



Regenerative Potential of Fibroblast Secretome: Keratinocyte Growth Factor (KGF) and Total Protein Effects on Senescent Cell Proliferation via Mek 1/2 Activation and Enhanced Collagen Type 1 Utilization

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SUPPLEMENTARY DATA AND STATISTIC

Doubling Time (DT) and Cumulative Population Doubling (CPD) of Fibroblast Cells Subculture.

Passage	Harvest Cells	Seeding Cells	DT (hour)	Total day <i>in vitro</i>	CPD
P1	2.000.000	300.000	61,42	7	2,74±2,74
P2	3.675.000	250.000	43,35	14	6,61±3,88
P3	1.912.500	250.000	57,26	21	9,54±2,93
P4	2.137.500	250.000	46,54	27	12,64±3,09
P5	2.000.000	250.000	56,03	34	15,64±2,99
P6	1.625.000	250.000	62,25	41	18,34±2,68
P7	2.075.000	250.000	55,06	48	21,39±3,05
P8	1.762.500	250.000	59,66	55	24,20±2,81
P9	1.812.500	250.000	67,22	63	27,06±2,86
P10	1.312.500	250.000	60,23	69	29,45±2,39
P11	1.525.000	250.000	64,43	76	32,06±2,61
P12	525.000	250.000	157,04	83	33,13±1,09
P13	1.550.000	250.000	63,86	90	35,76±2,63
P14	1.087.500	250.000	79,25	97	37,88±2,12
P15	950.000	250.000	87,28	104	39,80±1,92
P16	800.000	250.000	100,17	111	41,48±1,68
P17	1.275.000	250.000	81,73	119	43,83±2,35
P18	587.500	250.000	116,89	125	45,06±1,23
P19	650.000	250.000	121,94	132	46,44±1,17
P20	875.000	250.000	106,29	140	48,25±1,80

Passage	Harvest Cells	Seeding Cells	DT (hour)	Total day <i>in vitro</i>	CPD
P21	437.500	250.000	178,46	146	49,05±0,80
P22	575.000	250.000	139,89	153	50,25±1,20
P23	512.500	250.000	162,32	160	51,29±1,04
P24	362.500	250.000	313,58	167	51,82±0,54
P25	400.000	250.000	247,91	174	52,50±0,68

Cell Proliferation Profile After Treatment

Cell Proliferation After Treatment at 10⁴ cells / 24 hours (cells/well)

Hari ke-	P3-D10	P24-D10	P24-S10	P24-S20	p _X	p _{XX}
1	5207,11 ± 439,04	10797,89 ± 805,67	10980,22 ± 717,88	11354,89 ± 1162,5	0,37	0,11
3	22790,00 ± 437,66	15948,33 ± 2544,7	14050,67 ± 2158,43	15028,67 ± 1748,83	0,13	0,47
5	42268,67 ± 7536,39	14637 ± 2250,57	18245 ± 2304,27	21135,67 ± 1392,89	0,18	0,05
7	64703,34 ± 2729,01	21657,5 ± 867,13	25468,75 ± 3249,12	30342,5 ± 910,41	0,17	0,02

Note: p^z = normality, p^{xx} = homogeneity.

Normality Test For Cells Proliferation Day-1

One-Sample Kolmogorov-Smirnov Test

N		20
Normal Parameters ^{a,b}	Mean	76.40
	Std. Deviation	28.214
Most Extreme Differences	Absolute	.370
	Positive	.196
	Negative	-.370
Test Statistic		.370
Asymp. Sig. (2-tailed)		.000 ^c

Note: a. Test distribution is Normal.

b. Calculated from data.

c. Lilliefors Significance Correction.

d. This is a lower bound of the true significance.

One Way Anova Test For Cells Proliferation Day-1

Descriptives proliferasi

N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		
				Lower Bound	Upper Bound	
P3-D10	5	29.40	1.342	.600	27.73	31.07
P24-D10	5	90.60	4.930	2.205	84.48	96.72
P24-S10	5	91.60	4.450	1.990	86.07	97.13
P24-S20	5	94.00	6.782	3.033	85.58	102.42
Total	20	76.40	28.214	6.309	63.20	89.60

Test of Homogeneity of Variances.

Levene Statistic			df1	df2	Sig.
proliferasi	Based on Mean		2.358	3	.110
	Based on Median		1.016	3	.412
	Based on Median and with adjusted df		1.016	3	.420
	Based on trimmed mean		2.187	3	.129

ANOVA

Proliferasi

Sum of Squares		df	Mean Square	F	Sig.
Between Groups	14757.200	3	4919.067	214.105	.000
Within Groups	367.600	16	22.975		
Total	15124.800	19			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: proliferasi

	(I) klp	(J) klp	Mean Difference (I- J)	Std. Error	Sig.	95% Confidence Interval
						Lower Bound
Bonferroni	P3-D10	P24-D10	-61.200*	3.032	.000	-70.32
		P24-S10	-62.200*	3.032	.000	-71.32
		P24-S20	-64.600*	3.032	.000	-73.72
	P24-D10	P3-D10	61.200*	3.032	.000	52.08
		P24-S10	-1.000	3.032	1.000	-10.12
		P24-S20	-3.400	3.032	1.000	-12.52
	P24-S10	P3-D10	62.200*	3.032	.000	53.08
		P24-D10	1.000	3.032	1.000	-8.12
		P24-S20	-2.400	3.032	1.000	-11.52
	P24-S20	P3-D10	64.600*	3.032	.000	55.48
		P24-D10	3.400	3.032	1.000	-5.72
		P24-S10	2.400	3.032	1.000	-6.72
Games-Howell	P3-D10	P24-D10	-61.200*	2.285	.000	-69.93
		P24-S10	-62.200*	2.078	.000	-70.05
		P24-S20	-64.600*	3.092	.000	-76.74
	P24-D10	P3-D10	61.200*	2.285	.000	52.47
		P24-S10	-1.000	2.970	.986	-10.53
		P24-S20	-3.400	3.750	.802	-15.68
	P24-S10	P3-D10	62.200*	2.078	.000	54.35
		P24-D10	1.000	2.970	.986	-8.53
		P24-S20	-2.400	3.628	.908	-14.45
P24-S20	P3-D10	64.600*	3.092	.000	52.46	
	P24-D10	3.400	3.750	.802	-8.88	
	P24-S10	2.400	3.628	.908	-9.65	

