Chapter 6: Results

Chapter 6:

Results

Recapitulation:

The outcome measure - psychological assessments were made at baseline (BL) and on departing from Antarctica (P3). The biochemical assessments and Chemiluminescence assays were made on samples obtained on reaching Antarctica (P1), departing from the first Indian station (P2) and on departing from Antarctica (P3). Single colour global Gene Expression analysis were performed on samples obtained from baseline (BL), on reaching Antarctica (P1), and on departing from Antarctica (P3). BL serum samples were not available for analysis. Biochemical and Chemiluminescence assays were performed on samples obtained on reaching Antarctica (P1), departing from the first Indian station (P2) and on departing from Antarctica (P3)

The data from the samples were tested for normality. For biochemical tests and Chemiluminescence assessments, within group changes between any two timepoints were assessed using paired sample '*t*' test. Between group analysis was performed using Univariate ANCOVA adjusted for the baseline values.

Genes with more than 2-fold differential expression were pooled and tabulated from each samples of yoga and control groups. All the downstream analysis was performed with this list Also, a stringent, more than 2-fold differentially regulated gene list was prepared from genes which were commonly detected across both the groups and in all the samples. The stringent list was used to profile the transcription factors, processes and pathways that were consistently regulated in both the group.

The results of the study are described under the following headings:

6.1. Socio-demographic and medical characteristics of the study sample

6.2. Psychological Assessments

6.3. Biochemical Assessments

6.4. Molecular Biology Assessments

6.5. Gene Expression Analysis

6.1. Socio-demographic and Medical Characteristics of the study samples

There were 25 members at the start of the study, 24 males and 1 female. The average age of the expeditioners was 35±7.8 years. Twelve members volunteered to be part of the Yoga group and Thirteen members volunteered to be in the control group. The average age, weight, and BMI of both Yoga and Control group were similar at baseline *(table 6.1).*

Descriptive	**Yoga Group** (Mean±SD)	**Control Group** (Mean±SD)	**Significance**
Age (years)	34.0±9.0	37.0±6.6	NS
Weight (Kg)	71.1±11.69	78.22±11.34	NS
BMI (Kg/m^2)	24.66±2.74	26.78±3.30	NS

Table 6.1: Baseline demographic data (Mean±SD) and test for normality at baseline in both the groups

6.2.Psychological Assessments

6.2.1. Pittsburgh Sleep Quality Inventory:

Between groups analysis using analysis of covariance with respective baseline values as covariate, suggest that there was a significant contrasting change in the daytime dysfunction [$F_{(1,16)}$ =5.214, p=0.04]. The results suggest that the daytime dysfunction scores decreased by 62.5% in Yoga group, whereas, it increased by 49.25% in Control group. Also, a similar non-significant contrasting change was noted in the subjective sleep quality [$F_{(1,16)}$= 3.314, p=0.08]. The results suggest that

the subjective sleep quality increased by 44.4% in Yoga group, while it decreased by 32.84% in Control group at the end of the expedition *(table 6.2.1)*.

6.2.2. Perseverative Thinking Questionnaire [PTQ]

The perseverative cognition scores were similar in both groups at baseline. Following the expedition duration of ~3 months, results suggest that in Yoga group, a significant 33.56% reduction of overall perseverative thinking *(table 6.2.2)*. In contrary there was a 22.88% increase in Perseverative Thinking scores in the control group. Between groups analysis showed reduction in yoga group in overall PTQ scores [$F_{(1,16)}$ = 28.121, $p \leq 0.001$], Core RNT [$F_{(1,16)}$ = 25.65, $p \leq 0.001$], Unproductiveness RNT [$F_{(1,16)}$ = 10.50, p=0.037] and Mental Capacity [$F_{(1,16)}$ = 22.80, p=0.006].

6.3. Biochemical Assessments

P1_P2 Comparisons

Within group analysis showed a 32.84% reduction (p=0.02) in AST levels in the Control group. Yoga group showed a non-significant 15.72% reduction (p=0.24) in AST levels. Yoga group subjects showed significant increases in triglycerides (18.95%, p=0.02), HDL (5.26%, p=0.03), LDL (19.20%, p=0.003), VLDL (18.5%, p=0.05), Glucose (6.28%, p=0.024) and Cholesterol (16.62%, p=0.004). The increases in lipid profile measures were less in control group.

Between groups analysis showed non-significant greater increases in Urea [$F_{(1,14)}$=2.14, p=0.17] and Glucose [$F_{(1,14)}$=1.86, p=0.19] in control group. A contrasting change in creatinine levels [$F_{(1,14)}$= 3.69, p=0.08] were observed with 4.4% increase in Yoga group and 9.86% reduction in control group. A greater reduction in AST levels [$F_{(1,14)}$=1.99, p=0.18] are also noted in control group as compared to Yoga group. These

results suggest a rapid adaptation response by the body to the external environmental conditions *(Table 6.3.1)*.

P1_P3 Comparisons

Within group analysis showed that HDL levels increasing in both Yoga (15.46%, p=0.003) and Control (16.87%, p=0.005) groups. Bilirubin levels decreased by 100% and 66.67% in Yoga (p=0.04) and control group (p=0.17) respectively. Yoga group showed increases in LDL (36.18%, p=0.001), cholesterol (26.54%, p=0.001). The ALT levels increased by 28.03% in Yoga group (p=0.33), whereas, it remained unchanged in control group (p=0.95). Between group comparison showed a significant increase in LDL levels in Yoga group as compared to the control group ($F_{(1,13)}$=5.80, p=0.03) *(Table 6.3.2)*.

P2_P3 Comparisons

A similar increase was observed in HDL (Yoga: 10.33%, p=0.04; Control: 14.71%, p=0.01), AST (Yoga: 37.7%, p=0.01; Control: 49.23%, p=0.09) and GGT levels (Yoga: 25.14%, p=0.03; Control: 26.72%, p=0.08). Urea levels decreased by 9.8% and 17.28% in Yoga (p=0.05) and Control (p=0.06) groups respectively. Control group further showed 64.29% increase in ALT levels (p=0.08). Yoga group subjects demonstrated a significant increase in LDL (10.14%, p=0.02) and reductions in total proteins (4.8%, p=0.01), urea (9.8%, p=0.05) and albumin levels (5.76%, p=0.002). A contrasting change in glucose levels are observed, with reduction in Yoga group and increase in Control group ($F_{(1,10)}$= 7.44,p=0.02). Non-Significant greater increase in LDL levels was observed in Control group as compared to the Yoga group [$F_{(1,10)}$=2.31 ,p=0.16] *(Table 6.3.3)*.

	Yoga pre	Yoga post	% change	Wilcoxon Signed rank test	Control pre	Control post	%change	Wilcoxon Signed rank test	ANCOVA
Subjective Sleep Quality	0.9±0.74	0.5±0.53	-44.444	.102	0.67±0.5	0.89±0.6	32.83582	0.317	0.087
Sleep Latency	0.7±0.95	0.7±1.06	.000	.891	1±0.5	0.56±0.53	-44	0.157	0.725
Sleep Duration	0.7±0.67	0.7±0.82	.000	1.000	0.44±0.73	0.89±0.6	102.2727	0.102	0.366
Sleep Disturbance	1±0.67	1.1±0.32	10.000	.564	0.89±0.33	1±0	12.35955	0.317	0.434
Use of Sleep Medication	0±0	0±0			0±0	0±0			
Daytime Dysfunction	0.8±1.033	0.3±0.48	-62.500	.157	0.67±0.71	1±0.87	49.25373	0.257	**0.036***
PSQI (Total score)	4.1±2.38	3.3±2.06	-19.512	.491	3.67±1.5	4.33±1.66	17.98365	0.301	0.15

Table 6.2.1: Sleep quality in Yoga and Control groups (Mean±SD) at the baseline and completion (P3) of the expedition measured using Pittsburgh Sleep Quality Index. Within group changes were calculated using Wilcoxon-signed rank test and between group differences were calculated using ANCOVA.

Wilcoxon signed rank test: * $p \leq 0.05$; + $p \leq 0.001$;

ANCOVA: # $p \leq 0.05$; @ $p \leq 0.001$

Descriptive	Yoga Pre	Yoga post	% Change	Paired t test	Control Pre	Control Post	% Change	Paired t test	ANCOVA
Core RNT	9.6±9.04	5.9±5.45	-38.54	**0.004***	10.89±5.8	12.56±5.27	15.34	**0.03***	0.00012@
Unproductiveness RNT	2.2±2.04	2.2±2.04	0	1	3±1.5	4.33±1.87	44.33	**0.02***	0.04#
Mental Capacity	3.1±1.73	1.8±1.8	-41.94	0.07	3.11±2.67	4±2	28.62	0.104	0.006#
PTQ Total score	14.9±8.774	9.9±9.04	-33.56	**0.004***	17±8.7	20.89±8.09	22.88	**0.007***	0.000071@

Table 6.2.2.: Perseverative Thinking in Yoga and Control groups (Mean±SD) at the baseline and completion (P3) of expedition measured using Perseverative Thinking Questionnaire. Within group changes were calculated using paired t test and between group changes were calculated using ANCOVA

t-test: * $p \leq 0.05$; + $p \leq 0.001$;

ANCOVA: # $p \leq 0.05$; @ $p \leq 0.001$

	P1_P2 [7 Control + 10 Yoga]									*Normal range*
	P1_Control	**P2_Control**	**P1_P2_% Change Control**	**paired t test**	**P1_Yoga**	**P2_Yoga**	**P1_P2_% Change Yoga**	**paired t test**	**ANCOVA**	
TG (mg/dl)	101.14±22.46	106.86±15.66	5.65	0.54	99.2±23.31	118±34.54	18.95	**0.05***	0.32	*≤ 149*
HDL (mg/dl)	48.14±13.04	49.14±12.86	2.08	0.59	43.7±9.72	46±9.78	5.26	**0.03***	0.59	*≥ 40*
LDL (mg/dl)	115.29±39.12	128.86±25.17	11.77	0.36	102.6±20.35	122.3±24.11	19.20	**0.003***	0.95	*≤ 100*
VLDL (mg/dl)	20.29±4.57	21.29±3.25	4.93	0.58	20±4.59	23.7±6.83	18.50	**0.05***	0.30	*2-30*
Glucose (mg/dl)	95.29±8.75	99.29±3.73	4.20	0.14	86±10.22	91.4±7.65	6.28	**0.02***	0.19	*72-108*
Urea (mg/dl)	26.57±4.69	31.43±6.29	18.28	0.19	24.8±7.11	25.7±7.62	3.63	0.66	0.17	*7-20*
Uric Acid (mg/dl)	6.14±1.86	5.86±1.07	-4.65	0.52	5.6±1.26	5.7±1.34	1.79	0.68	0.61	*3.4-7.0*
Cholesterol (mg/dl)	196.86±68.44	205.71±37.88	4.50	0.73	167.9±27.09	195.8±30.09	16.62	**0.004***	0.96	*≤ 200*
ALT (units/litre)	18.14±8.47	14.14±9.96	-22.05	0.35	15.7±8.3	18.2±7.6	15.92	0.44	0.28	*7-56*
AST (units/litre)	38.29±9.38	25.71±5.35	-32.84	**0.02***	36.9±9.88	31.1±8.39	-15.72	0.24	0.18	*10-40*
GGT (units/litre)	32.71±7.91	28±11.6	-14.41	0.18	26±7.5	22.4±5.76	-13.85	0.16	0.72	*9-48*
Bilirubin (mg/dl)	0.29±0.49	0.57±0.53	100.00	0.17	0.5±0.53	0.4±0.52	-20.00	0.68	0.43	*0.1-1.2*
Total Protein (g/litre)	76.43±6.29	75.86±4.88	-0.75	0.79	78.9±5.4	78.8±4.26	-0.13	0.96	0.34	*60-80*
Albumin (g/litre)	49.71±7.11	47.71±1.98	-4.02	0.51	49.1±3.28	50±3.68	1.83	0.45	0.16	*35-55*
Creatinine (mg/dl)	1.01±0.24	0.91±0.09	-9.86	0.22	0.91±0.22	0.95±0.16	4.40	0.27	0.08	*0.6-1.2*

Table 6.3.1: Lipid profile, liver and kidney function tests in Yoga and Control groups at the timepoints P1 and P2 (Mean±SD). Within-group changes were calculated with t-test and between-group changes were calculated using ANCOVA.

t-test: * $p \leq 0.05$; + $p \leq 0.001$;

ANCOVA: # $p \leq 0.05$; @ $p \leq 0.001$

	P1_P3 [7 Control + 9 Yoga]									*Normal Range*
	P1_Control	**P3_Control**	**P1_P3 % change Control**	**paired t-test**	**P1_Yoga**	**P3_Yoga**	**P1_P3 %Change yoga**	**paired t-test**	**ANCOVA**	
TG (mg/dl)	100.86±24.94	104.29±34.69	3.40	0.71	94.89±23.55	94.78±19.19	-0.12	0.99	0.64	*≤ 149*
HDL (mg/dl)	47.43±9.24	55.43±10.34	16.87	**0.005***	43.11±10.03	49.78±10.73	15.46	0.003	0.58	*≥ 40*
LDL (mg/dl)	123.86±32.83	133.14±29.8	7.50	0.27	106.56±23.93	145.11±40.03	36.18	**0.001**$^{+}$	**0.03**$^{\#}$	*≤ 100*
VLDL (mg/dl)	20.29±4.99	20.86±6.89	2.82	0.75	19.22±4.68	18.89±3.79	-1.73	0.82	0.59	*2-30*
Glucose (mg/dl)	91.71±9.5	95.57±11.3	4.21	0.45	86.56±9.7	90.56±7.55	4.62	0.20	0.52	*72-108*
Urea (mg/dl)	25.43±6.73	24.57±6.73	-3.37	0.68	24.44±7.4	22.78±6.76	-6.82	0.52	0.67	*7-20*
Uric Acid (mg/dl)	5.57±1.9	5.43±1.4	-2.56	0.74	5.78±1.2	5.78±1.2	0.00	1.00	0.57	*3.4-7.0*
Cholesterol (mg/dl)	207.29±62.62	209.86±40.74	1.24	0.88	171.67±32.04	217.22±48.49	26.54	**0.002***	0.13	*≤ 200*
ALT (units/litre)	18.71±8.04	18.43±11.87	-1.53	0.95	14.67±7.94	18.78±11.21	28.03	0.33	0.74	*7-56*
AST (units/litre)	40±13.32	38.29±10.87	-4.29	0.55	35±10.26	39.56±14.72	13.02	0.51	0.72	*10-40*
GGT (units/litre)	32.14±6.96	32.43±6.82	0.89	0.84	27.56±9.03	27.89±9.84	1.21	0.94	0.51	*9-48*
Bilirubin (mg/dl)	0.43±0.53	0.14±0.38	-66.67	0.17	0.44±0.53	0±0	-100.00	**0.04***	0.26	*0.1-1.2*
Total Protein (g/litre)	76.14±7.82	75.29±4.79	-1.13	0.71	77.44±4.13	75.33±5.27	-2.73	0.33	0.86	*60-80*
Albumin (g/litre)	49.71±7.27	48.71±2.43	-2.01	0.75	48.56±3.09	47.56±4.07	-2.06	0.45	0.56	*35-55*
Creatinine (mg/dl)	0.96±0.21	0.91±0.07	-4.48	0.55	0.94±0.21	0.96±0.22	1.18	0.68	0.41	*0.6-1.2*

Table 6.3.2.: Lipid profile, liver and kidney function tests in Yoga and Control groups at the timepoints P1 and P3 (Mean±SD). Within-group changes were calculated with t-test and between-group changes were calculated using ANCOVA.

t-test: * $p \leq 0.05$; + $p \leq 0.001$;

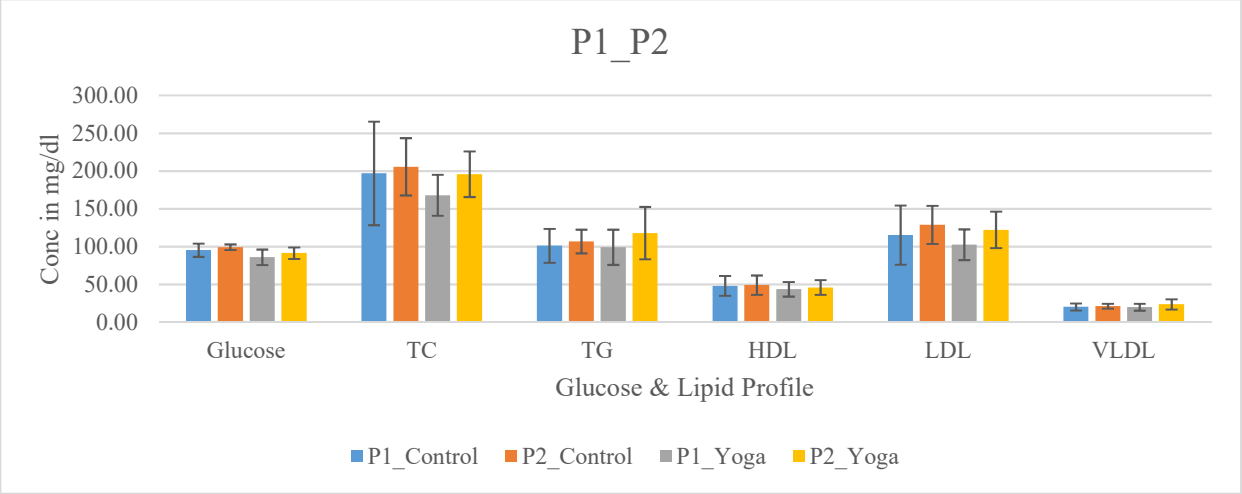
ANCOVA: # $p \leq 0.05$; @ $p \leq 0.001$

