank-sum test.

(https://pubmed.ncbi.nlm.nih.gov/25003868/)

Platelet Derived Growth Factor – BB decreases significantly across age:

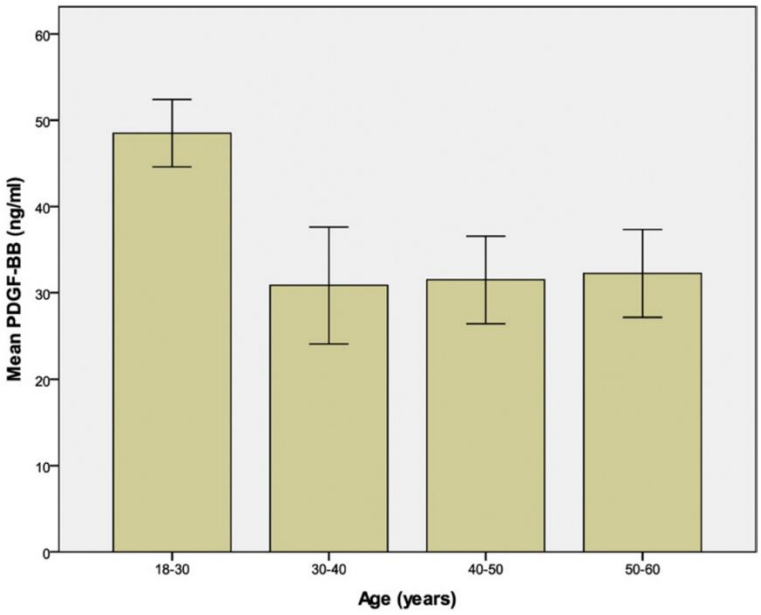

Figure 1 Bar graph of PDGF-BB by age. The error bars represent the standard error of the mean (SEM).

Table 2 Summary Statistics Including Correlation With Age for all 10 Analytes

Analyte	18-30 Years	30-40 Years	40-50 Years	50-60 Years	Correlation with Age	*P* Value
BMP-2 (pg/mL)	270 (±25)	326 (±81)	308 (±63)	235 (±38)	−0.088	0.587
BMP-4 (pg/mL)	361 (±92)	361 (±114)	146 (±41)	240 (±43)	−0.302	0.058
bFGF-2 (ng/mL)	9.56 (±4.3)	5.23 (±1.5)	2.95 (±0.73)	7.48 (±4.2)	−0.044	0.786
hGH (ng/mL)	2.18 (±0.68)	0.57 (±0.28)	5.91 (±4.57)	0.97 (±0.36)	−0.073	0.653
IGF-1 (μg/mL)	13.2 (±8.1)	2.69 (±1.3)	1.12 (±0.57)	0.27 (±0.06)	−0.457	0.003[a]
IGFBP-2 (ng/mL)	163 (±56)	87 (±20)	201 (±25)	118 (±25)	0.106	0.513
IGFBP-3 (ng/mL)	752 (±84)	287 (±95)	401 (±97)	363 (±77)	−0.443	0.004[a]
PDGF-BB (ng/mL)	48.5 (±3.9)	30.8 (±6.7)	31.5 (±5.0)	32.2 (±5.1)	−0.519	0.001[a]
TGF-β (ng/mL)	22.5 (±11)	76.8 (±33)	47.0 (±24)	72.7 (±28)	0.117	0.471
VEGF (ng/mL)	1.69 (±0.21)	2.46 (±0.79)	1.73 (±0.23)	1.87 (±0.25)	0.0.95	0.561

BMP-2, bone morphogenetic protein; BMP-4, bone morphogenetic proteins; bFGF-2, basic fibroblast growth factor 2; hGH, human growth hormone; IGF-1, insulin-like growth factor 1; IGFBP-2, insulin-like growth factor-binding protein 2; IGFBP-3, insulin-like growth factor-binding protein 3; PDGF-BB, platelet-derived growth factor BB; TGF-β, transforming growth factor beta 1; VEGF, vascular endothelial growth factor.

The values represent the mean (± standard error of the mean).

The Spearman correlation is listed along with its *P*-value.

[a]Denotes statistical significance after Bonferroni multitest correction.

https://www.researchgate.net/publication/257467546_Age-Related_Changes_of_Chondrogenic_Growth_Factors_in_Platelet-Rich_Plasma

Young Fresh Frozen Plasma is Superior to PRP

Young plasma benefits—excerpts from the Wyss-Coray lab at Stanford:

Intriguingly, we observed an almost universal loss of gene expression with age…aged blood reduces global gene expression, and young blood restores it.

- Immune cell accumulation in adipose depots is a fundamental feature of ageing, and indeed most types, including T cells, B cells, neutrophils, and plasma cells, accrue across diverse organs

- 1,000 hematopoietic stem cells genes are altered by young blood, perhaps indicating a tight-knit relationship between ageing of the immune system and changes in blood composition.

-Rejuvenation appears to be a much more concerted process: the core network of ageing rescued by rejuvenation consists of mitochondrial electron transport chain genes for multiple cell types

Young blood both reverses age-related profiles and initiates novel pathways. Systemic rejuvenation of genes encoding components of the electron transport chain is especially striking.

-young blood is a potent instigator of mitochondrial function

- mitochondrial genes arise even for cell types in which age-related decline is not evident, like marrow monocytes supporting the notion that young blood may indeed broadly enhance mitochondrial function.

Overall, these data indicate that nearly all cell types are amenable to reformation via changes blood composition, even those not directly exposed to blood.

1. Chen, M. B. *et al.* Brain Endothelial Cells Are Exquisite Sensors of Age-Related Circulatory Cues. *Cell Rep.* **30**, 4418-4432.e4 (2020). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7292569/

2. PRP a bust in placebo-controlled trial for knee OA https://www.physiciansweekly.com/platelet-rich-plasma-a-bust-in-placebo-controlled-trial-for-knee-oa

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