Normality Test For Cells Proliferation Day-3

One-Sample Kolmogorov-Smirnov Test

N		20
Normal Parameters ^{a,b}	Mean	106.95
	Std. Deviation	19.702
Most Extreme Differences	Absolute	.127
	Positive	.087
	Negative	-.127
Test Statistic		.127
Asymp. Sig. (2-tailed)		.200 ^{c,d}

Note: a. Test distribution is Normal.

b. Calculated from data.

c. Lilliefors Significance Correction.

d. This is a lower bound of the true significance.

One Way Anova Test For Cells Proliferation Day-3

Descriptives proliferasi

N		Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
P3-D10	5	81.60	13.297	5.946	65.09	98.11
P24-D10	5	121.20	15.320	6.851	102.18	140.22
P24-S10	5	109.60	12.818	5.732	93.68	125.52
P24-S20	5	115.40	10.621	4.750	102.21	128.59
Total	20	106.95	19.702	4.405	97.73	116.17

Test of Homogeneity of Variances

Levene Statistic			df1	df2	Sig.	
proliferasi	Based on Mean		.881	3	16	.472
	Based on Median		.465	3	16	.710
	Based on Median and with adjusted df		.465	3	14.871	.711
	Based on trimmed mean		.891	3	16	.467

ANOVA

proliferasi

Sum of Squares		df	Mean Square	F	Sig.
Between Groups	4620.550	3	1540.183	8.947	.001
Within Groups	2754.400	16	172.150		
Total	7374.950	19			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: proliferasi

	(I) klp	(J) klp	Mean Difference (I- J)	Std. Error	Sig.	95% Confidence Interval
						Lower Bound
Bonferroni	P3-D10	P24-D10	-39.600*	8.298	.001	-64.56
		P24-S10	-28.000*	8.298	.023	-52.96
		P24-S20	-33.800*	8.298	.005	-58.76
	P24-D10	P3-D10	39.600*	8.298	.001	14.64
		P24-S10	11.600	8.298	1.000	-13.36
		P24-S20	5.800	8.298	1.000	-19.16
	P24-S10	P3-D10	28.000*	8.298	.023	3.04
		P24-D10	-11.600	8.298	1.000	-36.56
		P24-S20	-5.800	8.298	1.000	-30.76
	P24-S20	P3-D10	33.800*	8.298	.005	8.84
		P24-D10	-5.800	8.298	1.000	-30.76
		P24-S10	5.800	8.298	1.000	-19.16
Games-Howell	P3-D10	P24-D10	-39.600*	9.072	.011	-68.78
		P24-S10	-28.000*	8.260	.038	-54.46
		P24-S20	-33.800*	7.611	.010	-58.45
	P24-D10	P3-D10	39.600*	9.072	.011	10.42
		P24-S10	11.600	8.933	.589	-17.21
		P24-S20	5.800	8.337	.896	-21.67
	P24-S10	P3-D10	28.000*	8.260	.038	1.54
		P24-D10	-11.600	8.933	.589	-40.41
		P24-S20	-5.800	7.444	.862	-29.83
P24-S20	P3-D10	33.800*	7.611	.010	9.15	
	P24-D10	-5.800	8.337	.896	-33.27	
	P24-S10	5.800	7.444	.862	-18.23	

Normality Test For Cells Proliferation Day-5

One-Sample Kolmogorov-Smirnov Test

N		20
Normal Parameters ^{a,b}	Mean	137.65
	Std. Deviation	21.192
Most Extreme Differences	Absolute	.176
	Positive	.176
	Negative	-.120
Test Statistic		.176
Asymp. Sig. (2-tailed)		.107 ^c

Note: a. Test distribution is Normal.
 b. Calculated from data.
 c. Lilliefors Significance Correction.

One Way Anova Test For Cells Proliferation Day-5

Descriptives proliferasi

N		Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
P3-D10	5	149.00	22.539	10.080	121.01	176.99
P24-D10	5	113.60	13.722	6.137	96.56	130.64
P24-S10	5	135.20	13.791	6.168	118.08	152.32
P24-S20	5	152.80	8.258	3.693	142.55	163.05
Total	20	137.65	21.192	4.739	127.73	147.57

Test of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.	
proliferasi		Based on Mean	3.276	3	16	.048
		Based on Median	1.562	3	16	.238
		Based on Median and with adjusted df	1.562	3	13.504	.244
		Based on trimmed mean	3.257	3	16	.049

ANOVA

proliferasi

Sum of Squares		df	Mean Square	F	Sig.
Between Groups	4713.750	3	1571.250	6.583	.004
Within Groups	3818.800	16	238.675		
Total	8532.550	19			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: proliferasi

		Mean Difference (I- J)	Sth. Error	Sig.	95% Confidence Interval	
(I) klp	(J) klp				Lower Bound	
Bonferroni	P3-D10	P24-D10	35.400*	9.771	.014	6.01
		P24-S10	13.800	9.771	1.000	-15.59
		P24-S20	-3.800	9.771	1.000	-33.19
	P24-D10	P3-D10	-35.400*	9.771	.014	-64.79
		P24-S10	-21.600	9.771	.252	-50.99
		P24-S20	-39.200*	9.771	.006	-68.59
	P24-S10	P3-D10	-13.800	9.771	1.000	-43.19
		P24-D10	21.600	9.771	.252	-7.79
		P24-S20	-17.600	9.771	.543	-46.99
	P24-S20	P3-D10	3.800	9.771	1.000	-25.59
		P24-D10	39.200*	9.771	.006	9.81
		P24-S10	17.600	9.771	.543	-11.79