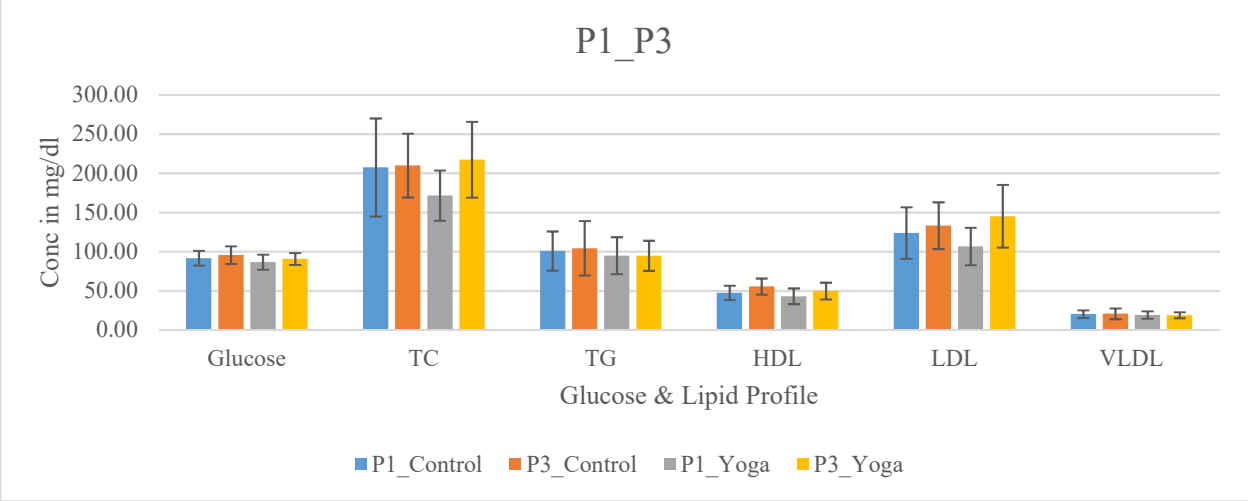
	P2_P3 [5 Control + 8 Yoga]									*Normal Range*
	P2_Control	**P3_Control**	**P2_P3 %Change Control**	**paired t-test**	**P2_Yoga**	**P3_Yoga**	**P2_P3 %Change Yoga**	**paired t-test**	**ANCOVA**	
TG (mg/dl)	108±16.66	113±35.53	4.63	0.77	107.38±28.93	93.38±20.01	-13.04	0.19	0.48	*≤ 149*
HDL (mg/dl)	47.6±9.66	54.6±11.93	14.71	**0.01***	46±10.43	50.75±11.04	10.33	**0.04***	0.98	*≥ 40*
LDL (mg/dl)	131.2±25.72	139±34.34	5.95	0.29	124.5±26.76	137.13±34.29	10.14	**0.02***	0.16	*≤ 100*
VLDL (mg/dl)	21.6±3.51	22.6±6.91	4.63	0.77	21.63±5.73	18.63±3.96	-13.87	0.15	0.43	*2-30*
Glucose (mg/dl)	99.6±3.21	101.2±7.19	1.61	0.69	90.13±6.33	88.88±6.01	-1.39	0.46	**0.02***	*72-108*
Urea (mg/dl)	32.4±7.3	26.8±3.77	-17.28	0.06	25.5±8.42	23±7.19	-9.80	**0.05***	0.53	*7-20*
Uric Acid (mg/dl)	5.8±1.1	5.8±1.1	0.00	1.00	6±1.31	5.75±1.28	-4.17	0.17	0.94	*3.4-7.0*
Cholesterol (mg/dl)	206.6±35.88	215.8±48.32	4.45	0.36	198.25±33.61	208±42.57	4.92	0.15	0.37	*≤ 200*
ALT (units/litre)	14±11.55	23±9.77	64.29	0.08	18.13±7.88	20.13±11.18	11.03	0.63	0.87	*7-56*
AST (units/litre)	26±6.16	38.8±9.58	49.23	0.09	30.5±9.09	42±13.65	37.70	**0.01***	0.74	*10-40*
GGT (units/litre)	26.2±7.19	33.2±8.14	26.72	0.08	22.38±6.48	28±10.52	25.14	**0.03***	0.70	*9-48*
Bilirubin (mg/dl)	0.8±0.45	0±0	-100.00	**0.02***	0.38±0.52	0±0	-100.00	0.08	NA	*0.1-1.2*
Total Protein (g/litre)	74.2±3.35	73.8±2.59	-0.54	0.75	78.13±4.55	74.38±4.72	-4.80	**0.01***	0.86	*60-80*
Albumin (g/litre)	47.2±1.64	47.6±1.52	0.85	0.59	49.86±4.16	47±3.96	-5.76	**0.05***	0.79	*35-55*
Creatinine (mg/dl)	0.92±0.08	0.94±0.05	2.17	0.62	0.96±0.18	0.93±0.22	-3.90	0.40	0.68	*0.6-1.2*

Table 6.3.3.: Lipid profile, liver and kidney function tests in Yoga and Control groups at the timepoints P2 and P3 (Mean±SD). Within-group changes were calculated with t-test and between-group changes were calculated using ANCOVA.

t-test: * $p \leq 0.05$; + $p \leq 0.001$;

ANCOVA: # $p \leq 0.05$; @ $p \leq 0.001$





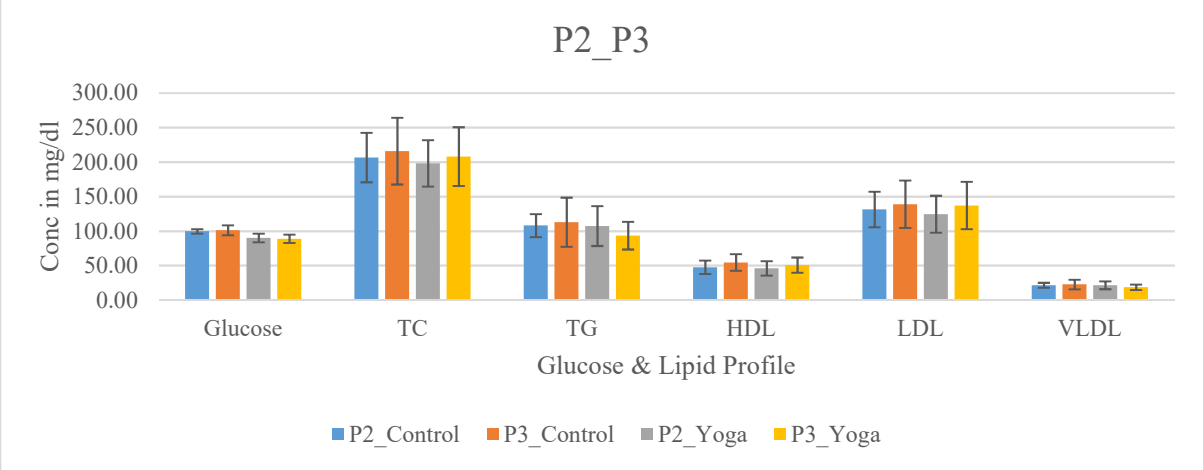
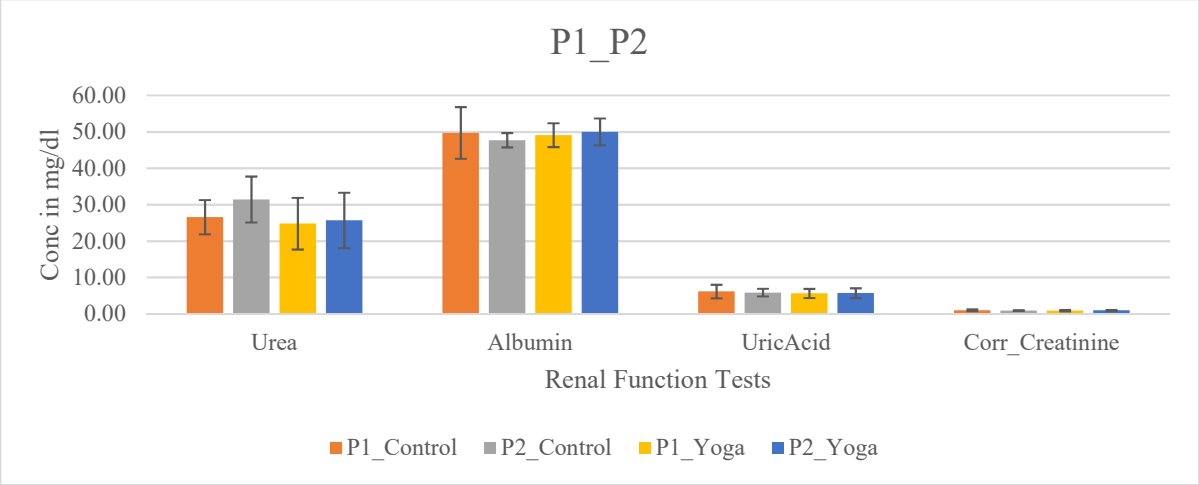
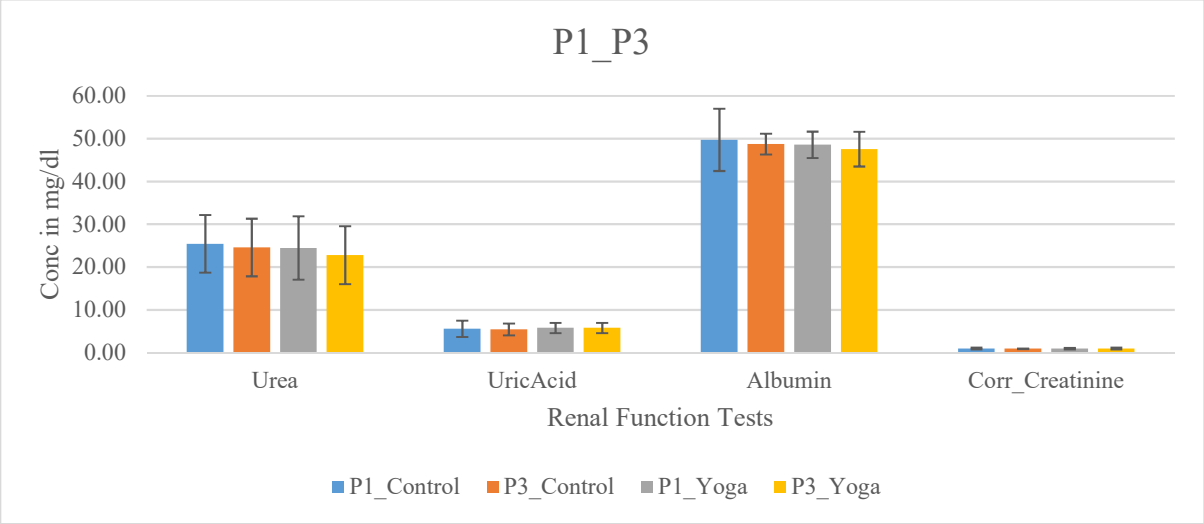


Fig 6.1a: Changes in Glucose and Lipid profile values in Yoga and Control groups in the timepoints P1, P2 and P3. Within-group changes were calculated using paired t-test and between-group changes were calculated using Analysis of Co-variance.

t-test: * $p \leq 0.05$; + $p \leq 0.001$;

ANCOVA: # $p \leq 0.05$; @ $p \leq 0.001$





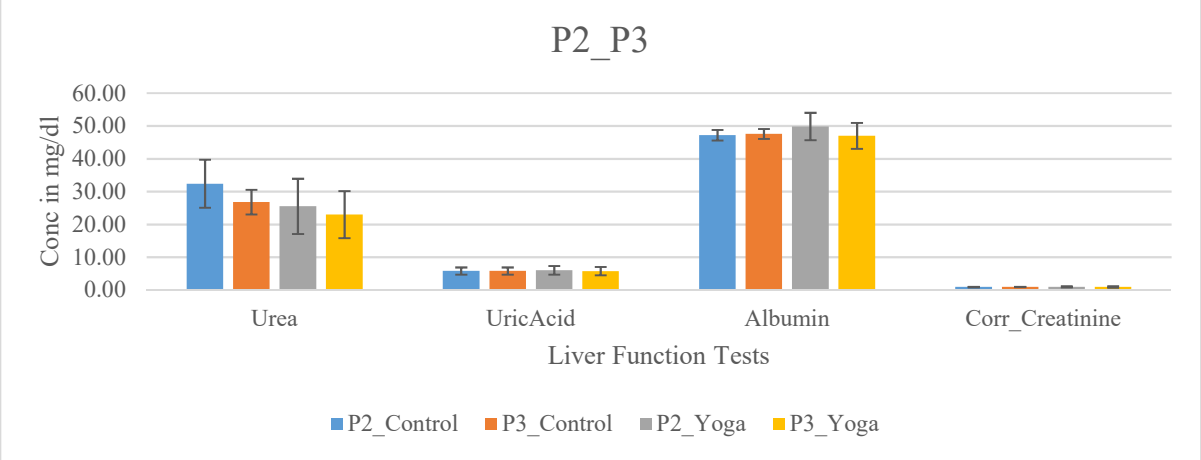
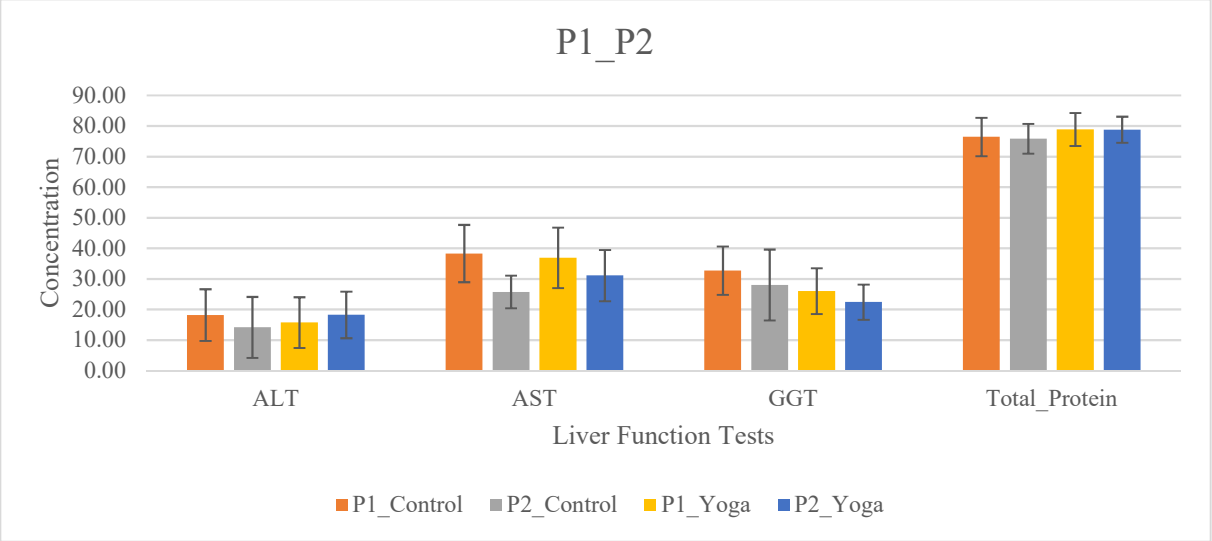
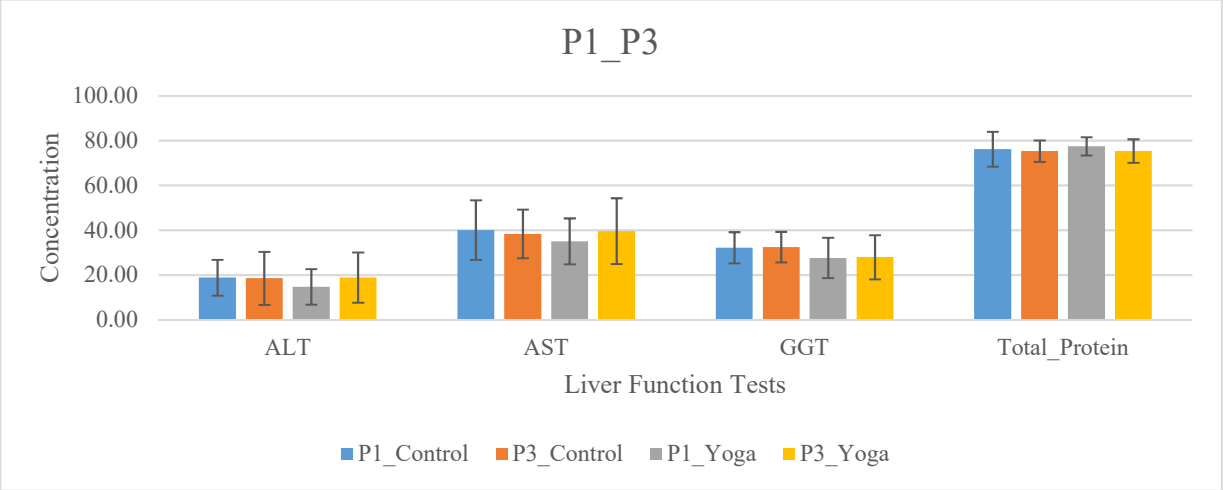


Fig 6.1b: Changes in Renal Function test values in Yoga and Control groups in the timepoints P1, P2 and P3. Within-group changes were calculated using paired t-test and between-group changes were calculated using Analysis of Co-variance.

t-test: * $p \leq 0.05$; + $p \leq 0.001$;

ANCOVA: # $p \leq 0.05$; @ $p \leq 0.001$





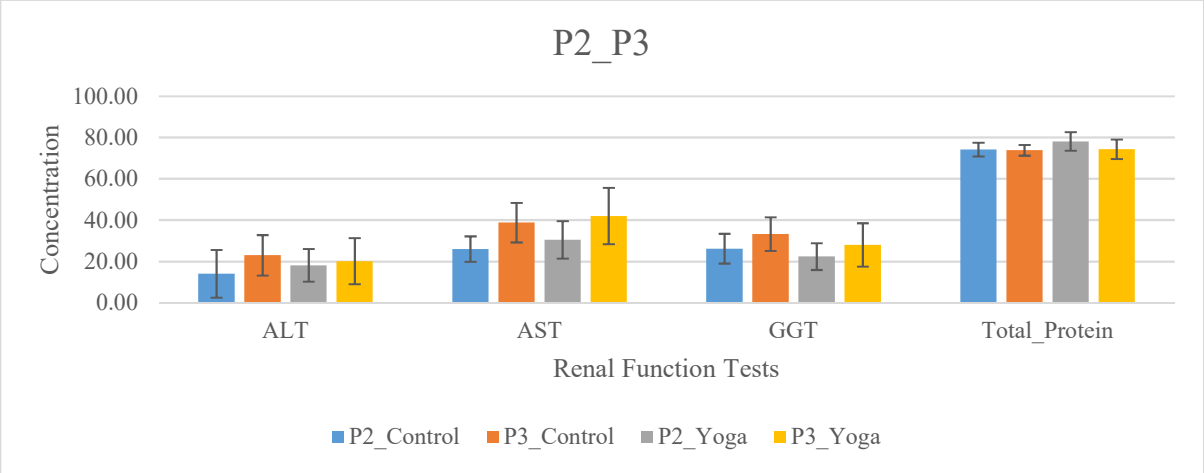


Fig 6.1 c: Changes in Liver Function test values in Yoga and Control groups in the timepoints P1, P2 and P3. Within-group changes were calculated using paired t-test and between-group changes were calculated using Analysis of Co-variance.

t-test: * $p \leq 0.05$; + $p \leq 0.001$;

ANCOVA: # $p \leq 0.05$; @ $p \leq 0.001$

6.4. Molecular Biology Assessments:

6.4.1. Cortisol Assay

Within-group comparison showed a significant increase in cortisol levels in the control group [$F_{(1,3)}$ =7.894, p=0.02] whereas, the Yoga group showed a non-significant increasing trend of Serum Cortisol levels [$F_{(1,3)}$=1.39, p= 0.32]. Between groups analysis did not show any significant changes.

