



CRP™ – Cytokine Rich Plasma

The Clear Advantage

CRP™

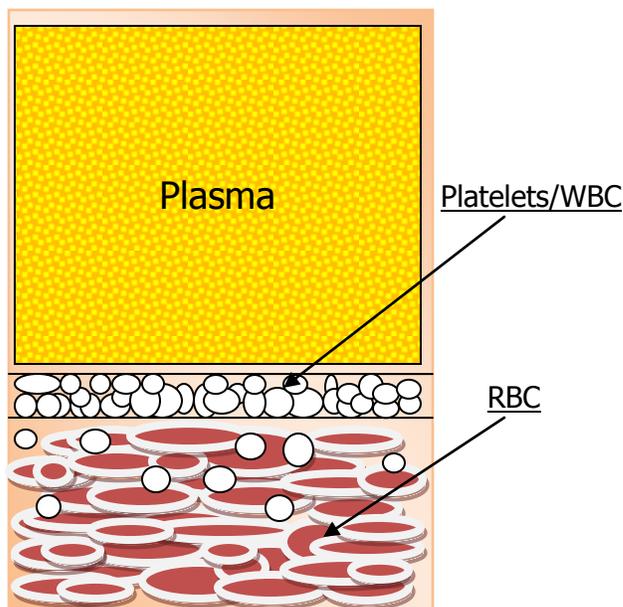
Orogen's Cytokine Rich Plasma was developed and designed to be the most efficacious Growth Factor composition on the market today. Orogen has proven through laboratory analysis and clinical outcomes that CRP™ is superior to any form of PRP currently available to healthcare providers. CRP™ is a growth factor plasma composition that arrives in an acellular form. Orogen's CRP™ eliminates all red blood cells and leukocytes, which include all inflammatory granulocytes and agranulocytes. The CRP™ device mechanically releases or extracts all growth factors or cytokines from all the platelets within a given sample of whole blood. Thus, leaving behind only ghost platelets or platelet membranes. This eliminates the need for platelet capture yields. Growth factor concentrations are 7 to 9 X baseline. Plasma protein concentrations are 2 to 3 X baseline. CRP™ also contains IL-1ra (IRAP) which is believed to aid in Osteoarthritis. The collected CRP™ sample is 8mL from 60mL of the patients' baseline whole blood. With Orogen's CRP™ system physicians can now offer the world's Richest form of growth factor technology, pure Gold cytokine rich plasma CRP™ without the inflammatory components.

No Leukocytes (White Blood Cells) or Erythrocytes (Red Blood Cells)

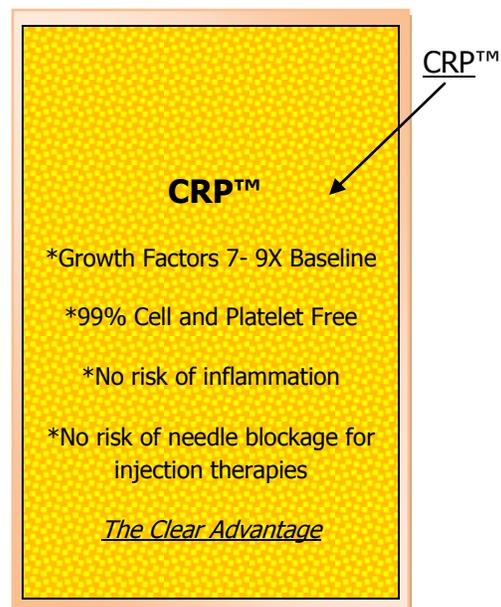
Orogen's CRP™ provides the highest level of growth factors in a pure plasma composition. It has no cells, cellular debris or platelet membranes (Ghost Platelets), making this the cleanest form of growth factor technology at the point of care. Why is this important? Red blood cells are reported to cause pain and aggravation when injected into a joint space. Additional unwanted cells and cellular debris increases the risk of needle blockage and injection resistance. Elimination of red blood cells gives the end product a very aesthetic appearance. This becomes very important in cosmetic applications such as face lifts, fillers and skin rejuvenation. The elimination of Leukocytes which include Granulocytes and some Agranulocytes can often increase healing times. Granulocytes and Agranulocytes (Neutrophils, Basophils, and Lymphocytes) in abundance will release additional cytokines that will amplify and pro-long inflammation periods. Acute inflammation periods are necessary for successful wound repair; long-term inflammation periods can be pernicious. Orogen's CRP™ is 99% cellular free, making it the cleanest growth factor composition for cosmetic application and non-inflammatory Orthobiologic injections.