	(I) klp	(J) klp	Mean Difference (I- J)	Sth. Error	Sig.	95% Confidence Interval
						Lower Bound
Games-Howell	P3-D10	P24-D10	35.400	11.801	.079	-4.29
		P24-S10	13.800	11.817	.664	-25.91
		P24-S20	-3.800	10.735	.983	-43.24
	P24-D10	P3-D10	-35.400	11.801	.079	-75.09
		P24-S10	-21.600	8.701	.138	-49.46
		P24-S20	-39.200*	7.162	.005	-63.34
	P24-S10	P3-D10	-13.800	11.817	.664	-53.51
		P24-D10	21.600	8.701	.138	-6.26
		P24-S20	-17.600	7.189	.160	-41.85
P24-S20	P3-D10	3.800	10.735	.983	-35.64	
	P24-D10	39.200*	7.162	.005	15.06	
	P24-S10	17.600	7.189	.160	-6.65	

Normality Test For Cells Proliferation Day-7

One-Sample Kolmogorov-Smirnov Test

N		20
Normal Parameters ^{a,b}	Mean	190.60
	Std. Deviation	25.918
Most Extreme Differences	Absolute	.170
	Positive	.153
	Negative	-.170
Test Statistic		.170
Asymp. Sig. (2-tailed)		.132 ^c

Note: a. Test distribution is Normal.

b. Calculated from data.

c. Lilliefors Significance Correction.

One Way Anova Test For Cells Proliferation Day-7

Descriptives proliferasi

N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		
				Lower Bound	Upper Bound	
P3-D10	5	211.80	15.498	6.931	192.56	231.04
P24-D10	5	156.80	5.357	2.396	150.15	163.45
P24-S10	5	183.00	17.986	8.044	160.67	205.33
P24-S20	5	210.80	5.119	2.289	204.44	217.16
Total	20	190.60	25.918	5.795	178.47	202.73

Test of Homogeneity of Variances

Levene Statistic			df1	df2	Sig.	
proliferasi	Based on Mean		4.620	3	16	.016
	Based on Median		1.234	3	16	.330
	Based on Median and with adjusted df		1.234	3	9.240	.352
	Based on trimmed mean		4.297	3	16	.021

ANOVA

proliferasi

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	10288.400	3	3429.467	22.176	.000
Within Groups	2474.400	16	154.650		
Total	12762.800	19			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: proliferasi

	(I) klp	(J) klp	Mean Difference (I - J)	Std. Error	Sig.	95% Confidence Interval
						Lower Bound
Bonferroni	P3-D10	P24-D10	55.000*	7.865	.000	31.34
		P24-S10	28.800*	7.865	.013	5.14
		P24-S20	1.000	7.865	1.000	-22.66
	P24-D10	P3-D10	-55.000*	7.865	.000	-78.66
		P24-S10	-26.200*	7.865	.025	-49.86
		P24-S20	-54.000*	7.865	.000	-77.66
	P24-S10	P3-D10	-28.800*	7.865	.013	-52.46
		P24-D10	26.200*	7.865	.025	2.54
		P24-S20	-27.800*	7.865	.017	-51.46
	P24-S20	P3-D10	-1.000	7.865	1.000	-24.66
		P24-D10	54.000*	7.865	.000	30.34
		P24-S10	27.800*	7.865	.017	4.14
Games-Howell	P3-D10	P24-D10	55.000*	7.333	.003	27.82
		P24-S10	28.800	10.618	.101	-5.37
		P24-S20	1.000	7.299	.999	-26.23
	P24-D10	P3-D10	-55.000*	7.333	.003	-82.18
		P24-S10	-26.200	8.393	.095	-57.93
		P24-S20	-54.000*	3.314	.000	-64.62
	P24-S10	P3-D10	-28.800	10.618	.101	-62.97
		P24-D10	26.200	8.393	.095	-5.53
		P24-S20	-27.800	8.363	.079	-59.59
P24-S20	P3-D10	-1.000	7.299	.999	-28.23	
	P24-D10	54.000*	3.314	.000	43.38	
	P24-S10	27.800	8.363	.079	-3.99	

Initial Total Protein In Medium

Medium	Total Protein (µg/ml)	p ^x	p ^{xx}
D10	5399,33 ± 180,69	0,38	0,32
S10	5154,33 ± 321,45		
S20	5830,67 ± 181,62		

Note: p^x = normality, p^{xx} = homogeneity.

Normality Test For Initial Total Protein In Medium**One-Sample Kolmogorov-Smirnov Test totalproteininitial**

N		9
Normal Parameters ^{ab}	Mean	4358044634.33
	Std. Deviation	2187062217.280
Most Extreme Differences	Absolute	.379
	Positive	.231
	Negative	-.379
Test Statistic		.379
Asymp. Sig. (2-tailed)		.001 ^c

Note: a. Test distribution is Normal.

b. Calculated from data.

c. Lilliefors Significance Correction.