Group	P1	P2	P3	ANOVA
Control	25.87±17.09	28.27±6.34	46.86±20.8	0.02
Yoga	19.72±3.71	23.68±16.41	32.58±22.38	0.32

Table 6.4.1.: Serum Cortisol levels (Mean±SD) in Yoga and Control groups at P1, P2 & P3

6.4.2. IL-2 Assay

The levels of IL-2 was in detectable range in only 6 out of 10 subjects.

6.5. Gene Expression – Exploratory Analysis:

6.5.1. Classification of Differentially Regulated Genes

The Differentially Expressed Genes (DEG) were analysed under three conditions for both Yoga and Control Groups:

a. Baseline Vs Post 1
b. Post 1 Vs Post 3
c. Baseline Vs Post 3

The DEGs of each condition were grouped according to the PANTHER protein class, GO Molecular Function, GO Biological Process and GO Cellular Component. Grouping the DEGs in every time-point according to the protein class, biological process and molecular function were most useful. The Details of classification for each timepoint is explained below. The number of genes belonging to the specific category in the Control group as compared to the Yoga group is expresses as percentage.

Baseline Vs Post 1

A total of 9498 and 6044 DEGs in Control and Yoga group respectively had annotations in the PANTHER database and were classified further *(Table 6.5.1A)*.

Biological Process:

For the Biological Process, the DEGs corresponding to cell killing (200%), growth (150%), metabolic process (62.6%), immune system process (59.17%), localisation (56.98%), Cellular Process (56.64%), biogenesis (55.15%), biological adhesion (55.05%), reproduction (52.75%) and biological regulation (51.08%) were upregulated in the control group as compared to the Yoga group *(fig 6.5.1a)*.

Molecular Function:

For the Molecular Functions, the DEGs corresponding to channel regulator activity (88.89%), catalytic activity (60.64%), antioxidant activity (60%), translation regulator activity (58.06%), structural module activity (56.57%), binding (55.48%), transporter activity (51.71%) and reporter activity (48.95%) were upregulated in the Control Group as compared to the Control Group *(fig 6.5.1b)*.

Protein Class:

For the Protein Class, DEGs corresponding to membrane traffic protein (75.45%), ligase (73.87%), hydrolase (65.8%), nucleic acid binding (65.7%), transcription factor (64.14%), isomerase (61.36%), chaperone (61.11%), cell adhesion molecule (60.23%), Oxidoreductase (59.03%), calcium binding protein (58.42%), transferase (57.62%), enzyme modulator (57.35%), transporter (53%), cell junction protein (50%), defence or immunity protein (46.15%) and cytoskeletal protein (45.28%) were up-regulated in Control group as compared to the Yoga group *(fig 6.5.1c)*.

Post 1 Vs Post 3

A total of 7789 and 6735 DEGs in Control and Yoga group respectively had annotations in the PANTHER database and were classified further *(Table 6.5.1B)*

Biological Process

For the Biological Process, the DEGs were almost similar in both Control and Yoga group except for the immune system process, where there were 31.21% more genes upregulated in the Control group than in the Yoga group *(fig 6.5.1d)*.

Molecular Function

For the molecular function, the DEGs corresponding to the channel regulator activity (87.5%) and antioxidant activity (54.55%) was upregulated in the Control group as compared to the Yoga group *(fig 6.5.1e)*.

Protein Class

For the Protein Class, DEGs were similar in both Control and Yoga groups *(fig 6.5.1f)*.

Baseline Vs Post 3

A total of 7897 and 5649 DEGs in Control and Yoga groups respectively had annotations in the PANTHER database and were classified further *(Table 6.5.1C)*

Biological Process

For the biological process, DEGs corresponding to growth (66.67%), biogenesis (57.20%), immune system process (50.96%), and metabolic process (50.25%) were upregulated in the Control group than the Yoga group.

In summary, it appears that more genes for any given function as classified under PANTHER database were regulated in the control group as compared to the Yoga group (*fig 6.5.1g)*.

Molecular Function

For the Molecular Function, DEGs corresponding to antioxidant activity (87.5%), translation regulator activity (50%), catalytic activity (48.7%) and structural molecule activity was upregulated in the Control Group as compared to the Yoga group *(fig 6.5.1h)*.

Protein Class:

For the protein class, DEGs corresponding to isomerase (75.76%), lyase (62.16%), calcium binding protein (56.04%), defence or immunity protein (54.84%), cell junction protein (54.17%), hydrolase (52.82%), oxidoreductase (50%), chaperone (48.08%), and nucleic acid binding (47.75%) were upregulated in Control group as compared to the Yoga group *(fig 6.5.1i)*.

The DEGs of all timepoints were visualised using InteractiVenn (Heberle, Meirelles, da Silva, Telles, & Minghim, 2015), a web-based tool to visualise the genes that are unique and that are expressed in common amongst groups and timepoints

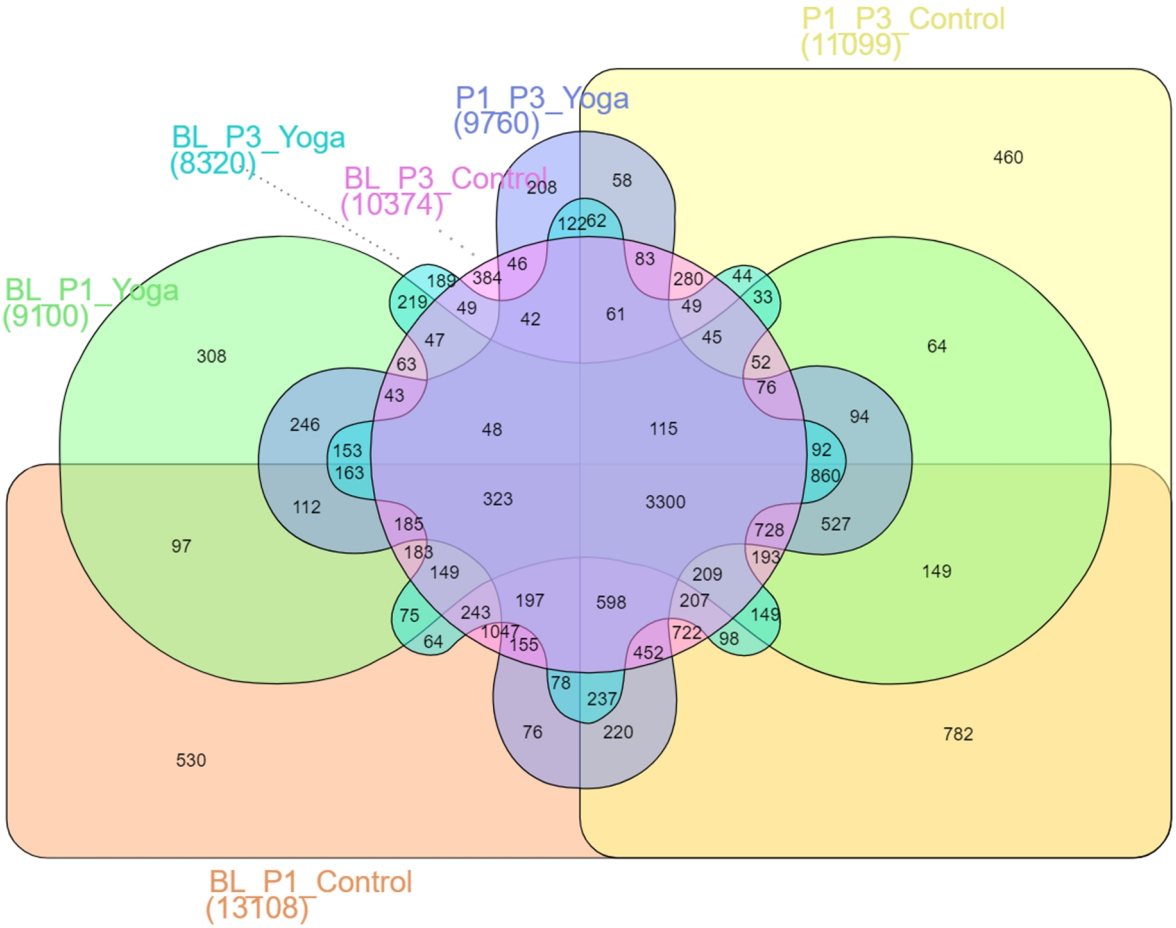


Fig 6.5.: Venn diagram representation of differentially expressed genes across groups and time-points

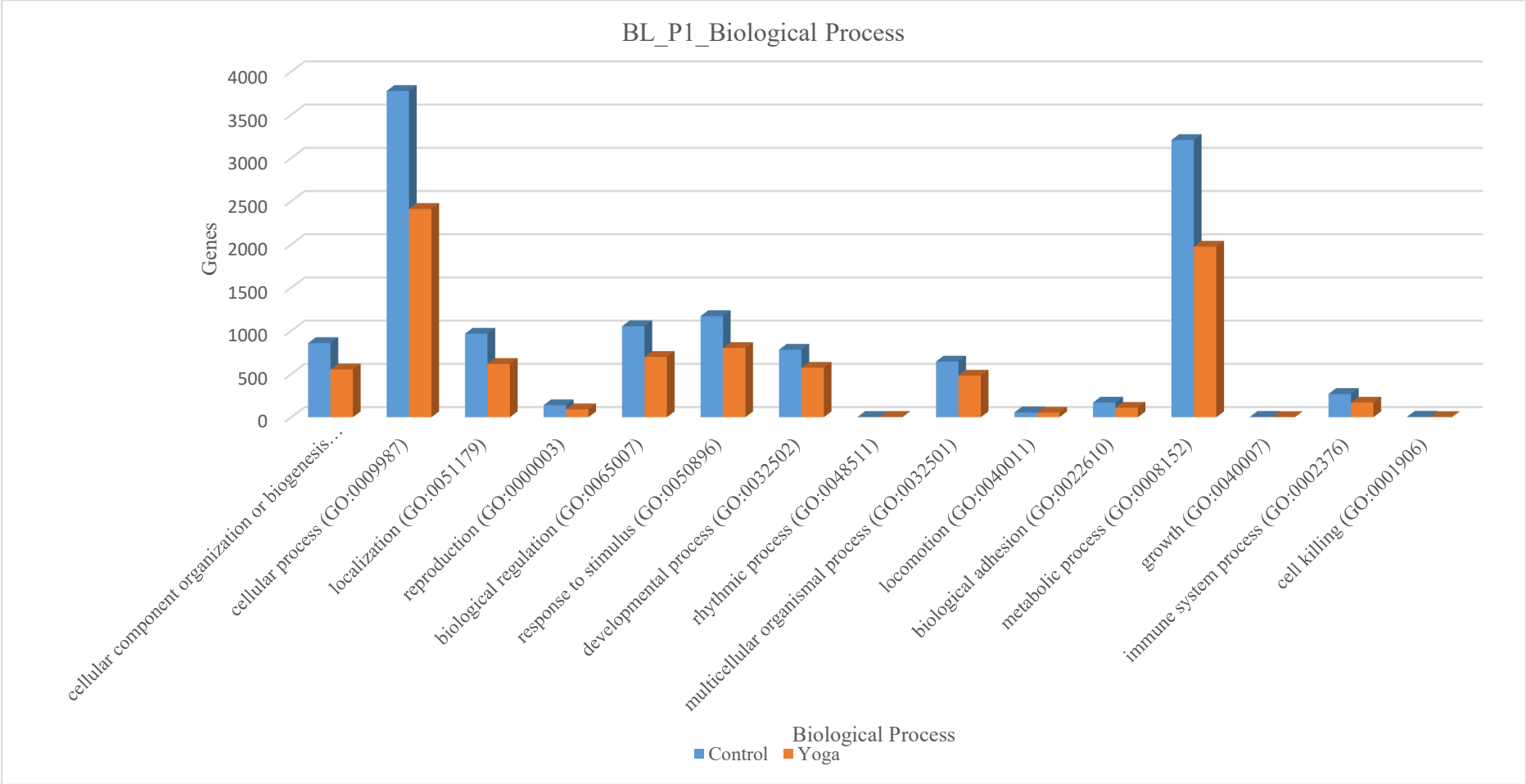


Fig6.5.1a: Classification of genes based on Gene Ontology– Biological Process of Differentially Regulated Genes for timepoint - Baseline versus Post1 in Control and Yoga groups

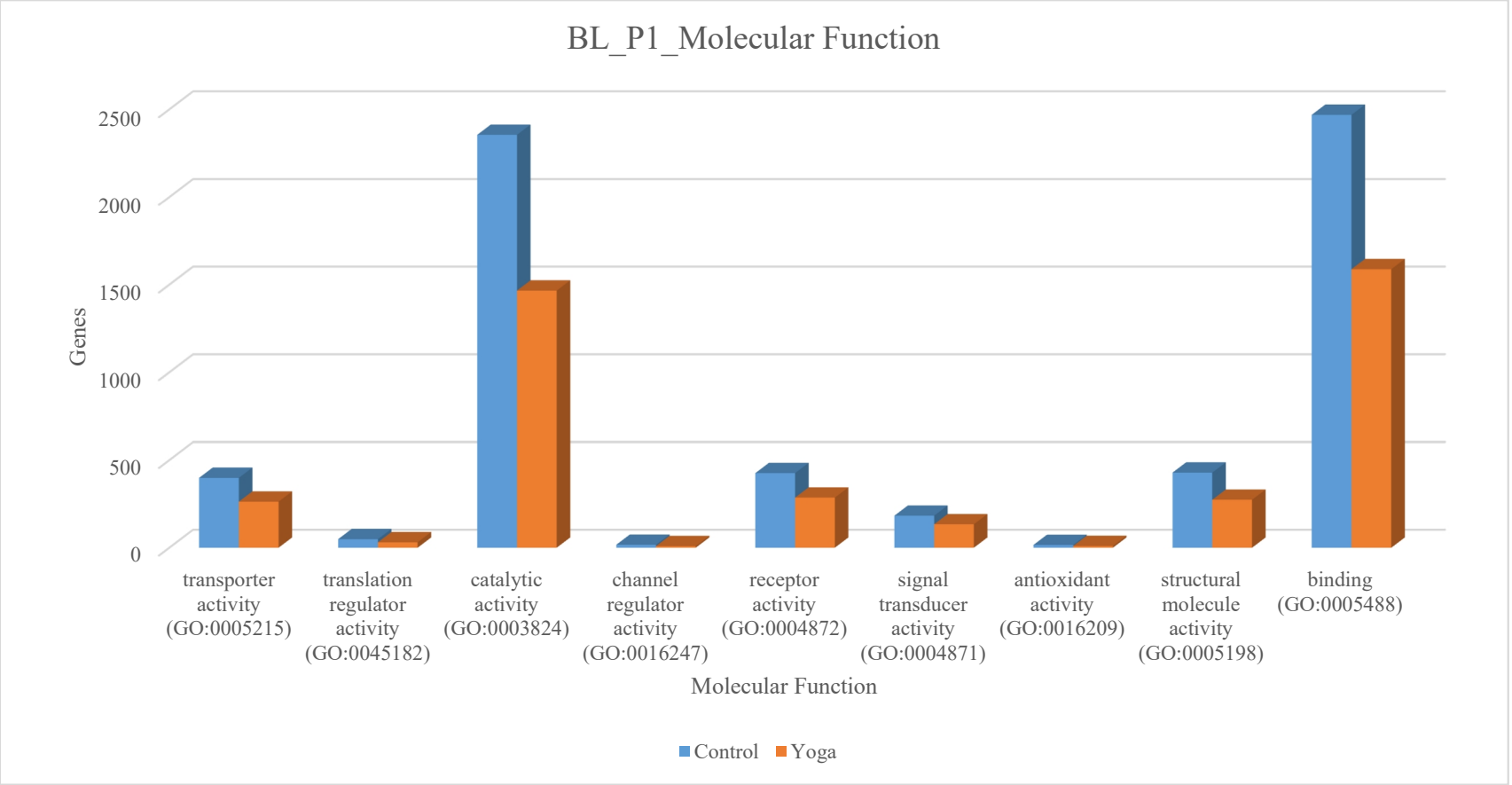


Fig 6.5.1b: Classification of genes based on Gene Ontology – Molecular Function of Differentially Regulated Genes for timepoint - Baseline versus Post1 in Control and Yoga groups