PRP: RBC/WBC Differentiation

CRP™: RBC/WBC Differentiation



Volume VS. Concentration



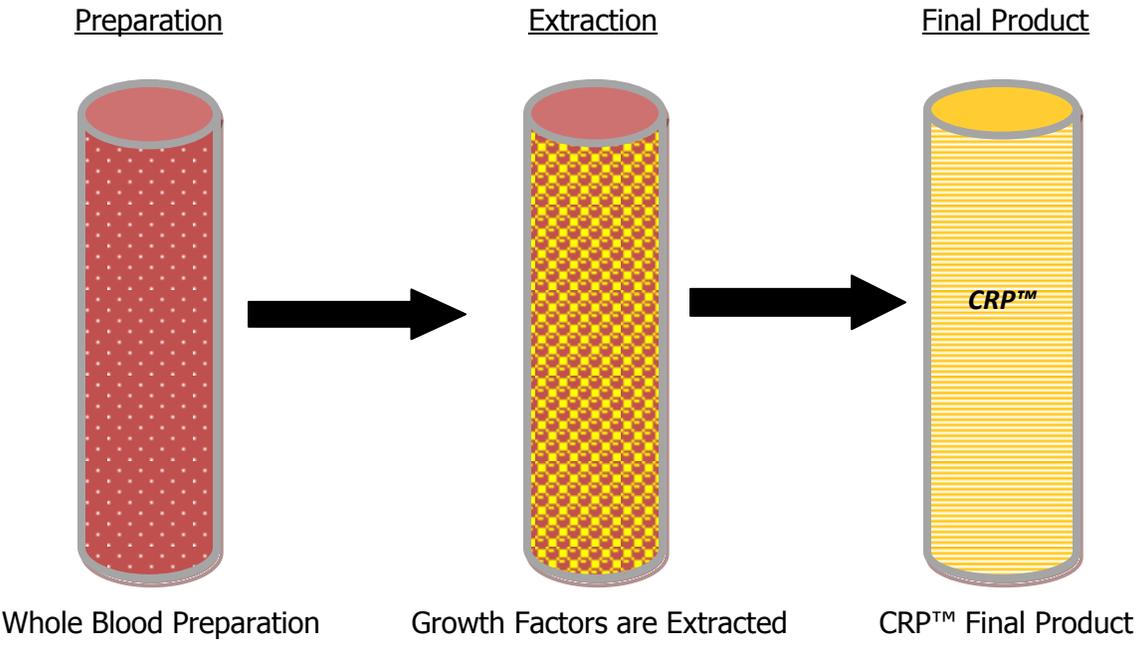
Volume VS. Concentration

****Values of differentiation reflect final end product(s) for that of patient point of care.**

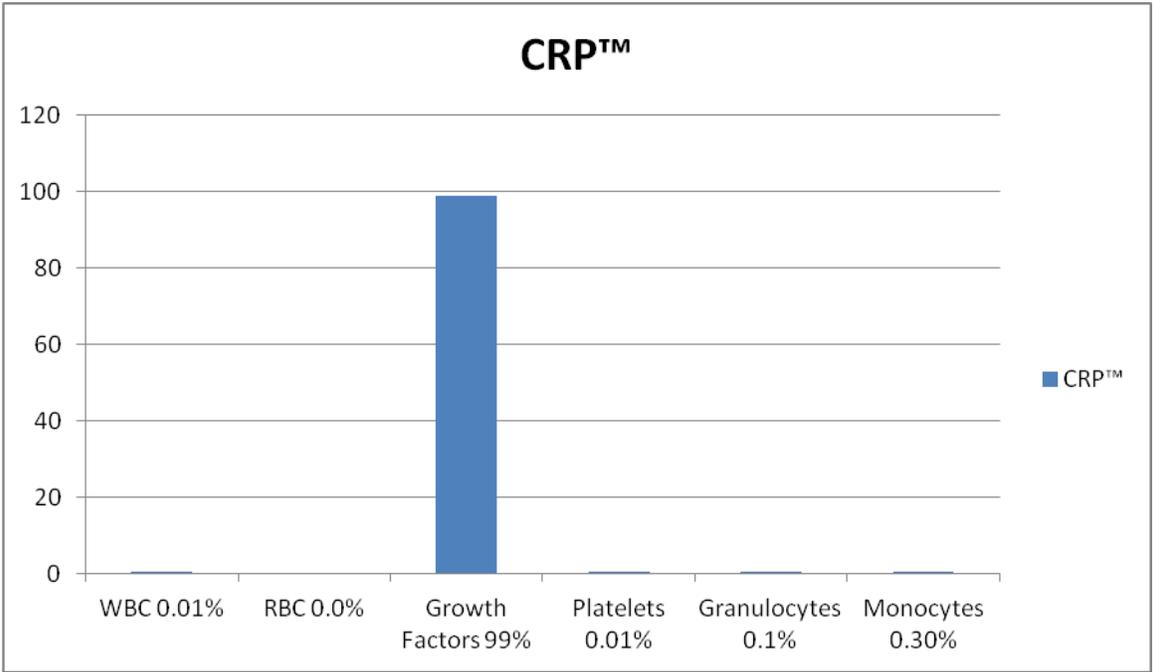
Refining the process of Growth Factor Extraction

CRP™ can only be obtained by utilizing Orogen's revolutionary Growth Factor Extraction process. The process is 100% mechanical, making this product safe and always effective. There are no additives such as Thrombin or Collagen needed to activate the platelets for release of Growth Factors/cytokines. The extraction process reaches all platelets in a given sample, even the heavy juvenile platelets. This removes the variables of platelet capture yields and human error. This process is completed in less than 12 minutes and provides the richest Growth Factor sample for clinical applications.