One Way Anova Test For Initial Total Protein In Medium**Descriptives totalproteininitial**

N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	
				Lower Bound	Upper Bound		
D10	3	5399.33	180.694	104.324	4950.46	5848.20	5214
S10	3	5154.33	321.455	185.592	4355.79	5952.87	4921
S20	3	5830.67	181.616	104.856	5379.51	6281.83	5625
Total	9	5461.44	360.804	120.268	5184.11	5738.78	4921

Test of Homogeneity of Variances

Levene Statistic			df1	df2	Sig.	
totalproteininitial	Based on Mean		1.398	2	6	.317
	Based on Median		.203	2	6	.822
	Based on Median and with adjusted df		.203	2	3.771	.825
	Based on trimmed mean		1.244	2	6	.353

ANOVA**totalproteininitial**

Sum of Squares		df	Mean Square	F	Sig.
Between Groups	703500.222	2	351750.111	6.245	.034
Within Groups	337936.000	6	56322.667		
Total	1041436.222	8			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: totalproteininitial

	(I) klp	(J) klp	Mean Difference (I- J)	Std. Error	Sig.	95% Confidence Interval
						Lower Bound
Bonferroni	D10	S10	245.000	193.774	.759	-392.02
		S20	-431.333	193.774	.203	-1068.36
	S10	D10	-245.000	193.774	.759	-882.02
		S20	-676.333*	193.774	.039	-1313.36
	S20	D10	431.333	193.774	.203	-205.69
		S10	676.333*	193.774	.039	39.31
Games-Howell	D10	S10	245.000	212.903	.550	-617.65
		S20	-431.333	147.913	.090	-958.50
	S10	D10	-245.000	212.903	.550	-1107.65
		S20	-676.333	213.165	.093	-1538.43
	S20	D10	431.333	147.913	.090	-95.83
		S10	676.333	213.165	.093	-185.76

Total Protein Post Treatment

Total Protein Post Treatment of 10⁴ cells / 24 hours (µg/ml)

Day-	P3-D10	P24-D10	P24-S10	P24-S20	p _X	p _{XX}
5	161,96 ± 11,29	0 ± 10,39	546,63 ± 13,56	310,34 ± 24,92	0,20	0,79
7	49,20 ± 14,32	0 ± 5,39	316,20 ± 0,83	254,57 ± 5,01	0,25	0,00

Note: p^v = normality, p^{xx} = homogeneity.

Normality Test for Total Protein Post Treatment Day-5

One-Sample Kolmogorov-Smirnov Test totalproteinperla kuan

N		12
Normal Parameters ^{a,b}	Mean	2.17
	Std. Deviation	8.737
Most Extreme Differences	Absolute	.205
	Positive	.168
	Negative	-.205
Test Statistic		.205
Asymp. Sig. (2-tailed)		.177 ^c

Note: a. Test distribution is Normal.

b. Calculated from data.

c. Lilliefors Significance Correction.

One Way Anova Test for Total Protein Post Treatment Day-5

Descriptives totalproteinperlakuan

N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		
				Lower Bound	Upper Bound	
P3-D10	3	2.33	1.155	.667	-.54	5.20
P24-D10	3	-11.00	1.000	.577	-13.48	-8.52
P24-S10	3	11.67	1.155	.667	8.80	14.54
P24-S20	3	5.67	1.528	.882	1.87	9.46
Total	12	2.17	8.737	2.522	-3.38	7.72

Test of Homogeneity of Variances

Levene Statistic			df1	df2	Sig.	
totalproteinperlakuan	Based on Mean		.356	3	8	.787
	Based on Median		.083	3	8	.967
	Based on Median and with adjusted df		.083	3	6.857	.967
	Based on trimmed mean		.320	3	8	.811

ANOVA

totalproteinperlakuan

Sum of Squares		df	Mean Square	F	Sig.
Between Groups	827.667	3	275.889	183.926	.000
Within Groups	12.000	8	1.500		
Total	839.667	11			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: totalproteinperlakuan

	(I) klp	(J) klp	Mean Difference (I- J)	Std. Error	Sig.	95% Confidence Interval
						Lower Bound
Bonferroni	P3-D10	P24-D10	13.333*	1.000	.000	9.85
		P24-S10	-9.333*	1.000	.000	-12.81
		P24-S20	-3.333	1.000	.062	-6.81
	P24-D10	P3-D10	-13.333*	1.000	.000	-16.81
		P24-S10	-22.667*	1.000	.000	-26.15
		P24-S20	-16.667*	1.000	.000	-20.15
	P24-S10	P3-D10	9.333*	1.000	.000	5.85
		P24-D10	22.667*	1.000	.000	19.19
		P24-S20	6.000*	1.000	.002	2.52
	P24-S20	P3-D10	3.333	1.000	.062	-.15
		P24-D10	16.667*	1.000	.000	13.19
		P24-S10	-6.000*	1.000	.002	-9.48
Games-Howell	P3-D10	P24-D10	13.333*	.882	.000	9.71
		P24-S10	-9.333*	.943	.002	-13.17
		P24-S20	-3.333	1.106	.131	-8.00
	P24-D10	P3-D10	-13.333*	.882	.000	-16.96
		P24-S10	-22.667*	.882	.000	-26.29
		P24-S20	-16.667*	1.054	.001	-21.32
	P24-S10	P3-D10	9.333*	.943	.002	5.50
		P24-D10	22.667*	.882	.000	19.04
		P24-S20	6.000*	1.106	.022	1.33
P24-S20	P3-D10	3.333	1.106	.131	-1.34	
	P24-D10	16.667*	1.054	.001	12.02	
	P24-S10	-6.000*	1.106	.022	-10.67	

Normality Test for Total Protein Post Treatment Day-7**One-Sample Kolmogorov-Smirnov Test
totalproteinperla kuan**

N		12
Normal Parameters ^{a,b}	Mean	2.17
	Std. Deviation	2.725
Most Extreme Differences	Absolute	.249
	Positive	.249
	Negative	-.184
Test Statistic		.249
Asymp. Sig. (2-tailed)		.038 ^c

Note: a. Test distribution is Normal.

b. Calculated from data.

c. Lilliefors Significance Correction.