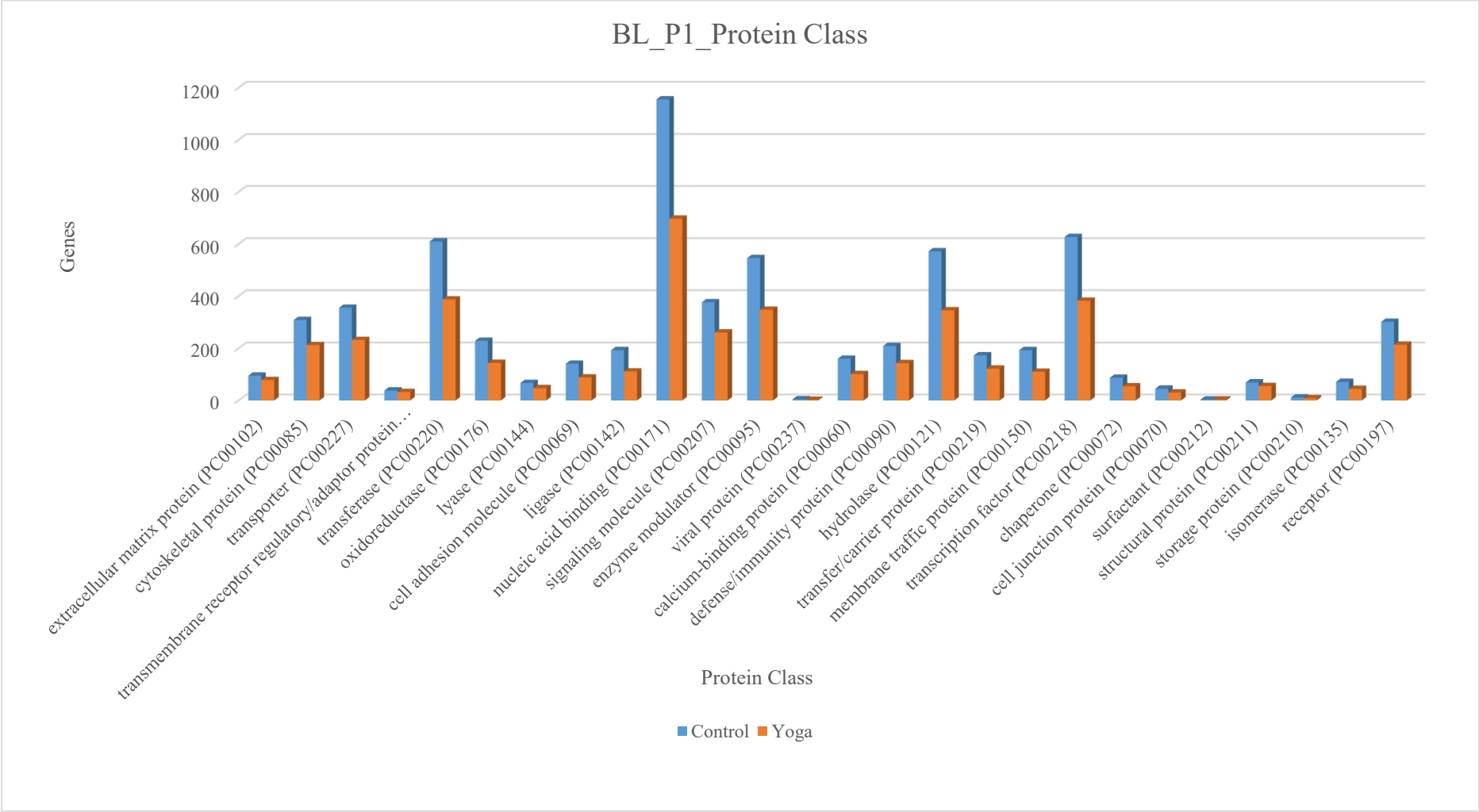


Fig 6.5.1c: Classification of genes based on Gene Ontology – Protein Class of Differentially Regulated Genes for timepoint - Baseline versus Post1 in Control and Yoga groups

Gene Ontology Classification [Baseline versus Post 1]	**Control** (No of genes)	**Yoga** (No of genes)
Biological Process		
Cellular component organization or biogenesis (GO:0071840)	858	553
Cellular process (GO:0009987)	3775	2410
Localization (GO:0051179)	967	616
Reproduction (GO:0000003)	139	91
Biological regulation (GO:0065007)	1053	697
Response to stimulus (GO:0050896)	1170	801
Developmental process (GO:0032502)	781	573
Rhythmic process (GO:0048511)	3	3
Multicellular organismal process (GO:0032501)	644	481
Locomotion (GO:0040011)	56	52
Biological adhesion (GO:0022610)	169	109
Metabolic process (GO:0008152)	3208	1973
Growth (GO:0040007)	5	2
Immune system process (GO:0002376)	269	169
Cell killing (GO:0001906)	6	2
Molecular Function		
Transporter activity (GO:0005215)	399	263
Translation regulator activity (GO:0045182)	49	31
Catalytic activity (GO:0003824)	2355	1466
Channel regulator activity (GO:0016247)	17	9
Receptor activity (GO:0004872)	426	286
Signal transducer activity (GO:0004871)	183	134
Antioxidant activity (GO:0016209)	16	10
Structural molecule activity (GO:0005198)	429	274
Binding (GO:0005488)	2469	1588
Protein Class		

Extracellular matrix protein (PC00102)	95	78
Cytoskeletal protein (PC00085)	308	212
Transporter (PC00227)	355	232
Transmembrane receptor regulatory/adaptor protein (PC00226)	38	32
Transferase (PC00220)	610	387
Oxidoreductase (PC00176)	229	144
Lyase (PC00144)	67	47
Cell adhesion molecule (PC00069)	141	88
Ligase (PC00142)	193	111
Nucleic acid binding (PC00171)	1155	697
Signaling molecule (PC00207)	376	261
Enzyme modulator (PC00095)	546	347
Viral protein (PC00237)	4	2
Calcium-binding protein (PC00060)	160	101
Defense/immunity protein (PC00090)	209	143
Hydrolase (PC00121)	572	345
Transfer/carrier protein (PC00219)	173	122
Membrane traffic protein (PC00150)	193	110
Transcription factor (PC00218)	627	382
Chaperone (PC00072)	87	54
Cell junction protein (PC00070)	45	30
Surfactant (PC00212)	3	3
Structural protein (PC00211)	69	55
Storage protein (PC00210)	11	8
Isomerase (PC00135)	71	44
Receptor (PC00197)	301	214

Tab 6.5.1A: Gene Ontology classifications of Differentially Expressed Genes for timepoint - Baseline versus Post1 in Control and Yoga groups

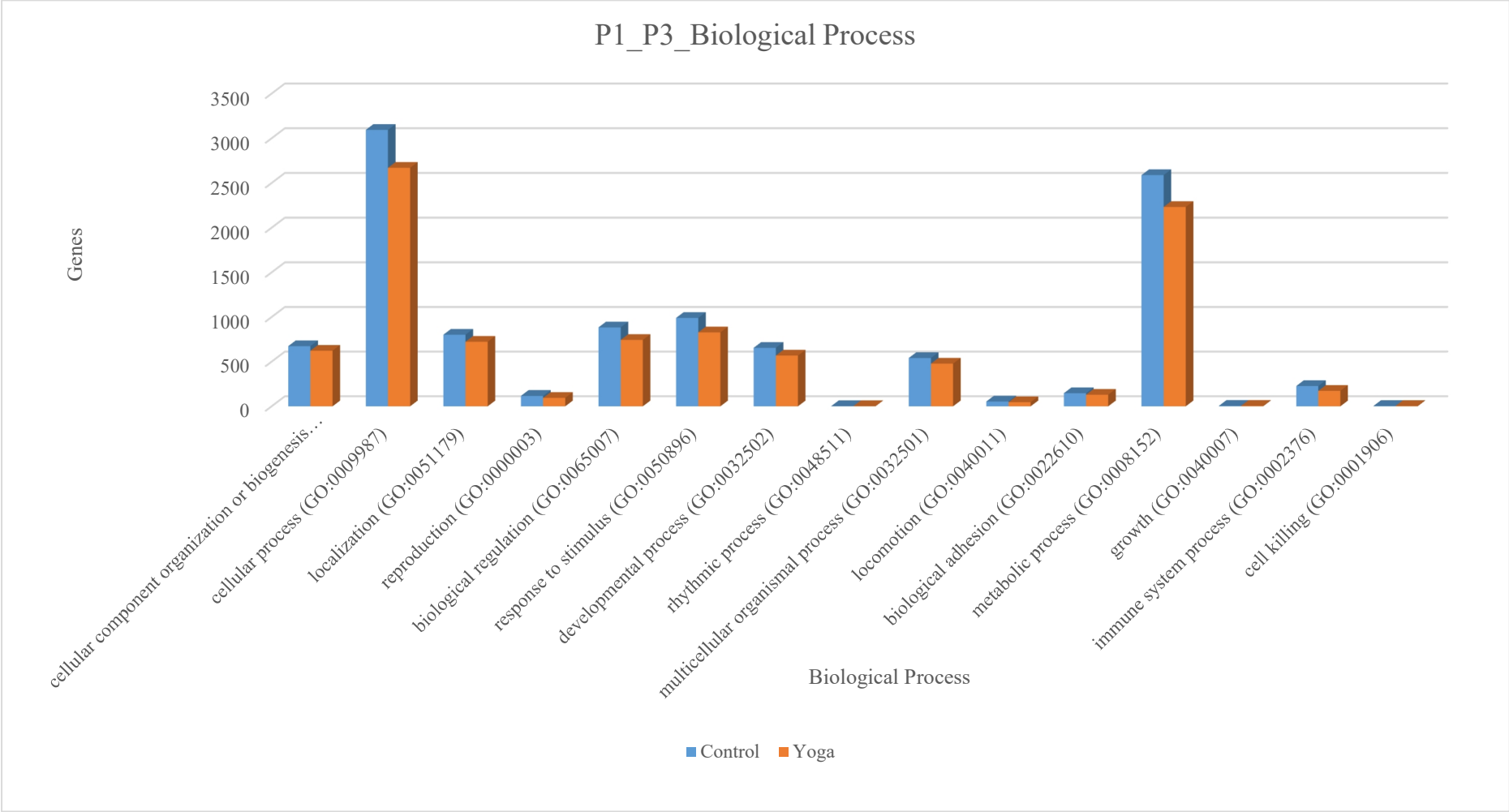


Fig 6.5.1d: Classification of genes based on Gene Ontology – Biological Process of Differentially Regulated Genes for timepoint – Post1 versus Post3 in Control and Yoga groups.

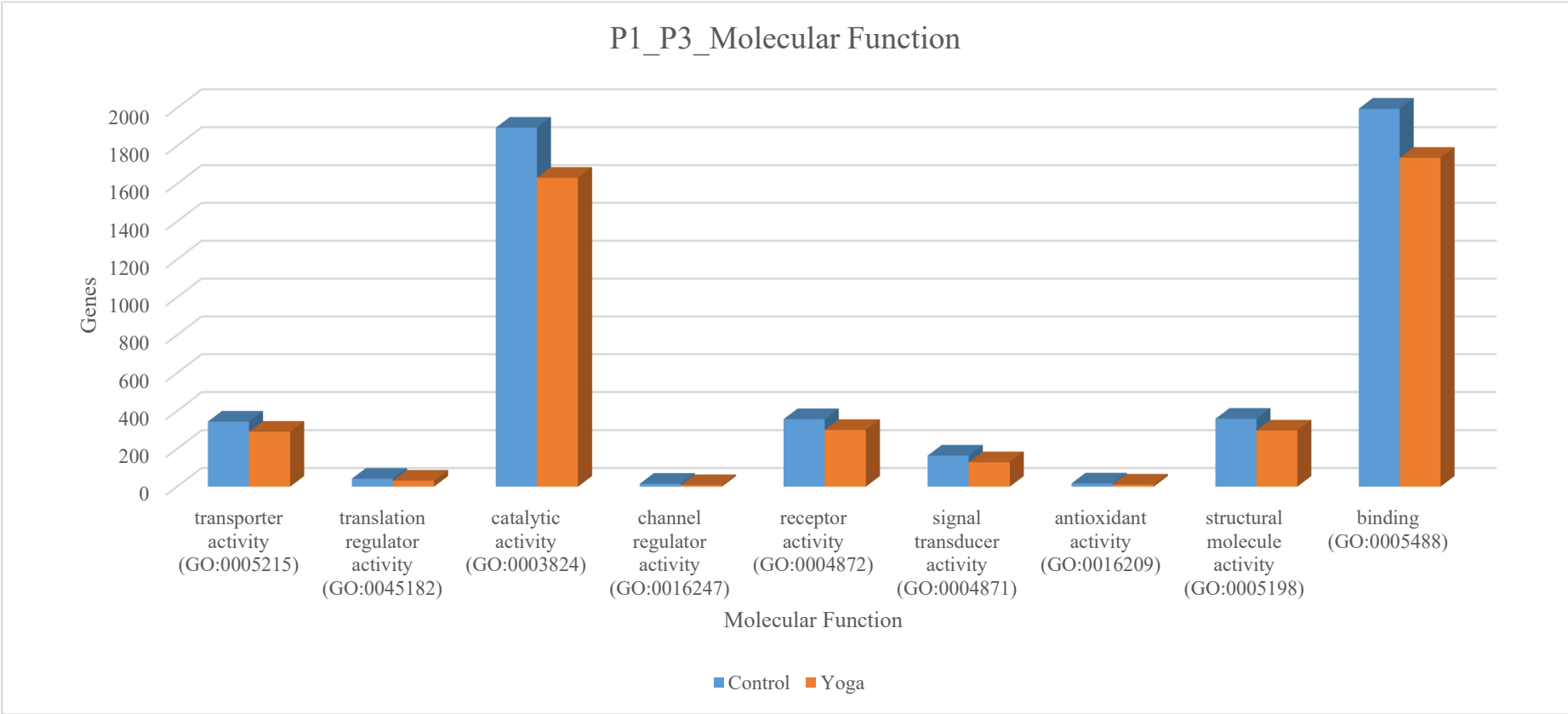


Fig 6.5.1e: Classification of genes based on Gene Ontology – Molecular Function of Differentially Regulated Genes for timepoint – Post1 versus Post3 in Control and Yoga groups.

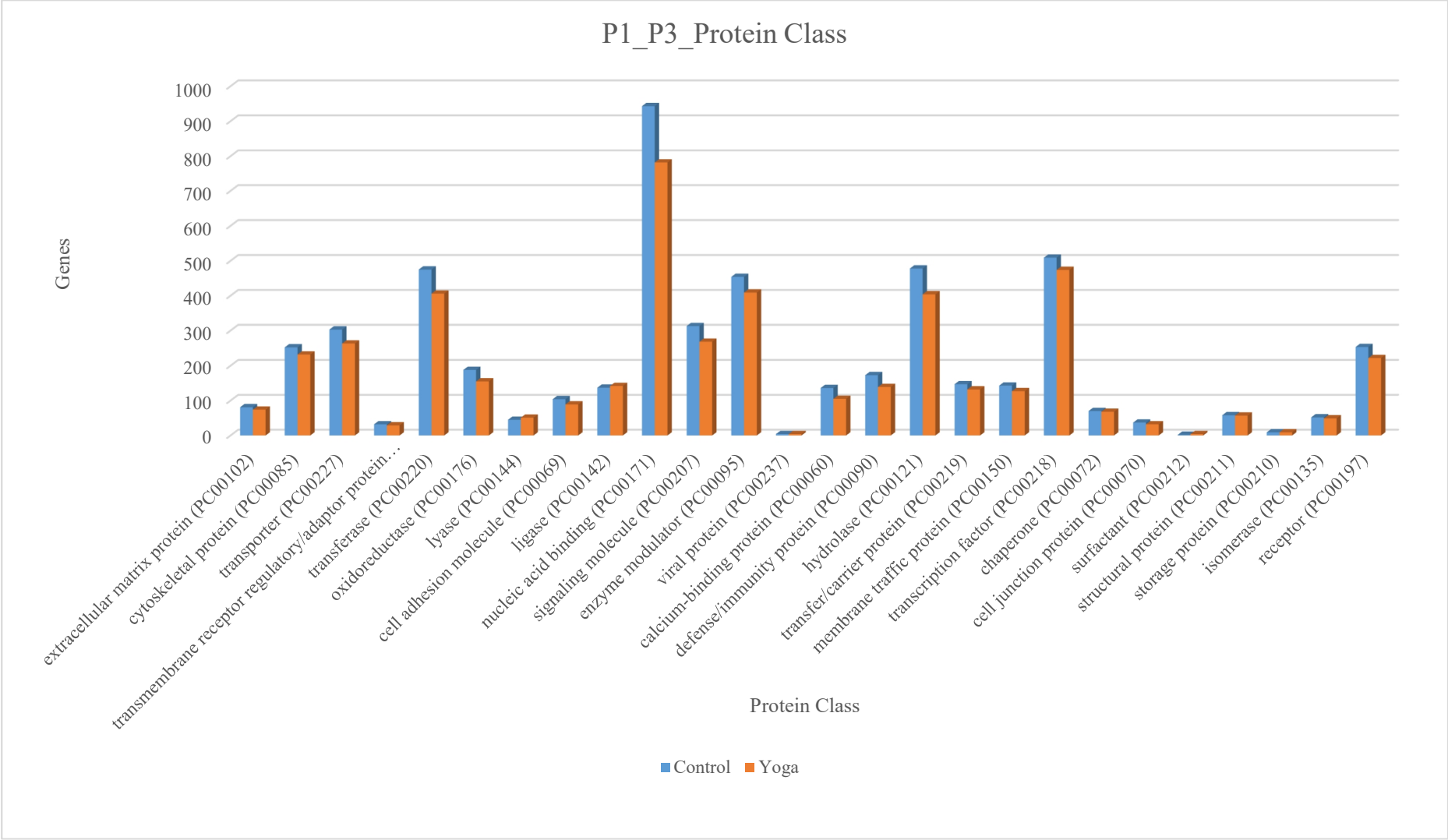


Fig 6.5.1f: Classification of genes based on Gene Ontology – Protein Class of Differentially Regulated Genes for timepoint – Post1 versus Post3 in Control and Yoga groups.