Refining the Process of Growth Factor Extraction CRP™



Orogen CRP™ Performance Metric – When Less Is More



Orogen CRP™ Laboratory Evaluation – Plasma

Blood was obtained from two (2) normal donors with consent. Blood collection protocols met all requirements of the AABB, FDA and CBER. Fifty (50)mL of blood was drawn from each patient into a 60mL Syringe (Terumo SS-60L) filled with 6mL of Anticoagulant Citrate Dextrose Solution (ACD-A). Blood samples were processed according to manufacturers (Orogen) instructions for processing CRP™. Approximately 8mL of CRP™ was collected. Complete ELISA Immunoassay analysis was done with third party laboratories.

Average Concentration, ug/ml	Sample ID	Fibrinogen	Fibronectin	Vitronectin
Baseline 1	1	1222.0	301.8	123.3
Baseline 2	2	1245.4	292.4	106.0
Test Sample 1	3	1602.4	767.7	198.0
Test Sample 2	4	2098.8	1182.3	264.3
By-product - H2O	5	<0.01	<0.03	<0.02

Replicate 1	Sample ID	Fibrinogen	Fibronectin	Vitronectin
Baseline 1	1	1356.5	290.6	128.6
Baseline 2	2	1394.8	284.4	112.8
Test Sample 1	3	1650.5	829.6	214.8
Test Sample 2	4	2203.8	1290.5	264.5
By-product - H2O	5	<0.01	<0.03	<0.02

Replicate 2	Sample ID	Fibrinogen	Fibronectin	Vitronectin
Baseline 1	1	1087.6	312.9	118.0
Baseline 2	2	1095.9	300.4	99.2
Test Sample 1	3	1554.4	705.7	181.1
Test Sample 2	4	1993.9	1074.1	264.1
By-product - H2O	5	<0.01	<0.03	<0.02

Discussion

The Orogen CRP™ system presents an absolute solution for growth factor technology. Plasma proteins play a very important role in the healing cascade. Plasma proteins are cellular adhesion molecules that allow cells to migrate easily to the wound site. By concentrating the levels of these proteins, it promotes rapid healing rates. To date, there has been no other point of care growth factor product that can accomplish these levels of plasma proteins.

Orogen CRP™ Laboratory Evaluation – Growth Factors/Cytokines

Analyte Concentration, pg/ml	Sample #	IL-2	PDGF-AA	TGF-b1	VEGF
Baseline 1	*1	5.9	644.3	3046.1	625.2
Baseline 2	2	2.1	362.6	2693.4	774.3
Test Sample 1	**3	230.9	2062.0	5046.3	1538.6
Test Sample 2	4	156.2	1886.3	4462.0	808.16
By-product - H2O	5	0.5	22.3	<18.3	<1.0

Replicate 1, pg/ml	Sample #	IL-2	PDGF-AA	TGF-b1	VEGF
Baseline 1	*1	6.1	737.8	2967.8	652.3
Baseline 2	2	2.1	406.9	2650.4	791.7
Test Sample 1	**3	254.6	1986.7	5181.4	1510.9
Test Sample 2	4	167.1	1860.2	4673.6	858.35
By-product - H2O	5	0.5	20.3	<18.3	<1.0

Replicate 2, pg/ml	Sample #	IL-2	PDGF-AA	TGF-b1	VEGF
Baseline 1	*1	5.8	550.9	3124.3	598.2
Baseline 2	2	2.1	318.3	2736.4	756.9
Test Sample 1	**3	207.2	2137.3	4911.2	1566.3
Test Sample 2	4	145.2	1912.4	4250.4	757.97
By-product - H2O	5	0.5	24.4	<18.3	<1.0

Discussion

Orogen's CRP™ system presents the most plausible solution for growth factor technology where growth factors (Cytokines) are released and retained to a degree that is greater to or equal than any PRP system available to health care providers. The system offers only what is necessary for rapid wound repair and discards virtually all RBC's, WBC's and platelet membranes. To date, there has been no other point of care system capable of achieving all of these components into one product. Orogen's CRP™ offers an aggressive product that can be produced within the current standard processing time. The testing from in vitro studies, intended to analyze product characterization, has demonstrated that the functional ability of the product is compatible and equivalent to predicate products in the regenerative medicine space. Orogen's CRP™ has provided consistent results with predictable growth factor yields without cells, cellular debris and inflammatory components. The Clear Advantage.



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