One Way Anova for Total Protein Post Treatment Day-7**Descriptives totalproteinperlakuan**

N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		
				Lower Bound	Upper Bound	
P3-D10	3	1.00	.000	.000	1.00	1.00
P24-D10	3	-1.00	.000	.000	-1.00	-1.00
P24-S10	3	4.33	2.887	1.667	-2.84	11.50
P24-S20	3	4.33	1.155	.667	1.46	7.20
Total	12	2.17	2.725	.787	.44	3.90

Test of Homogeneity of Variances

Levene Statistic		df1	df2	Sig.	
totalproteinperlakuan	Based on Mean	12.322	3	8	.002
	Based on Median	.770	3	8	.542
	Based on Median and with adjusted df	.770	3	2.624	.590
	Based on trimmed mean	9.705	3	8	.005

ANOVA**totalproteinperlakuan**

Sum of Squares	df	Mean Square	F	Sig.	
Between Groups	62.333	3	20.778	8.598	.007
Within Groups	19.333	8	2.417		
Total	81.667	11			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: totalproteinperlakuan

	(I) klp	(J) klp	Mean Difference (I- J)	Std. Error	Sig.	95% Confidence Interval
						Lower Bound
Bonferroni	P3-D10	P24-D10	2.000	1.269	.922	-2.42
		P24-S10	-3.333	1.269	.182	-7.75
		P24-S20	-3.333	1.269	.182	-7.75
	P24-D10	P3-D10	-2.000	1.269	.922	-6.42
		P24-S10	-5.333*	1.269	.018	-9.75
		P24-S20	-5.333*	1.269	.018	-9.75
	P24-S10	P3-D10	3.333	1.269	.182	-1.08
		P24-D10	5.333*	1.269	.018	.92
		P24-S20	.000	1.269	1.000	-4.42
	P24-S20	P3-D10	3.333	1.269	.182	-1.08
		P24-D10	5.333*	1.269	.018	.92
		P24-S10	.000	1.269	1.000	-4.42
Games-Howell	P3-D10	P24-D10	2.000	.000	.	2.00
		P24-S10	-3.333	1.667	.406	-14.88
		P24-S20	-3.333	.667	.092	-7.95
	P24-D10	P3-D10	-2.000	.000	.	-2.00
		P24-S10	-5.333	1.667	.202	-16.88
		P24-S20	-5.333*	.667	.038	-9.95
	P24-S10	P3-D10	3.333	1.667	.406	-8.21
		P24-D10	5.333	1.667	.202	-6.21
		P24-S20	.000	1.795	1.000	-9.58
P24-S20	P3-D10	3.333	.667	.092	-1.29	
	P24-D10	5.333*	.667	.038	.71	
	P24-S10	.000	1.795	1.000	-9.58	

Initial KGF in Medium

Medium	Total Protein (pg/ml)	p ^x	p ^{xx}
D10	0,00 ± 4,48	0,36	0,12
S10	1457,27 ± 12,94		
S20	1712,67 ± 7,19		

Note: p^x = normality, p^{xx} = homogeneity.

Normality Test for KGF in Medium

One-Sample Kolmogorov-Smirnov Test

kgfinitial

N		9
Normal Parameters ^{a,b}	Mean	10017.89
	Std. Deviation	8817.636
Most Extreme Differences	Absolute	.358
	Positive	.240
	Negative	-.358
Test Statistic		.358
Asymp. Sig. (2-tailed)		.001 ^c

Note: a. Test distribution is Normal.

b. Calculated from data.

c. Lilliefors Significance Correction.

One Way Anova Test for Initial KGF in Medium

Descriptives kgfinitial

N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	
				Lower Bound	Upper Bound		
D10	3	-1645.67	44.837	25.887	-1757.05	-1534.29	-1696
S10	3	14572.67	129.404	74.711	14251.21	14894.12	14424
S20	3	17126.67	71.975	41.555	16947.87	17305.46	17047
Total	9	10017.89	8817.636	2939.212	3240.05	16795.72	-1696

Test of Homogeneity of Variances

Levene Statistic			df1	df2	Sig.	
kgfinitial	Based on Mean		3.107	2	6	.119
	Based on Median		.346	2	6	.721
	Based on Median and with adjusted df		.346	2	3.107	.732
	Based on trimmed mean		2.664	2	6	.149

ANOVA

kgfinitial

Sum of Squares		df	Mean Square	F	Sig.
Between Groups	621957750.889	2	310978875.444	38976.296	.000
Within Groups	47872.000	6	7978.667		
Total	622005622.889	8			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: kgfinitial

	(I) klp	(J) klp	Mean Difference (I- J)	Std. Error	Sig.	95% Confidence Interval
						Lower Bound
Bonferroni	D10	S10	-16218.333*	72.932	.000	-16458.09
		S20	-18772.333*	72.932	.000	-19012.09
	S10	D10	16218.333*	72.932	.000	15978.57
		S20	-2554.000*	72.932	.000	-2793.76
	S20	D10	18772.333*	72.932	.000	18532.57
		S10	2554.000*	72.932	.000	2314.24
Games-Howell	D10	S10	-16218.333*	79.069	.000	-16599.29
		S20	-18772.333*	48.958	.000	-18963.57
	S10	D10	16218.333*	79.069	.000	15837.38
		S20	-2554.000*	85.490	.000	-2901.75
	S20	D10	18772.333*	48.958	.000	18581.09
		S10	2554.000*	85.490	.000	2206.25

KGF Post Treatment

KGF Post Treatment of 10⁴ cells / 24 hours (pg/ml)

Day-	P3-D10	P24-D10	P24-S10	P24-S20	p ^x	p ^{xx}
5	199,24	488,95	123,18	45,29	0,28	0,33
7	127,57	369,20	87,96	53,02	0,34	0,23

Note: p^x = normality, p^{xx} = homogeneity.

Normality Test KGF Post Treatment Day-5

**One-Sample Kolmogorov-Smirnov Test
kgf**

N		12
Normal Parameters ^{a,b}	Mean	21416.42
	Std. Deviation	17520.241
Most Extreme Differences	Absolute	.277
	Positive	.277
	Negative	-.189
Test Statistic		.277
Asymp. Sig. (2-tailed)		.011 ^c

Note: a. Test distribution is Normal.

b. Calculated from data.

c. Lilliefors Significance Correction.