Gene Ontology Classification [Post1 versus Post 3]	**Control** (No of genes)	**Yoga** (No of genes)
Biological Process		
Cellular component organization or biogenesis (GO:0071840)	674	623
Cellular process (GO:0009987)	3094	2670
Localization (GO:0051179)	802	723
Reproduction (GO:0000003)	117	94
Biological regulation (GO:0065007)	884	743
Response to stimulus (GO:0050896)	990	828
Developmental process (GO:0032502)	655	568
Rhythmic process (GO:0048511)	2	2
Multicellular organismal process (GO:0032501)	541	478
Locomotion (GO:0040011)	54	46
Biological adhesion (GO:0022610)	147	130
Metabolic process (GO:0008152)	2588	2232
Growth (GO:0040007)	6	5
Immune system process (GO:0002376)	227	173
Cell killing (GO:0001906)	4	4
Molecular Function		
Transporter activity (GO:0005215)	344	290
Translation regulator activity (GO:0045182)	42	32
Catalytic activity (GO:0003824)	1896	1632
Channel regulator activity (GO:0016247)	15	8
Receptor activity (GO:0004872)	357	300
Signal transducer activity (GO:0004871)	164	129
Antioxidant activity (GO:0016209)	17	11
Structural molecule activity (GO:0005198)	359	297
Binding (GO:0005488)	1996	1737

Protein Class		
Extracellular matrix protein (PC00102)	81	74
Cytoskeletal protein (PC00085)	252	232
Transporter (PC00227)	303	263
Transmembrane receptor regulatory/adaptor protein (PC00226)	32	29
Transferase (PC00220)	475	406
Oxidoreductase (PC00176)	188	155
Lyase (PC00144)	45	51
Cell adhesion molecule (PC00069)	104	89
Ligase (PC00142)	137	142
Nucleic acid binding (PC00171)	943	782
Signaling molecule (PC00207)	313	268
Enzyme modulator (PC00095)	454	409
Viral protein (PC00237)	4	4
Calcium-binding protein (PC00060)	136	105
Defence/immunity protein (PC00090)	173	139
Hydrolase (PC00121)	478	404
Transfer/carrier protein (PC00219)	147	132
Membrane traffic protein (PC00150)	143	127
Transcription factor (PC00218)	509	474
Chaperone (PC00072)	70	68
Cell junction protein (PC00070)	37	32
Surfactant (PC00212)	2	4
Structural protein (PC00211)	58	57
Storage protein (PC00210)	9	9
Isomerase (PC00135)	52	49
Receptor (PC00197)	253	222

Tab 6.5.1B: Classification of genes based on Gene Ontology of Differentially Regulated Genes for timepoint – Post1 versus Post3 in Control and Yoga groups.

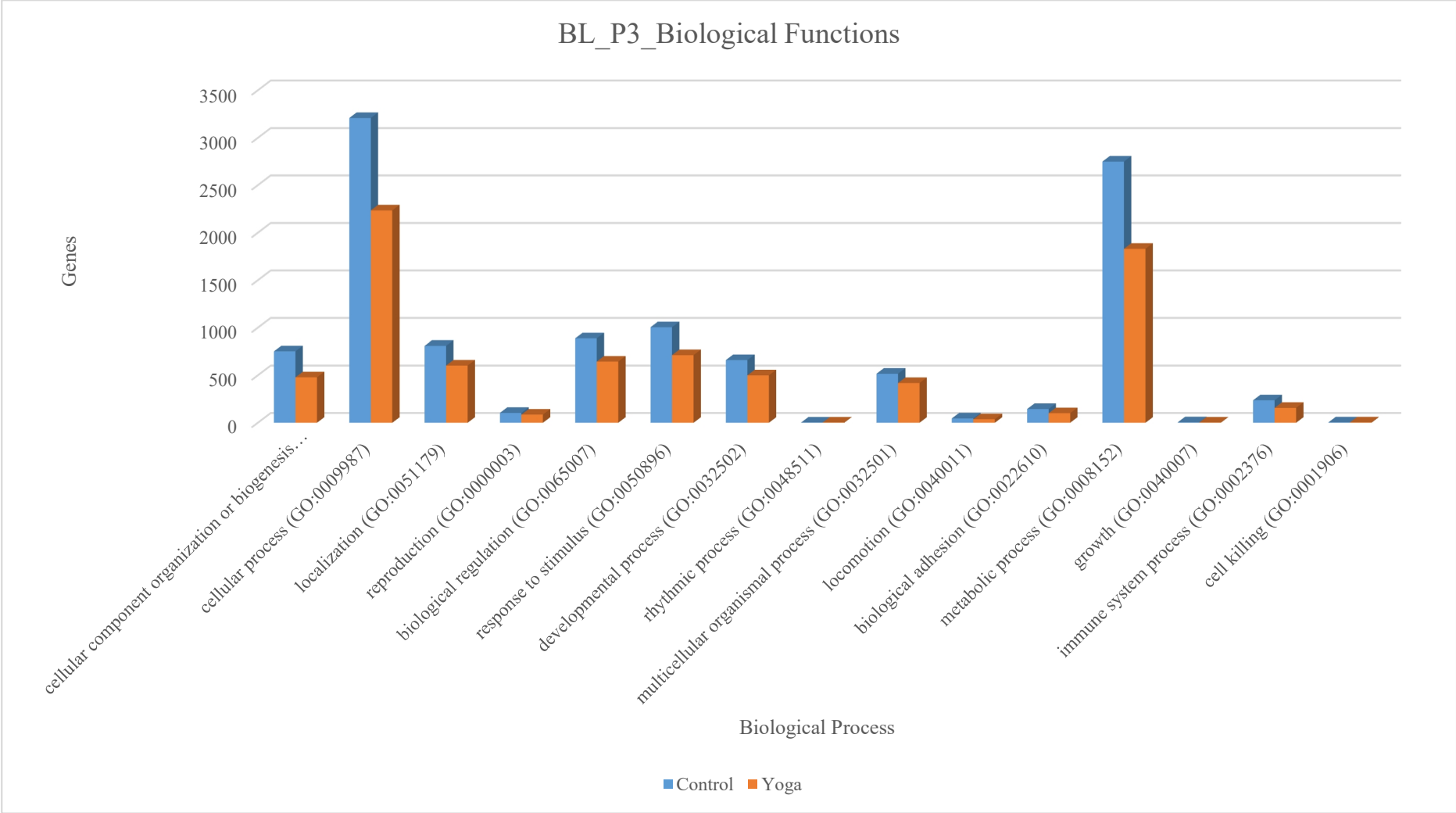


Fig 6.5.1g: Classification of genes based on Gene Ontology – Biological Process of Differentially Regulated Genes for timepoint – Baseline versus Post3 in Control and Yoga groups

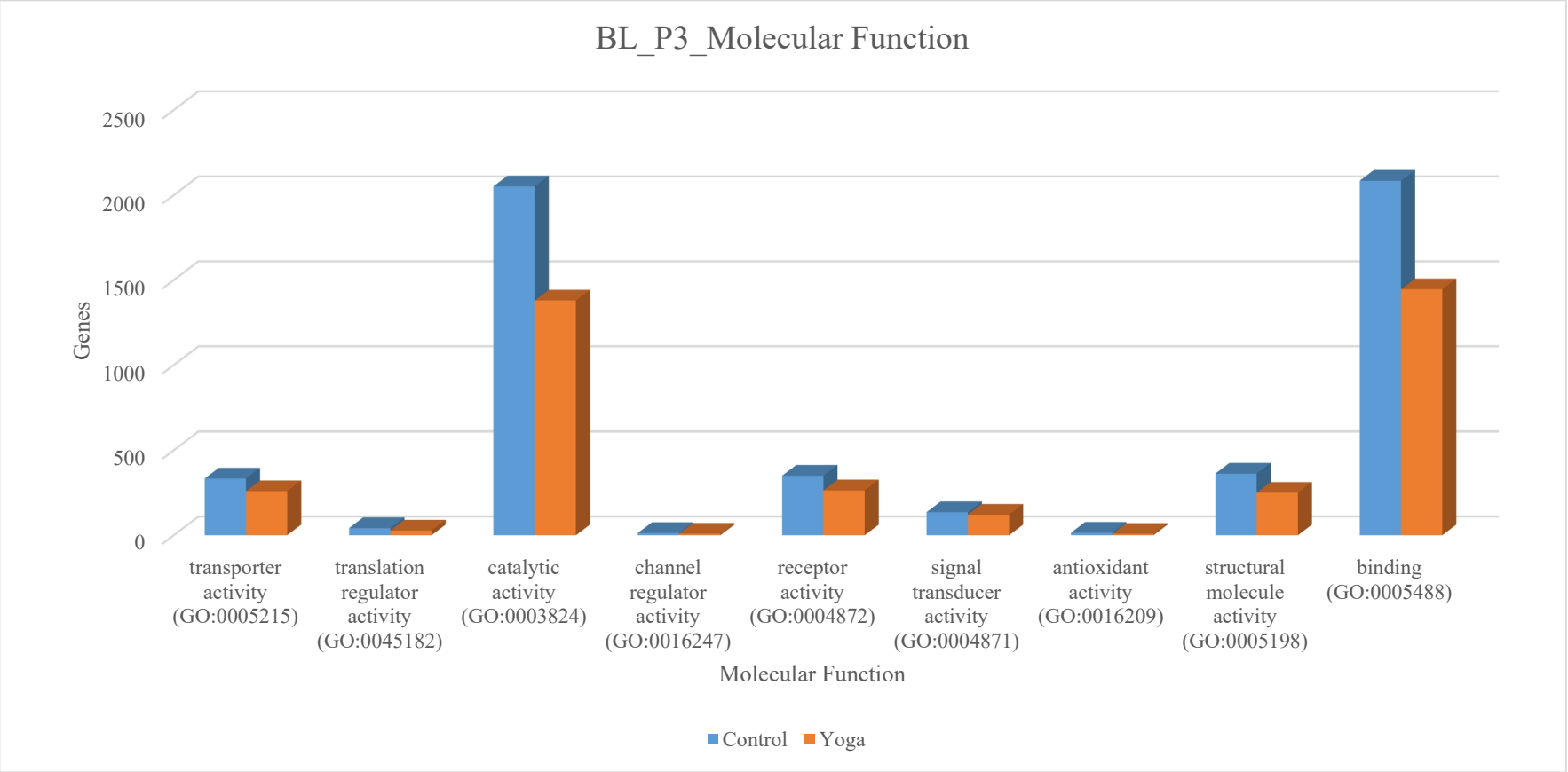


Fig 6.5.1h: Classification of genes based on Gene Ontology – Molecular Function of Differentially Regulated Genes for timepoint – Baseline versus Post3 in Control and Yoga groups

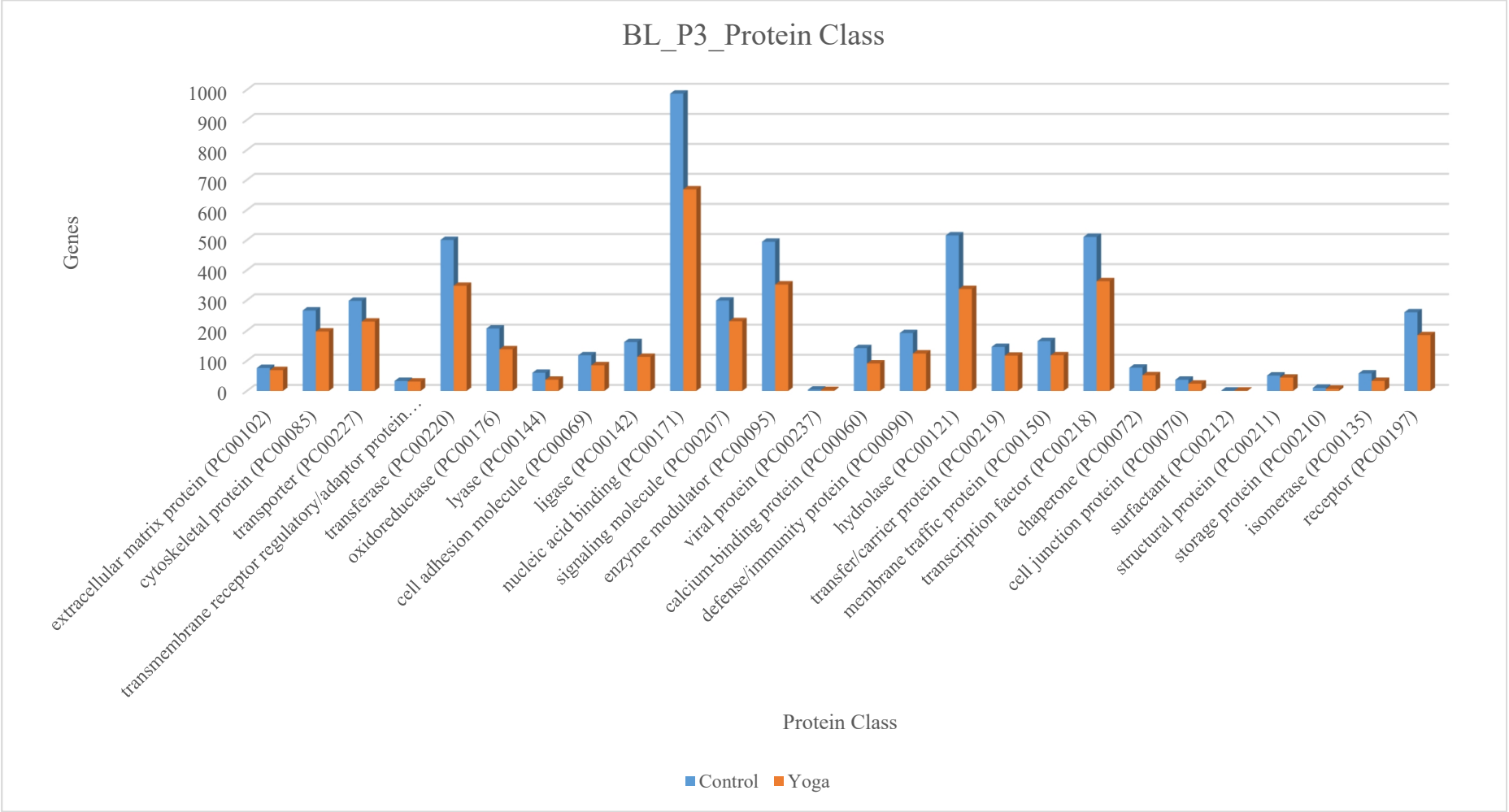


Fig 6.5.1i: Figure representing Gene Ontology classification – Molecular Function of Differentially Regulated Genes for timepoint – Baseline versus Post3 between Control and Yoga groups

Gene Ontology Classification [Baseline versus Post 3]	**Control** (No of genes)	**Yoga** (No of genes)
Biological Process		
Cellular component organization or biogenesis (GO:0071840)	753	479
Cellular process (GO:0009987)	3209	2235
Localization (GO:0051179)	810	603
Reproduction (GO:0000003)	104	86
Biological regulation (GO:0065007)	888	645
Response to stimulus (GO:0050896)	1005	713
Developmental process (GO:0032502)	661	500
Rhythmic process (GO:0048511)	3	3
Multicellular organismal process (GO:0032501)	517	419
Locomotion (GO:0040011)	46	37
Biological adhesion (GO:0022610)	145	101
Metabolic process (GO:0008152)	2751	1831
Growth (GO:0040007)	5	3
Immune system process (GO:0002376)	237	157
Cell killing (GO:0001906)	4	4
Molecular Function		
Transporter activity (GO:0005215)	334	259
Translation regulator activity (GO:0045182)	42	28
Catalytic activity (GO:0003824)	2052	1380
Channel regulator activity (GO:0016247)	13	9
Receptor activity (GO:0004872)	351	264
Signal transducer activity (GO:0004871)	136	121
Antioxidant activity (GO:0016209)	15	8
Structural molecule activity (GO:0005198)	363	250
Binding (GO:0005488)	2085	1446

Protein Class		
Extracellular matrix protein (PC00102)	76	69
Cytoskeletal protein (PC00085)	266	197
Transporter (PC00227)	298	230
Transmembrane receptor regulatory/adaptor protein (PC00226)	33	31
Transferase (PC00220)	500	348
Oxidoreductase (PC00176)	207	138
Lyase (PC00144)	60	37
Cell adhesion molecule (PC00069)	118	85
Ligase (PC00142)	162	113
Nucleic acid binding (PC00171)	987	668
Signaling molecule (PC00207)	299	231
Enzyme modulator (PC00095)	494	352
Viral protein (PC00237)	4	3
Calcium-binding protein (PC00060)	142	91
Defense/immunity protein (PC00090)	192	124
Hydrolase (PC00121)	515	337
Transfer/carrier protein (PC00219)	146	117
Membrane traffic protein (PC00150)	165	118
Transcription factor (PC00218)	510	363
Chaperone (PC00072)	77	52
Cell junction protein (PC00070)	37	24
Surfactant (PC00212)	1	1
Structural protein (PC00211)	51	44
Storage protein (PC00210)	10	7
Isomerase (PC00135)	58	33
Receptor (PC00197)	260	185

Table 6.5.1C: Classification of genes based on Gene Ontology of Differentially Regulated Genes for timepoint – Baseline versus Post3 in Control and Yoga groups

6.5.2. Overrepresentation Analysis of Differentially Regulated Genes

Overrepresentation analysis with Bonferroni correction for multiple testing was performed using PANTHER database [version 12, released 10-07-2017] on the Differentially Expressed Genes (DEG) under three conditions for both Yoga and Control Groups:

a. Baseline Vs Post 1

b. Post 1 Vs Post 3

c. Baseline Vs Post 3

The overrepresented DEGs were classified according to PANTHER protein class, GO Slim Molecular Function, GO Slim Biological Process and GO Slim Cellular Component. The Details of classification for each time point is explained below.

Baseline Vs Post 1

GO Slim Biological Process:

In the Control group, GO terms corresponding to the 'Biological Process' the following processes were over-represented- mRNA splicing, via spliceosome (GO:0000398) [p=0.02], mRNA processing (GO:0006397) [p=0.003], translation (GO:0006412) [p=0.002], transcription from RNA polymerase II promoter (GO:0006366) [p=0.05], RNA metabolic process (GO:0016070) [p≤0.001], cellular component biogenesis (GO:0044085) [p≤0.001], transcription, DNA-dependent (GO:0006351) [p≤0.001], organelle organization (GO:0006996) [p=0.003], phosphate-containing compound metabolic process (GO:0006796) [p=0.02], biosynthetic process (GO:0009058) [p≤0.001], nitrogen compound metabolic process (GO:0006807) [p≤0.001], protein metabolic process (GO:0019538) [p=0.001], cellular component organization or biogenesis (GO:0071840) [p=0.02], nucleobase-containing compound metabolic process (GO:0006139) [p≤0.001], metabolic process

(GO:0008) [p≤0.001], primary metabolic process (GO:0044238) [p≤0.001], cellular process (GO:0009987) [p≤0.001].