One Way Anova Test for KGF Post Treatment Day-5

Descriptives kgf

N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		
				Lower Bound	Upper Bound	
P3-D10	3	19923.67	392.383	226.542	18948.93	20898.40
P24-D10	3	48895.33	304.935	176.054	48137.83	49652.83
P24-S10	3	12318.00	234.928	135.636	11734.41	12901.59
P24-S20	3	4528.67	164.044	94.711	4121.16	4936.17
Total	12	21416.42	17520.241	5057.658	10284.59	32548.25

Test of Homogeneity of Variances

Levene Statistic		df1	df2	Sig.	
kgf	Based on Mean	1.340	3	8	.328
	Based on Median	.219	3	8	.880
	Based on Median and with adjusted df	.219	3	5.853	.880
	Based on trimmed mean	1.181	3	8	.376

ANOVA

kgf

Sum of Squares		Df	Mean Square	F	Sig.
Between Groups	3375889348.917	3	1125296449.639	13679.295	.000
Within Groups	658102.000	8	82262.750		
Total	3376547450.917	11			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: kgf

	(I) klp	(J) klp	Mean Difference (I- J)	Std. Error	Sig.	95% Confidence Interval
						Lower Bound
Bonferroni	P3-D10	P24-D10	-28971.667*	234.183	.000	-29786.36
		P24-S10	7605.667*	234.183	.000	6790.97
		P24-S20	15395.000*	234.183	.000	14580.30
	P24-D10	P3-D10	28971.667*	234.183	.000	28156.97
		P24-S10	36577.333*	234.183	.000	35762.64
		P24-S20	44366.667*	234.183	.000	43551.97
	P24-S10	P3-D10	-7605.667*	234.183	.000	-8420.36
		P24-D10	-36577.333*	234.183	.000	-37392.03
		P24-S20	7789.333*	234.183	.000	6974.64
	P24-S20	P3-D10	-15395.000*	234.183	.000	-16209.70
		P24-D10	-44366.667*	234.183	.000	-45181.36
		P24-S10	-7789.333*	234.183	.000	-8604.03
Games-Howell	P3-D10	P24-D10	-28971.667*	286.909	.000	-30175.84
		P24-S10	7605.667*	264.043	.000	6402.25
		P24-S20	15395.000*	245.543	.000	14105.79
	P24-D10	P3-D10	28971.667*	286.909	.000	27767.49
		P24-S10	36577.333*	222.243	.000	35642.64
		P24-S20	44366.667*	199.913	.000	43416.72
P24-S10	P3-D10	-7605.667*	264.043	.000	-8809.08	
	P24-D10	-36577.333*	222.243	.000	-37512.02	
	P24-S20	7789.333*	165.430	.000	7074.49	
P24-S20	P3-D10	-15395.000*	245.543	.000	-16684.21	
	P24-D10	-44366.667*	199.913	.000	-45316.62	
	P24-S10	-7789.333*	165.430	.000	-8504.18	

Normality Test for KGF Post Treatment Day-7

One-Sample Kolmogorov-Smirnov Test
kgf

N		12
Normal Parameters ^{a,b}	Mean	15943.58
	Std. Deviation	12946.153
Most Extreme Differences	Absolute	.344
	Positive	.344
	Negative	-.203
Test Statistic		.344
Asymp. Sig. (2-tailed)		.000 ^c

Note: a. Test distribution is Normal.
 b. Calculated from data.
 c. Lilliefors Significance Correction.

One Way Anova Test for KGF Post Treatment Day-7

Descriptives kgf

N		Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
P3-D10	3	12756.3 3	116.105	67.033	12467.91	13044.75
P24-D10	3	36919.6 7	50.083	28.916	36795.25	37044.08
P24-S10	3	8796.33	246.901	142.549	8183.00	9409.67
P24-S20	3	5302.00	130.985	75.624	4976.62	5627.38
Total	12	15943.5 8	12946.153	3737.23 2	7717.99	24169.18

Test of Homogeneity of Variances

Levene Statistic		df1	df2	Sig.	
kgf	Based on Mean	1.762	3	8	.232
	Based on Median	.913	3	8	.477
	Based on Median and with adjusted df	.913	3	4.909	.499
	Based on trimmed mean	1.701	3	8	.244

ANOVA

kgf

Sum of Squares		df	Mean Square	F	Sig.
Between Groups	1843443338.917	3	614481112.972	26118.679	.000
Within Groups	188212.000	8	23526.500		
Total	1843631550.917	11			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: kgf

	(I) klp	(J) klp	Mean Difference (I- J)	Std. Error	Sig.	95% Confidence Interval
						Lower Bound
Bonferroni	P3-D10	P24-D10	-24163.333*	125.237	.000	-24599.02
		P24-S10	3960.000*	125.237	.000	3524.32
		P24-S20	7454.333*	125.237	.000	7018.65
	P24-D10	P3-D10	24163.333*	125.237	.000	23727.65
		P24-S10	28123.333*	125.237	.000	27687.65
		P24-S20	31617.667*	125.237	.000	31181.98
	P24-S10	P3-D10	-3960.000*	125.237	.000	-4395.68
		P24-D10	-28123.333*	125.237	.000	-28559.02
		P24-S20	3494.333*	125.237	.000	3058.65
	P24-S20	P3-D10	-7454.333*	125.237	.000	-7890.02
		P24-D10	-31617.667*	125.237	.000	-32053.35
		P24-S10	-3494.333*	125.237	.000	-3930.02
Games-Howell	P3-D10	P24-D10	-24163.333*	73.004	.000	-24542.08
		P24-S10	3960.000*	157.523	.001	3170.00
		P24-S20	7454.333*	101.057	.000	7039.98
	P24-D10	P3-D10	24163.333*	73.004	.000	23784.59
		P24-S10	28123.333*	145.452	.000	27197.43
		P24-S20	31617.667*	80.964	.000	31178.39
P24-S10	P3-D10	-3960.000*	157.523	.001	-4750.00	
	P24-D10	-28123.333*	145.452	.000	-29049.24	
	P24-S20	3494.333*	161.366	.001	2723.27	
P24-S20	P3-D10	-7454.333*	101.057	.000	-7868.69	
	P24-D10	-31617.667*	80.964	.000	-32056.94	
	P24-S10	-3494.333*	161.366	.001	-4265.40	

pMEK 1/2 Post Treatment

pMEK 1/2 Post Treatment of 10⁴ cells (pg/ml)