Following processes were under-represented: biological regulation (GO:0065007) [p=0.03], regulation of biological process (GO:0050789) [p=0.006], cell surface receptor signalling pathway (GO:0007166) [p=0.05], single-multicellular organism process (GO:0044707) [p≤0.001], multicellular organismal process (GO:0032501) [p≤0.001], system process (GO:0003008) [p≤0.001], G-protein coupled receptor signalling pathway (GO:0007186) [p≤0.001], neurological system process (GO:0050877) [p≤0.001], muscle organ development (GO:0007517) [p=0.03], sensory perception (GO:0007600) [p≤0.001], sensory perception of chemical stimulus (GO:0007606) [p≤0.001], sensory perception of smell (GO:0007608) [p≤0.001].

In the Yoga group, GO terms corresponding to the 'Biological Process' - metabolic process (GO:0008152) [p=0.05] and cellular process (GO:0009987) [p=0.02] were over represented. DEG's related to GO terms system process (GO:0003008) [p=0.007], neurological system process (GO:0050877) [p≤0.001], sensory perception (GO:0007600) [p≤0.001], sensory perception of smell (GO:0007608) [p≤0.001], sensory perception of chemical stimulus (GO:0007606) [p≤0.001] were underrepresented *(Fig 6.5.2a)*.

GO Slim Molecular Function:

In the Control group GO terms corresponding to the 'Molecular Function' - structural constituent of ribosome (GO:0003735) [p≤0.001], chromatin binding (GO:0003682) [p=0.03], RNA binding (GO:0003723) [p≤0.001], transferase activity (GO:0016740) [p≤0.001], nucleic acid binding (GO:0003676) [p≤0.001], catalytic activity (GO:0003824) [p≤0.001], binding (GO:0005488) [p≤0.001] were over expressed and

the functions corresponding to receptor activity (GO:0004872) [p≤0.001], G-protein coupled receptor activity (GO:0004930) [p≤0.001], signal transducer activity (GO:0004871) [p≤0.001] were underrepresented.

In the Yoga group, GO terms corresponding to only binding (GO:0005488) [p=0.03] was overrepresented and functions corresponding to the receptor activity (GO:0004872) [p≤0.001], signal transducer activity (GO:0004871) [p≤0.001] were underrepresented *(Fig 6.5.2b)*.

GO Slim Protein Class

In the Control group, the protein class corresponding to ribosomal protein (PC00202) [p≤0.001], RNA binding protein (PC00031) [p≤0.001], transferase (PC00220) [p≤0.001], and nucleic acid binding (PC00171) [p≤0.001] were overrepresented and the GO terms in protein class corresponding to homeobox transcription factor (PC00119) [p≤0.001], helix-turn-helix transcription factor (PC00116) [p≤0.001] were underrepresented.

In the yoga group, GO terms corresponding to the protein class RNA binding protein (PC00031) [p≤0.001], transferase (PC00220) [p=0.02] and nucleic acid binding (PC00171) [p=0.04] were over-represented *(Fig 6.5.2c)*.

Post 1 Vs Post 3

GO Slim Biological Process

In the Control group, GO terms corresponding to the 'Biological Process' – translation (GO:0006412) [p≤0.001], transcription, DNA-dependent (GO:0006351) [p=0.003], RNA metabolic process (GO:0016070) [p≤0.001], biosynthetic process (GO:0009058) [p≤0.001]

nucleobase-containing compound metabolic process (GO:0006139) [p≤0.001], metabolic process (GO:0008152) [p≤0.001], primary metabolic process

(GO:0044238) [p=0.001], and cellular process (GO:0009987) [p=0.004] were overrepresented and the GO terms corresponding to single-multicellular organism process (GO:0044707) [p≤0.001], multicellular organismal process (GO:0032501) [p≤0.001], G-protein coupled receptor signalling pathway (GO:0007186) [p=0.015], system process (GO:0003008) [p≤0.001], neurological system process (GO:0050877) [p≤0.001], defense response to bacterium (GO:0042742) [p=0.04], sensory perception (GO:0007600) [p≤0.001], sensory perception of chemical stimulus (GO:0007606) [p≤0.001] and sensory perception of smell (GO:0007608) [p≤0.001] were underrepresented.

In the Yoga group, GO terms corresponding to Biological process, - cellular component organization or biogenesis (GO:0071840) [p=0.05], metabolic process (GO:0008152) [p≤0.001], primary metabolic process (GO:0044238) [p=0.01] and cellular process (GO:0009987) [p=0.02] were overrepresented. And, the processes, single-multicellular organism process (GO:0044707) [p≤0.001], multicellular organismal process (GO:0032501) [p≤0.001], system process (GO:0003008) [p≤0.001], neurological system process (GO:0050877) [p≤0.001], sensory perception (GO:0007600) [p≤0.001], sensory perception of smell (GO:0007608) [p≤0.001] and sensory perception of chemical stimulus (GO:0007606) [p≤0.001] were underrepresented *(Fig 6.5.2d)*.

GO Slim Molecular Functions

In the Control group, GO terms corresponding to the 'Molecular Functions', - structural constituent of ribosome (GO:0003735) [p≤0.001], RNA binding (GO:0003723) [p=0.013] and nucleic acid binding (GO:0003676) [p=0.0012] were overrepresented and GO terms corresponding to receptor activity (GO:0004872)

[p≤0.001], G-protein coupled receptor activity (GO:0004930) [p≤0.001], and signal transducer activity (GO:0004871) [p≤0.001] were underrepresented.

In the Yoga group, the GO term associated with the Molecular Function, nucleic acid binding (GO:0003676) [p≤0.001] was significantly overrepresented and receptor activity (GO:0004872) [p≤0.001], G-protein coupled receptor activity (GO:0004930) [p≤0.001], signal transducer activity (GO:0004871) [p≤0.001] and ligand-gated ion channel activity (GO:0015276) [p=0.03] were underrepresented *(Fig 6.5.2e)*

GO Slim Protein Class

In the Control group, GO terms corresponding to the 'Protein Class' - ribosomal protein (PC00202) [p≤0.001], RNA binding protein (PC00031) [p≤0.001] and nucleic acid binding (PC00171) [p≤0.001] were overrepresented and no class of proteins were underrepresented under the set criteria.

In the Yoga group, GO terms corresponding to the Protein Class, RNA binding protein (PC00031) [p=0.04] and nucleic acid binding (PC00171) [p=0.005] were overrepresented and no other GO protein class was underrepresented in the set criteria *(Fig 6.5.2f)*.

Baseline Vs Post 3

GO Slim Biological Process

In the Control Group, GO terms corresponding to the 'Biological Process' – mRNA processing (GO:0006397) [p≤0.001], translation (GO:0006412) [p≤0.001], mRNA splicing, via spliceosome (GO:0000398) [p=0.01], cellular component biogenesis (GO:0044085) [p≤0.001], organelle organization (GO:0006996) [p=0.0000697], RNA metabolic process (GO:0016070) [p≤0.001], catabolic process (GO:0009056) [p≤0.001], protein metabolic process (GO:0019538) [p≤0.001], biosynthetic process (GO:0009058) [p≤0.001], cellular component organization or biogenesis

(GO:0071840) [p≤0.001], cellular component organization (GO:0016043) [p=0.0483], metabolic process (GO:0008152) [p≤0.001], nitrogen compound metabolic process (GO:0006807) [p=0.003], primary metabolic process (GO:0044238) [p≤0.001], nucleobase-containing compound metabolic process (GO:0006139) [p≤0.001], cellular process (GO:0009987) [p≤0.001], were overrepresented and the GO terms, single-multicellular organism process (GO:0044707) [p≤0.001], multicellular organismal process (GO:0032501) [p≤0.001], G-protein coupled receptor signaling pathway (GO:0007186) [p≤0.001], system process (GO:0003008) [p≤0.001], neurological system process (GO:0050877) [p≤0.001], sensory perception (GO:0007600) [p≤0.001], sensory perception of smell (GO:0007608) [p≤0.001], sensory perception of chemical stimulus (GO:0007606) [p≤0.001], sensory perception of taste (GO:0050909) [p=0.006] were underrepresented.

In the Yoga group, GO process corresponding to single-multicellular organism process (GO:0044707) [p=0.003], multicellular organismal process (GO:0032501) [p=0.001], system process (GO:0003008) [p=0.01], neurological system process (GO:0050877) [p=0.003], sensory perception (GO:0007600) [p≤0.001], sensory perception of chemical stimulus (GO:0007606) [p≤0.001] and sensory perception of smell (GO:0007608) [p≤0.001] were all underrepresented. Interestingly no Biological process was overrepresented *(Fig 6.5.2g)*.

GO Slim Molecular Function

In the Control group, GO terms corresponding to the 'Molecular Functions', - structural constituent of ribosome (GO:0003735) [p≤0.001], RNA binding (GO:0003723) [p≤0.001], kinase activity (GO:0016301) [p=0.03], enzyme regulator activity (GO:0030234) [p=0.04], transferase activity (GO:0016740) [p=0.02], nucleic

acid binding (GO:0003676) [p=0.001], catalytic activity (GO:0003824) [p≤0.001] and binding (GO:0005488) [p=0.000636] were overrepresented. The GO terms with functions corresponding to receptor activity (GO:0004872) [p≤0.001], G-protein coupled receptor activity (GO:0004930) [p≤0.001], signal transducer activity (GO:0004871) [p≤0.001] and cytokine receptor binding (GO:0005126) [p=0.03] were underrepresented.

In the Yoga group, the GO terms corresponding to the Molecular function, receptor activity (GO:0004872) [p≤0.001], signal transducer activity (GO:0004871) [p≤0.001] were underrepresented. No GO function categories were overrepresented *(Fig 6.5.2h)*.

Go Slim Protein Class

In the Control group, GO terms corresponding to the 'Protein Class" - ribosomal protein (PC00202) [p≤0.001], RNA binding protein (PC00031) [p≤0.001], nucleic acid binding (PC00171) [p≤0.001], transferase (PC00220) [p=0.004] were overrepresented and the GO class corresponding to G-protein coupled receptor (PC00021) [p=0.02], homeobox transcription factor (PC00119) [p=0.001] and helix-turn-helix transcription factor (PC00116) [p=0.001] were underrepresented.

In the Yoga group, GO terms corresponding to RNA binding protein (PC00031) [p=0.002] and nucleic acid binding (PC00171) [p=0.004] were overrepresented and no GO terms were overrepresented *(Fig 6.5.2i)*.

The overrepresented functions, process and protein class are mentioned below

Condition	Molecular Function	Biological process	Protein Class
BL_P1 Yoga ↑	binding (GO:0005488)	metabolic process (GO:0008152) cellular process (GO:0009987)	RNA binding protein (PC00031) transferase (PC00220) nucleic acid binding (PC00171)
BL_P1 Yoga ↓	receptor activity (GO:0004872) signal transducer activity (GO:0004871)	system process (GO:0003008) neurological system process (GO:0050877) sensory perception (GO:0007600) sensory perception of smell (GO:0007608) sensory perception of chemical stimulus(GO:0007606)	
BL_P1 Control ↑	structural constituent of ribosome (GO:0003735) chromatin binding (GO:0003682) RNA binding (GO:0003723) transferase activity (GO:0016740) nucleic acid binding (GO:0003676) catalytic activity (GO:0003824)	mRNA splicing, via spliceosome (GO:0000398) mRNA processing (GO:0006397) translation (GO:0006412) transcription from RNA polymerase II promoter (GO:0006366) RNA metabolic process (GO:0016070) cellular component biogenesis (GO:0044085)	ribosomal protein (PC00202) RNA binding protein (PC00031) transferase (PC00220) nucleic acid binding (PC00171)

	binding (GO:0005488)	transcription, DNA-dependent (GO:0006351) organelle organization (GO:0006996) phosphate-containing compound metabolic process (GO:0006796) biosynthetic process (GO:0009058) nitrogen compound metabolic process (GO:0006807) protein metabolic process (GO:0019538) cellular component organization or biogenesis (GO:0071840) nucleobase-containing compound metabolic process (GO:0006139) metabolic process (GO:0008152) primary metabolic process (GO:0044238) cellular process (GO:0009987)	
BL_P1 Control ↓	receptor activity (GO:0004872) G-protein coupled receptor activity (GO:0004930) signal transducer activity (GO:0004871)	biological regulation (GO:0065007) regulation of biological process (GO:0050789) cell surface receptor signalling pathway (GO:0007166) single-multicellular organism process (GO:0044707)	homeobox transcription factor (PC00119) helix-turn-helix transcription factor (PC00116)

		multicellular organismal process (GO:0032501) system process (GO:0003008) G-protein coupled receptor signalling pathway (GO:0007186) neurological system process (GO:0050877) muscle organ development (GO:0007517) sensory perception (GO:0007600) sensory perception of chemical stimulus (GO:0007606) sensory perception of smell (GO:0007608)	
P1_P3 Yoga ↑	nucleic acid binding (GO:0003676)	cellular component organization or biogenesis (GO:0071840) metabolic process (GO:0008152) primary metabolic process (GO:0044238) cellular process (GO:0009987)	RNA binding protein (PC00031) nucleic acid binding (PC00171)
P1_P3 Yoga ↓	receptor activity (GO:0004872) G-protein coupled receptor activity (GO:0004930) signal transducer activity (GO:0004871)	single-multicellular organism process (GO:0044707) multicellular organismal process (GO:0032501) system process (GO:0003008) neurological system process (GO:0050877) sensory perception (GO:0007600)	NIL

	ligand-gated ion channel activity (GO:0015276)	sensory perception of smell (GO:0007608) sensory perception of chemical stimulus(GO:0007606)	
P1_P3 Control ↑	structural constituent of ribosome (GO:0003735) RNA binding (GO:0003723) nucleic acid binding (GO:0003676)	translation (GO:0006412) transcription, DNA-dependent (GO:0006351) RNA metabolic process (GO:0016070) biosynthetic process (GO:0009058) nucleobase-containing compound metabolic process (GO:0006139) metabolic process (GO:0008152) primary metabolic process (GO:0044238) cellular process (GO:0009987)	ribosomal protein (PC00202) RNA binding protein (PC00031) nucleic acid binding (PC00171)
P1_P3 Control ↓	receptor activity (GO:0004872) G-protein coupled receptor activity (GO:0004930) signal transducer activity (GO:0004871)	cell surface receptor signalling pathway (GO:0007166) single-multicellular organism process (GO:0044707) multicellular organismal process (GO:0032501) G-protein coupled receptor signalling pathway (GO:0007186) system process (GO:0003008) neurological system process (GO:0050877)	

		defence response to the bacterium (GO:0042742) sensory perception (GO:0007600) sensory perception of chemical stimulus (GO:0007606) sensory perception of smell (GO:0007608)	
BL_P3 Yoga ↑			RNA binding protein (PC00031) nucleic acid binding (PC00171)
BL_P3 Yoga ↓	receptor activity (GO:0004872) signal transducer activity (GO:0004871)	single-multicellular organism process (GO:0044707) multicellular organismal process (GO:0032501) system process (GO:0003008) neurological system process (GO:0050877) sensory perception (GO:0007600) sensory perception of chemical stimulus (GO:0007606) sensory perception of smell (GO:0007608)	
BL_P3 Control ↑	structural constituent of ribosome (GO:0003735) RNA binding (GO:0003723)	mRNA processing (GO:0006397) translation (GO:0006412) mRNA splicing, via spliceosome (GO:0000398)	ribosomal protein (PC00202) RNA binding protein (PC00031)

	kinase activity (GO:0016301) enzyme regulator activity (GO:0030234) transferase activity (GO:0016740) nucleic acid binding (GO:0003676) catalytic activity (GO:0003824) binding (GO:0005488)	cellular component biogenesis (GO:0044085) organelle organization (GO:0006996) RNA metabolic process (GO:0016070) catabolic process (GO:0009056) protein metabolic process (GO:0019538) biosynthetic process (GO:0009058) cellular component organization or biogenesis (GO:0071840) cellular component organization (GO:0016043) metabolic process (GO:0008152) nitrogen compound metabolic process (GO:0006807) primary metabolic process (GO:0044238) nucleobase-containing compound metabolic process (GO:0006139) cellular process (GO:0009987)	nucleic acid binding (PC00171) transferase (PC00220)
BL_P3 Control ↓	receptor activity (GO:0004872) G-protein coupled receptor activity (GO:0004930) signal transducer activity (GO:0004871)	single-multicellular organism process (GO:0044707) multicellular organismal process (GO:0032501) G-protein coupled receptor signalling pathway (GO:0007186)	G-protein coupled receptor (PC00021) homeobox transcription factor (PC00119)

	cytokine receptor binding (GO:0005126)	system process (GO:0003008) neurological system process (GO:0050877) sensory perception (GO:0007600) sensory perception of smell (GO:0007608) sensory perception of chemical stimulus (GO:0007606) sensory perception of taste (GO:0050909)	helix-turn-helix transcription factor (PC00116)

Table 6.5.2: Over-representation analysis of Differentially Expressed Genes for each timepoint comparison in Yoga and Control groups using PANTHER database.