Day - Minute / Hours	P3-D10	P24-D10	P24-S10	P24-S20	pX	pXX
5 - 45	0,00 ± 0,00	0,01 ± 0,00	0,01 ± 0,00	0,01 ± 0,00	0,37	0,06
5 - 24	0,08 ± 0,00	0,22 ± 0,03	0,22 ± 0,02	0,18 ± 0,03		
7 - 45	0,00 ± 0,00	0,01 ± 0,00	0,01 ± 0,00	0,01 ± 0,00		
7 - 24	0,06 ± 0,00	0,15 ± 0,00	0,14 ± 0,01	0,11 ± 0,00		

Note: p¹ = normality, p^{xx} = homogeneity.

Normality Test for pMEK 1/2

**One-Sample Kolmogorov-Smirnov Test
mek**

N		12
Normal Parameters ^{a,b}	Mean	51527765.83
	Std. Deviation	63208916.191
Most Extreme Differences	Absolute	.369
	Positive	.369
	Negative	-.247
Test Statistic		.369
Asymp. Sig. (2-tailed)		.000 ^c

Note: a. Test distribution is Normal.
 b. Calculated from data.
 c. Lilliefors Significance Correction.

One Way Anova Test for pMEK 1/2

Descriptives mek

N		Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean
					Lower Bound
P24-S20-div5-45menit	3	8.67	.577	.333	7.23
P24-S20-div5-24jam	3	179.33	20.502	11.837	128.40
P24-S20-div7-45menit	3	12.33	1.528	.882	8.54
P24-S20-div7-24jam	3	107.33	.577	.333	105.90
Total	12	76.92	74.819	21.598	29.38

Test of Homogeneity of Variances

Levene Statistic			df1	df2	Sig.	
mek	Based on Mean		3.797	3	8	.058
	Based on Median		3.640	3	8	.064
	Based on Median and with adjusted df		3.640	3	2.048	.219
	Based on trimmed mean		3.788	3	8	.059

ANOVA

mek

-	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	60730.250	3	20243.417	191.276	.000
Within Groups	846.667	8	105.833		
Total	61576.917	11			

Post Hoc Tests
Multiple Comparisons
Dependent Variable: mek

	(I) klp	(J) klp	Mean Difference (I-J)	Std. Error	Sig.
Bonferroni	P24-S20-div5-45menit	P24-S20-div5-24jam	-170.667*	8.400	.000
		P24-S20-div7-45menit	-3.667	8.400	1.000
		P24-S20-div7-24jam	-98.667*	8.400	.000
	P24-S20-div5-24jam	P24-S20-div5-45menit	170.667*	8.400	.000
		P24-S20-div7-45menit	167.000*	8.400	.000
		P24-S20-div7-24jam	72.000*	8.400	.000
	P24-S20-div7-45menit	P24-S20-div5-45menit	3.667	8.400	1.000
		P24-S20-div5-24jam	-167.000*	8.400	.000
		P24-S20-div7-24jam	-95.000*	8.400	.000
	P24-S20-div7-24jam	P24-S20-div5-45menit	98.667*	8.400	.000
		P24-S20-div5-24jam	-72.000*	8.400	.000
			P24-S20-div7-45menit	95.000*	8.400
Games- Howell	P24-S20-div5-45menit	P24-S20-div5-24jam	-170.667*	11.842	.012
		P24-S20-div7-45menit	-3.667	.943	.107
		P24-S20-div7-24jam	-98.667*	.471	.000
	P24-S20-div5-24jam	P24-S20-div5-45menit	170.667*	11.842	.012
		P24-S20-div7-45menit	167.000*	11.870	.012
		P24-S20-div7-24jam	72.000	11.842	.064
	P24-S20-div7-45menit	P24-S20-div5-45menit	3.667	.943	.107
		P24-S20-div5-24jam	-167.000*	11.870	.012
		P24-S20-div7-24jam	-95.000*	.943	.000
	P24-S20-div7-24jam	P24-S20-div5-45menit	98.667*	.471	.000
		P24-S20-div5-24jam	-72.000	11.842	.064
		P24-S20-div7-45menit	95.000*	.943	.000

Type-1 Collagen Post Treatment

Type-1 Collagen Post Treatment of 10⁴ cells / 24 hours (ng/ml)

Day-	P3-D10	P24-D10	P24-S10	P24-S20	p ^x	p ^{xx}
5	1,23 ± 0,04	3,02 ± 0,03	3,00 ± 0,06	2,67 ± 0,03	0,33	0,55
7	0,91 ± 0,06	2,73 ± 0,26	2,56 ± 0,05	1,76 ± 0,11	0,26	0,02

Note: p^x = normality, p^{xx} = homogeneity.

Normality Test for Type-1 Collagen Post Treatment Day-5

**One-Sample Kolmogorov-Smirnov Test
kolagen**

N		12
Normal Parameters ^{a,b}	Mean	248.00
	Std. Deviation	76.885
Most Extreme Differences	Absolute	.332
	Positive	.225
	Negative	-.332
Test Statistic		.332
Asymp. Sig. (2-tailed)		.001 ^c

Note: a. Test distribution is Normal.

b. Calculated from data.

c. Lilliefors Significance Correction.