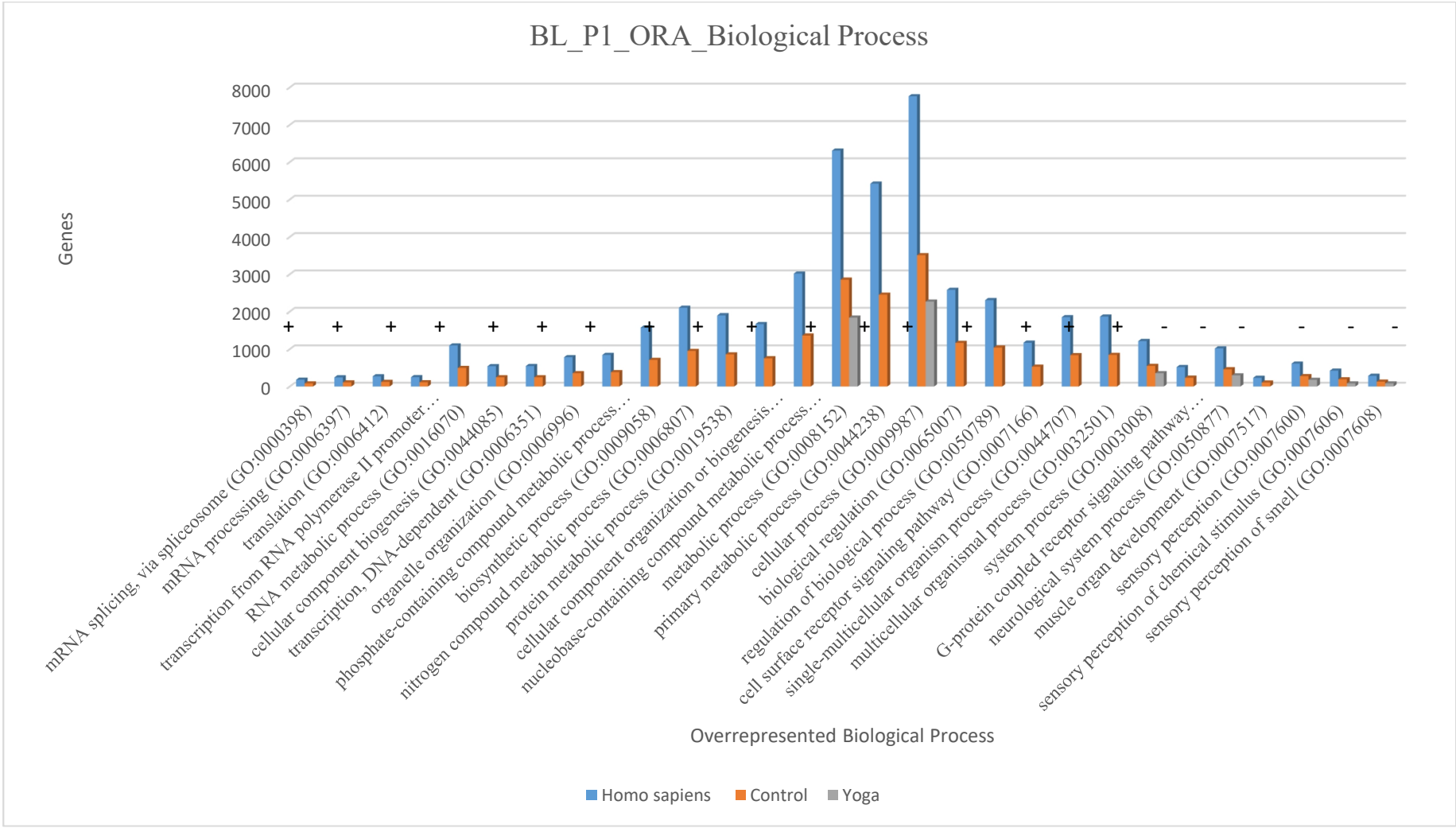


Fig 6.5.2a: Over-Representation analysis of over(+) and under(-) represented Biological Processes for DEGs in Baseline-Post1 timepoints in Yoga and Control groups and human annotated genes in PANTHER database

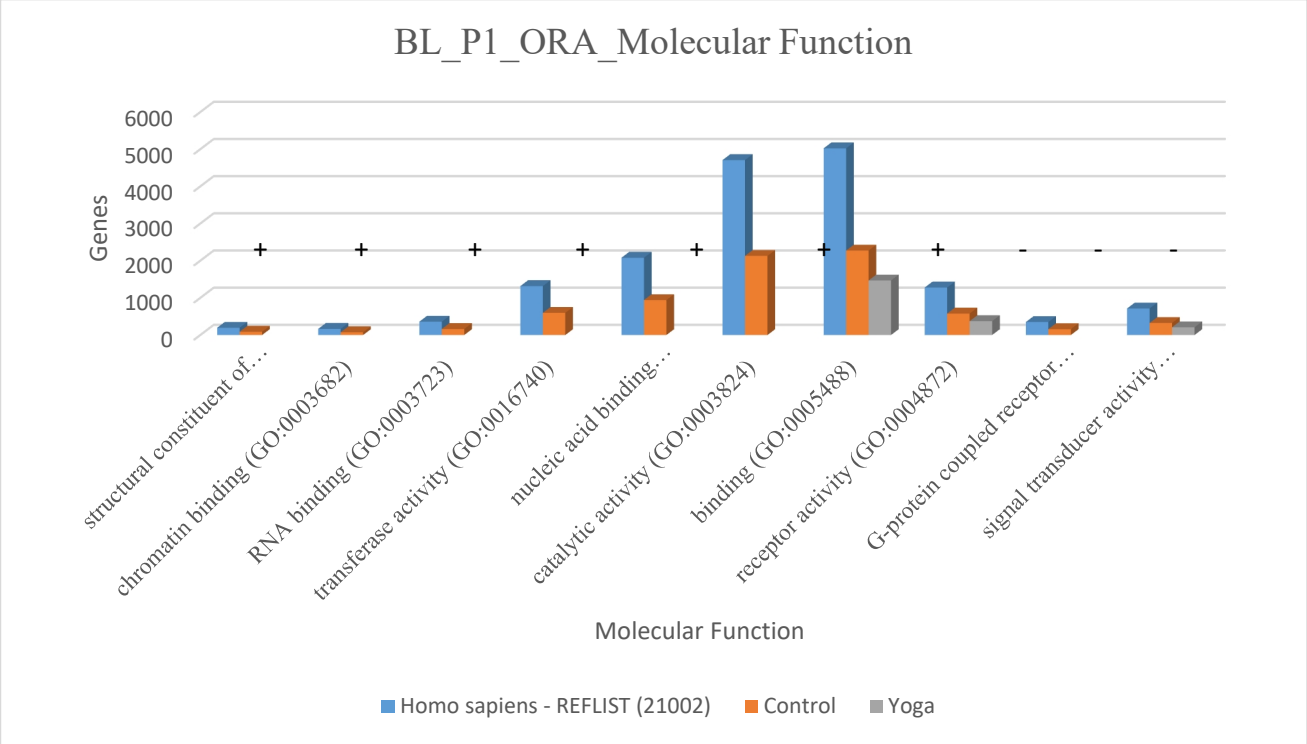


Fig 6.5.2b: Over-Representation analysis of over(+) and under(-) represented Molecular Functions for DEGs in Baseline-Post1 timepoints in Yoga and Control groups and human annotated genes in PANTHER database

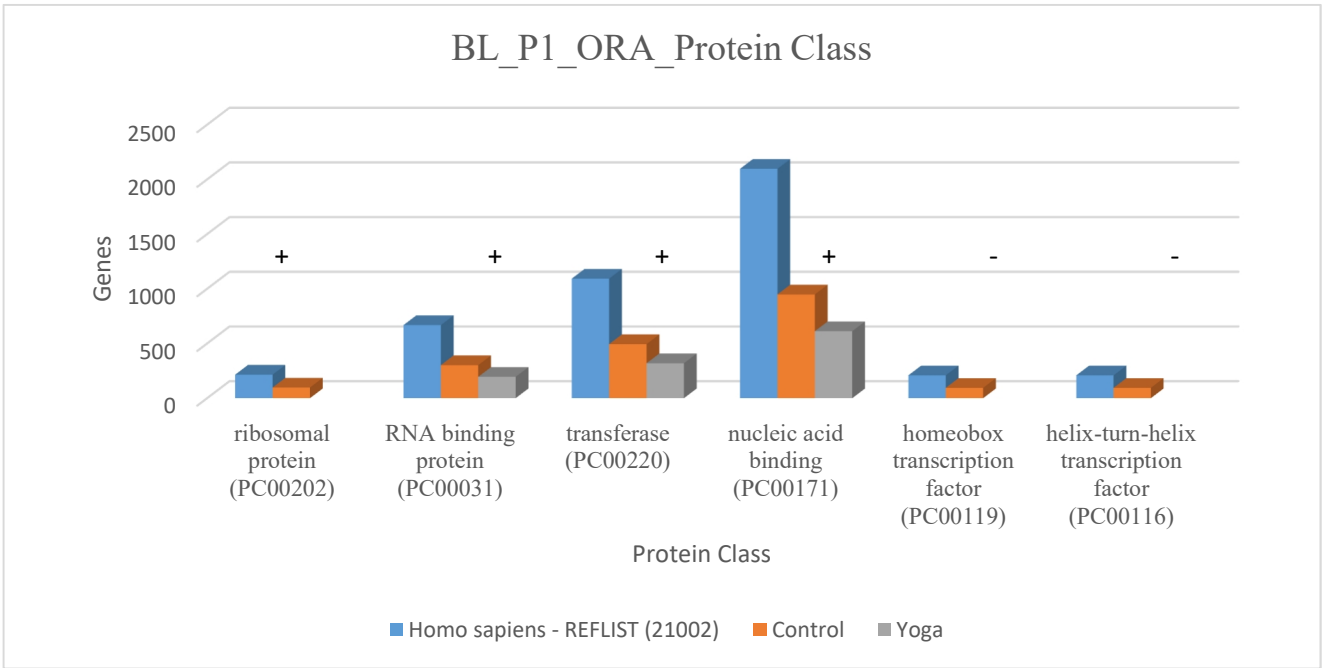


Fig 6.5.2c: Over-Representation analysis of over(+) and under(-) represented Protein Class for DEGs in Baseline-Post1 timepoints in Yoga and Control groups and human annotated genes in PANTHER database

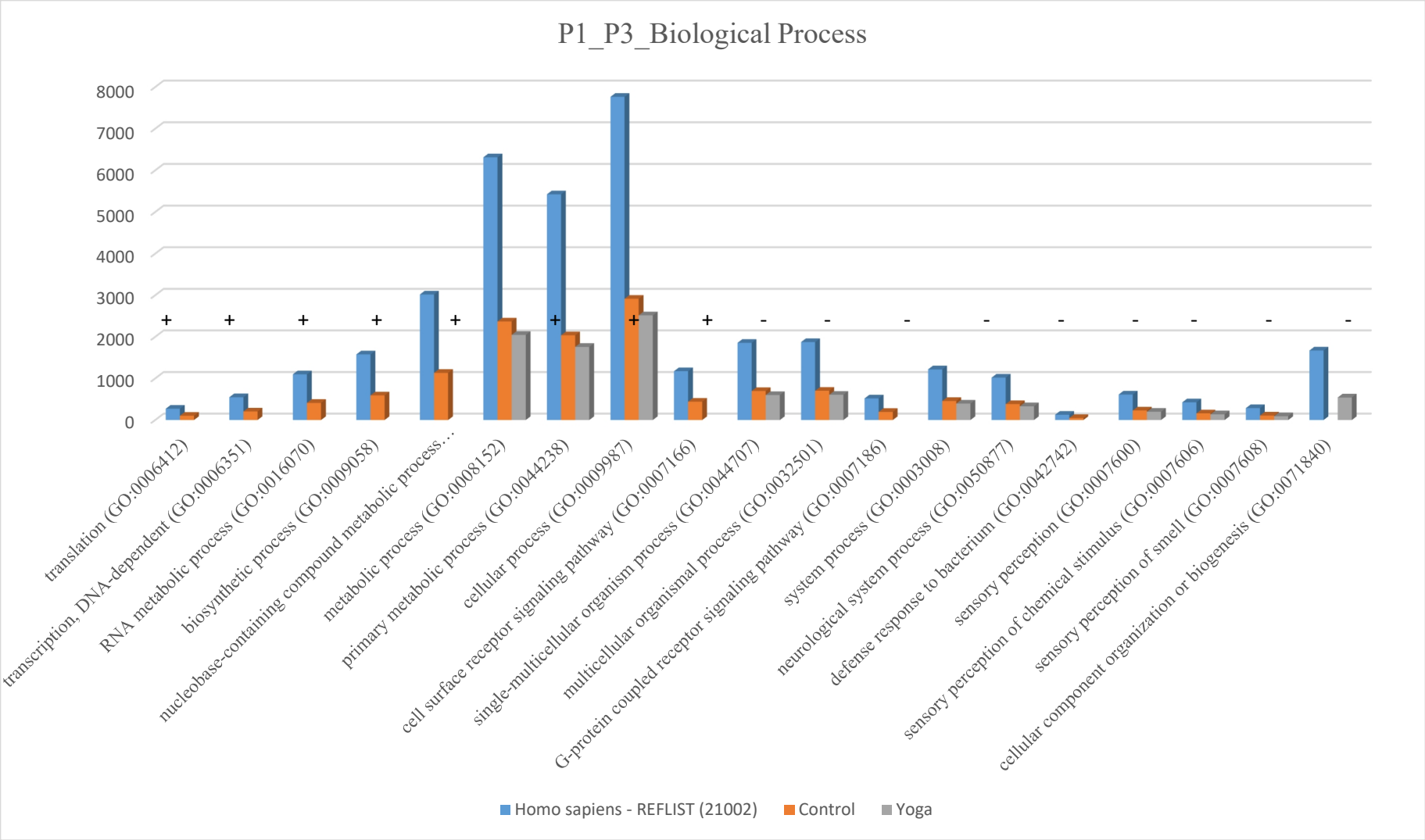


Fig 6.5.2d: Over-Representation analysis of over(+) and under(-) represented Biological Processes for DEGs in Post1-Post3 timepoints in Yoga and Control groups and human annotated genes in PANTHER database

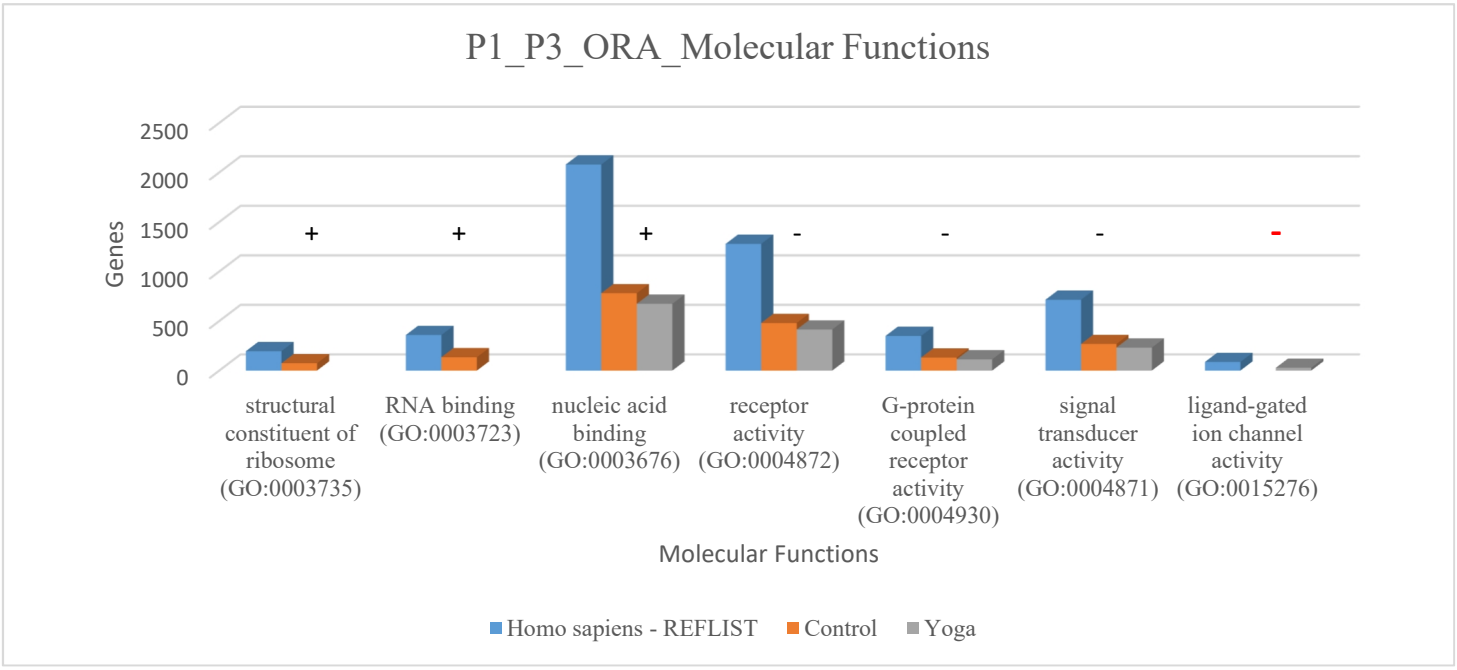


Fig 6.5.2e: Over-Representation analysis of over(+) and under(-) represented Molecular functions for DEGs in Post1-Post3 timepoints in Yoga and Control groups and human annotated genes in PANTHER database

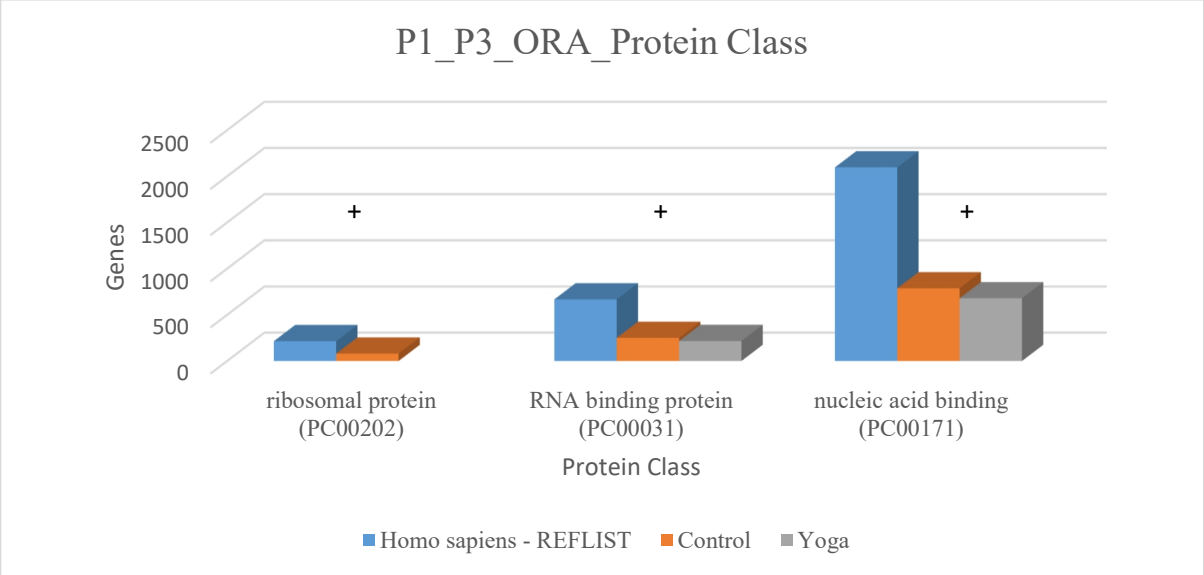


Fig 6.5.2f: Over-Representation analysis of over(+) and under(-) represented Protein Class for DEGs in Post1-Post3 timepoints in Yoga and Control groups and human annotated genes in PANTHER database