One Way Anova Test for Type-1 Collagen Post Treatment Day-5

**Descriptives
kolagen**

N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		
				Lower Bound	Upper Bound	
P3-D10	3	123.00	4.359	2.517	112.17	133.83
P24-D10	3	302.33	2.887	1.667	295.16	309.50
P24-S10	3	300.00	5.568	3.215	286.17	313.83
P24-S20	3	266.67	3.055	1.764	259.08	274.26
Total	12	248.00	76.885	22.195	199.15	296.85

Test of Homogeneity of Variances

Levene Statistic		df1	df2	Sig.	
kolagen	Based on Mean	.758	3	8	.548
	Based on Median	.239	3	8	.867
	Based on Median and with adjusted df	.239	3	6.867	.866
	Based on trimmed mean	.703	3	8	.576

ANOVA

kolagen

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	64888.667	3	21629.556	1278.594	.000
Within Groups	135.333	8	16.917		
Total	65024.000	11			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: kolagen

	(I) klp	(J) klp	Mean Difference (I- J)	Std. Error	Sig.	95% Confidence Interval
						Lower Bound
Bonferroni	P3-D10	P24-D10	-179.333*	3.358	.000	-191.02
		P24-S10	-177.000*	3.358	.000	-188.68
		P24-S20	-143.667*	3.358	.000	-155.35
	P24-D10	P3-D10	179.333*	3.358	.000	167.65
		P24-S10	2.333	3.358	1.000	-9.35
		P24-S20	35.667*	3.358	.000	23.98
	P24-S10	P3-D10	177.000*	3.358	.000	165.32
		P24-D10	-2.333	3.358	1.000	-14.02
		P24-S20	33.333*	3.358	.000	21.65
	P24-S20	P3-D10	143.667*	3.358	.000	131.98
		P24-D10	-35.667*	3.358	.000	-47.35
		P24-S10	-33.333*	3.358	.000	-45.02
Games-Howell	P3-D10	P24-D10	-179.333*	3.018	.000	-192.60
		P24-S10	-177.000*	4.082	.000	-194.11
		P24-S20	-143.667*	3.073	.000	-156.93
	P24-D10	P3-D10	179.333*	3.018	.000	166.07
		P24-S10	2.333	3.621	.911	-15.13
		P24-S20	35.667*	2.427	.000	25.77
	P24-S10	P3-D10	177.000*	4.082	.000	159.89
		P24-D10	-2.333	3.621	.911	-19.80
		P24-S20	33.333*	3.667	.008	16.05
	P24-S20	P3-D10	143.667*	3.073	.000	130.40
		P24-D10	-35.667*	2.427	.000	-45.56
		P24-S10	-33.333*	3.667	.008	-50.62

Normality Test for Type-1 Collagen Post Treatment Day-7

One-Sample Kolmogorov-Smirnov Test

kolagen

N		12
Normal Parameters ^{a,b}	Mean	207.33
	Std. Deviation	73.721
Most Extreme Differences	Absolute	.259
	Positive	.179
	Negative	-.259
Test Statistic		.259
Asymp. Sig. (2-tailed)		.025 ^c

Note: a. Test distribution is Normal.

b. Calculated from data.

c. Lilliefors Significance Correction.

One Way Anova Test for Type-1 Collagen Post Treatment Day-7

Descriptives kolagen

N		Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
P3-D10	3	91.33	6.658	3.844	74.79	107.87
P24-D10	3	272.67	25.423	14.678	209.51	335.82
P24-S10	3	256.00	5.292	3.055	242.86	269.14
P24-S20	3	176.00	10.583	6.110	149.71	202.29
Total	12	199.00	76.308	22.028	150.52	247.48

Test of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.	
kolagen		Based on Mean	6.231	3	8	.017
		Based on Median	.484	3	8	.702
		Based on Median and with adjusted df	.484	3	2.874	.718
		Based on trimmed mean	5.079	3	8	.029

ANOVA

kolagen

Sum of Squares		df	Mean Square	F	Sig.
Between Groups	62390.667	3	20796.889	100.146	.000
Within Groups	1661.333	8	207.667		
Total	64052.000	11			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: kolagen

	(I) klp	(J) klp	Mean Difference (I- J)	Std. Error	Sig.	95% Confidence Interval
						Lower Bound
Bonferroni	P3-D10	P24-D10	-181.333*	11.766	.000	-222.27
		P24-S10	-164.667*	11.766	.000	-205.60
		P24-S20	-84.667*	11.766	.001	-125.60
	P24-D10	P3-D10	181.333*	11.766	.000	140.40
		P24-S10	16.667	11.766	1.000	-24.27
		P24-S20	96.667*	11.766	.000	55.73
	P24-S10	P3-D10	164.667*	11.766	.000	123.73
		P24-D10	-16.667	11.766	1.000	-57.60
		P24-S20	80.000*	11.766	.001	39.07
	P24-S20	P3-D10	84.667*	11.766	.001	43.73
		P24-D10	-96.667*	11.766	.000	-137.60
		P24-S10	-80.000*	11.766	.001	-120.93

			Mean Difference (I- J)	Std. Error	Sig.	95% Confidence Interval
	(I) klp	(J) klp				Lower Bound
Games-Howell	P3-D10	P24-D10	-181.333*	15.173	.011	-273.33
		P24-S10	-164.667*	4.910	.000	-185.17
		P24-S20	-84.667*	7.219	.002	-116.97
	P24-D10	P3-D10	181.333*	15.173	.011	89.34
		P24-S10	16.667	14.993	.718	-78.38
		P24-S20	96.667*	15.899	.035	13.05
	P24-S10	P3-D10	164.667*	4.910	.000	144.16
		P24-D10	-16.667	14.993	.718	-111.72
		P24-S20	80.000*	6.831	.004	46.57
P24-S20	P3-D10	84.667*	7.219	.002	52.36	
	P24-D10	-96.667*	15.899	.035	-180.28	
	P24-S10	-80.000*	6.831	.004	-113.43	

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