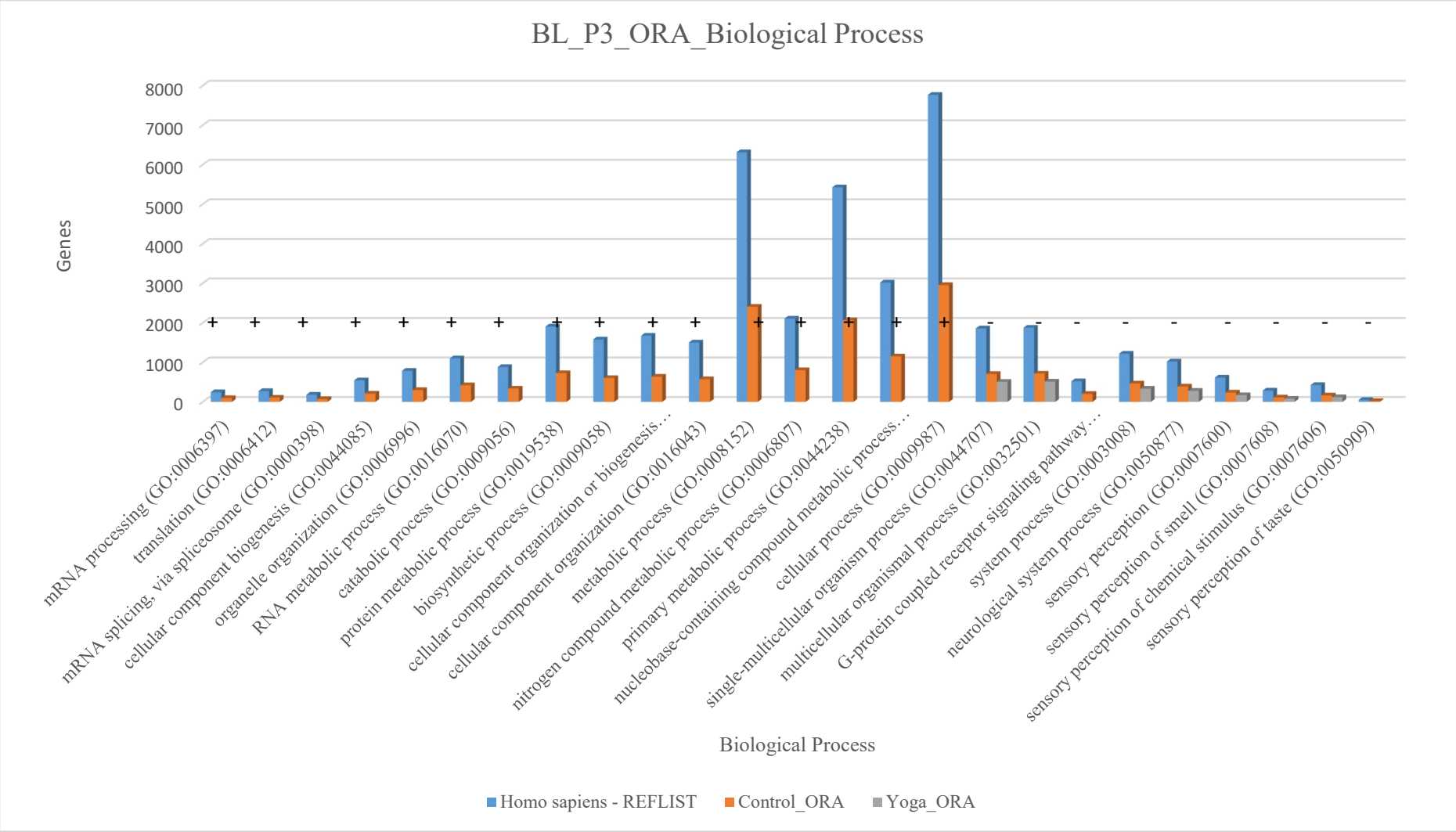


Fig 6.5.2g: Over-Representation analysis of over(+) and under(-) represented Biological Process for DEGs in Baseline-Post3 timepoints in Yoga and Control groups and human annotated genes in PANTHER database

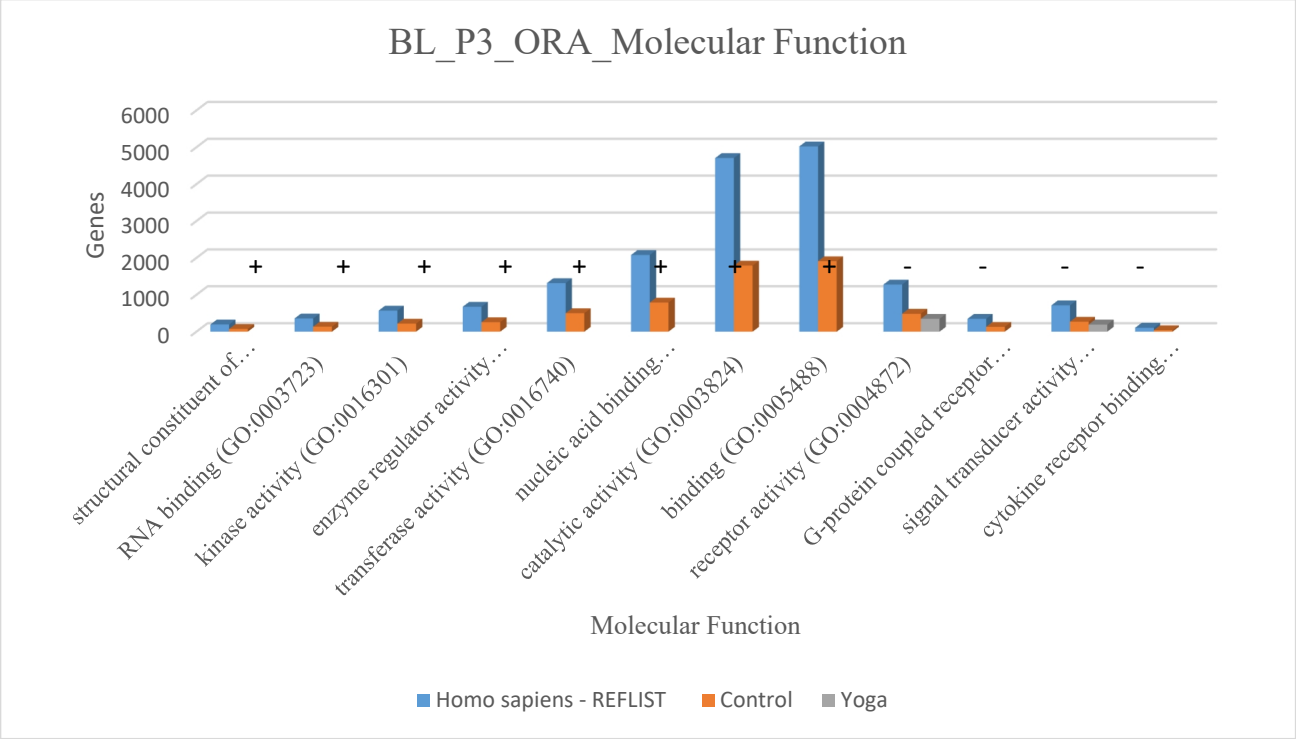


Fig 6.5.2h: Over-Representation analysis of over(+) and under(-) represented Molecular functions for DEGs in Baseline-Post3 timepoints in Yoga and Control groups and human annotated genes in PANTHER database

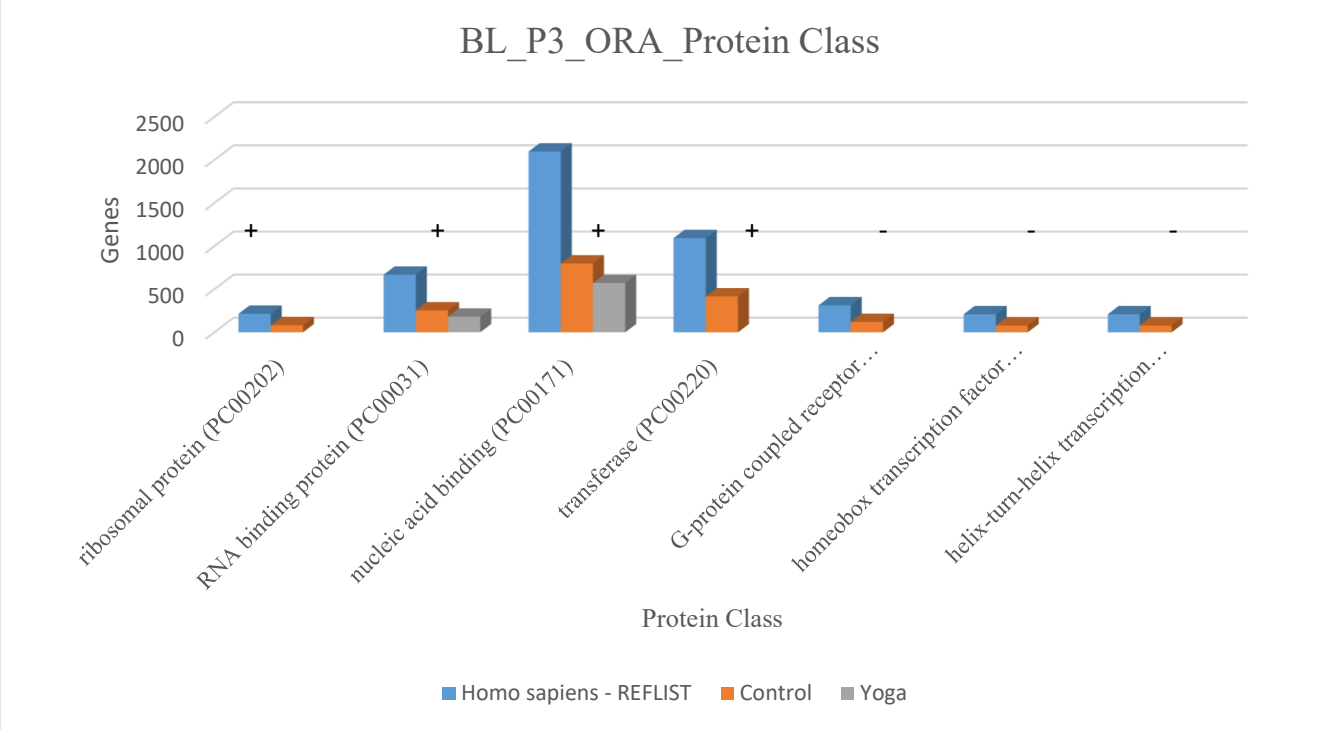


Fig 6.5.2i: Over-Representation analysis of over(+) and under(-) represented Protein Class for DEGs in Baseline-Post3 timepoints in Yoga and Control groups and human annotated genes in PANTHER database

6.5.3. Gene Set Enrichment Analysis

The fold change values of DEG from two groups with Entrez ID alone were enriched against the reference human genes in the Consensus database. The enriched pathways were obtained from 11 databases: Wikipathways, Netpath, Kegg, Humancyc, Ehmn, Inoh, Smpdb, Biocarta, Reactome, Signalink, and Pid.

The fold change values of a timepoint across both the groups were tabulated considering the common genes between both the groups and the DEG unique to either of the groups.

The criterion for enrichment was set with a minimum number of measured genes in a given pathway to be four and p-value cut-off was set at 0.01.

Top 20 pathways for each timepoint comparison are listed in *Table 6.5.3*. Complete list of the significant pathways is listed as *Appendix-11*

Baseline – Post 1 Enriched Pathways

BL_P1 pathways	source	external_id	p-value	q-value
Metabolism	Reactome	R-HSA-1430728	2.96E-07	0.000991
Gene Expression	Reactome	R-HSA-74160	8.24E-07	0.001382
Signal Transduction	Reactome	R-HSA-162582	1.60E-05	0.01524
Immune System	Reactome	R-HSA-168256	1.88E-05	0.01524
Cell Cycle	Reactome	R-HSA-1640170	3.06E-05	0.01524
Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC)	Reactome	R-HSA-975957	3.46E-05	0.01524
Nonsense-Mediated Decay (NMD)	Reactome	R-HSA-927802	3.46E-05	0.01524
The citric acid (TCA) cycle and respiratory electron transport	Reactome	R-HSA-1428517	3.64E-05	0.01524
Cell Cycle, Mitotic	Reactome	R-HSA-69278	5.43E-05	0.020246
SRP-dependent cotranslational protein targeting to membrane	Reactome	R-HSA-1799339	6.44E-05	0.021059
Cytoplasmic Ribosomal Proteins	Wikipathways	WP477	6.91E-05	0.021059

Nonsense Mediated Decay (NMD) independent of the Exon Junction Complex (EJC)	Reactome	R-HSA-975956	8.14E-05	0.022763
Metabolism of amino acids and derivatives	Reactome	R-HSA-71291	0.000116	0.029919
Antigen processing: Ubiquitination & Proteasome degradation	Reactome	R-HSA-983168	0.000128	0.030557
Cellular responses to stress	Reactome	R-HSA-2262752	0.000137	0.030694
Respiratory electron transport	Reactome	R-HSA-611105	0.000244	0.051225
Transcriptional Regulation by TP53	Reactome	R-HSA-3700989	0.000287	0.052609
Eukaryotic Translation Termination	Reactome	R-HSA-72764	0.000291	0.052609
Extension of Telomeres	Reactome	R-HSA-180786	0.000298	0.052609
Ribosome - Homo sapiens (human)	KEGG	path:hsa03010	0.000316	0.05299
Translation	Reactome	R-HSA-72766	0.000418	0.06027

Table 6.5.3A: Top 20 significantly regulated pathways in Baseline – Post1 timepoints

Post 1 – Post 3 Enriched Pathways

P1_P3 pathways	source	external_id	p-value	q-value
Ribosome - Homo sapiens (human)	KEGG	path:hsa03010	3.12E-11	1.01E-07
Selenocysteine synthesis	Reactome	R-HSA-2408557	3.95E-10	6.39E-07
Eukaryotic Translation Termination	Reactome	R-HSA-72764	8.15E-10	8.78E-07
Eukaryotic Translation Elongation	Reactome	R-HSA-156842	1.44E-09	1.16E-06
Peptide chain elongation	Reactome	R-HSA-156902	2.16E-09	1.37E-06
SRP-dependent cotranslational protein targeting to membrane	Reactome	R-HSA-1799339	2.54E-09	1.37E-06
Nonsense Mediated Decay (NMD) independent of the Exon Junction Complex (EJC)	Reactome	R-HSA-975956	3.21E-09	1.48E-06
Gene Expression	Reactome	R-HSA-74160	4.04E-09	1.63E-06

Formation of a pool of free 40S subunits	Reactome	R-HSA-72689	5.82E-09	2.09E-06
Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC)	Reactome	R-HSA-975957	1.26E-08	3.72E-06
Nonsense-Mediated Decay (NMD)	Reactome	R-HSA-927802	1.26E-08	3.72E-06
Selenoamino acid metabolism	Reactome	R-HSA-2408522	1.50E-08	3.99E-06
GTP hydrolysis and joining of the 60S ribosomal subunit	Reactome	R-HSA-72706	1.60E-08	3.99E-06
L13a-mediated translational silencing of Ceruloplasmin expression	Reactome	R-HSA-156827	2.38E-08	5.12E-06
3, -UTR-mediated translational regulation	Reactome	R-HSA-157279	2.38E-08	5.12E-06
Translation	Reactome	R-HSA-72766	3.12E-08	6.30E-06
Cap-dependent Translation Initiation	Reactome	R-HSA-72737	4.41E-08	7.92E-06
Eukaryotic Translation Initiation	Reactome	R-HSA-72613	4.41E-08	7.92E-06
Metabolism	Reactome	R-HSA-1430728	6.36E-08	1.08E-05

Table 6.5.3B: Top 20 significantly regulated pathways in Post1 – Post3 timepoints

Baseline – Post 3 Enriched Pathways

BL_P3 pathways	**source**	**external_id**	**p-value**	**q-value**
Gene Expression	Reactome	R-HSA-74160	1.27E-34	4.15E-31
Metabolism of proteins	Reactome	R-HSA-392499	1.24E-30	2.03E-27
Immune System	Reactome	R-HSA-168256	6.57E-27	7.18E-24
Metabolism	Reactome	R-HSA-1430728	3.76E-26	3.08E-23
Signal Transduction	Reactome	R-HSA-162582	1.69E-23	1.11E-20
Post-translational protein modification	Reactome	R-HSA-597592	5.99E-18	3.27E-15
Innate Immune System	Reactome	R-HSA-168249	7.68E-18	3.59E-15

Vesicle-mediated transport	Reactome	R-HSA-5653656	7.60E-17	3.11E-14
Membrane Trafficking	Reactome	R-HSA-199991	1.00E-16	3.64E-14
Cell Cycle	Reactome	R-HSA-1640170	1.89E-16	6.19E-14
Cellular responses to stress	Reactome	R-HSA-2262752	6.32E-13	1.72E-10
Class I MHC mediated antigen processing & presentation	Reactome	R-HSA-983169	1.97E-12	4.96E-10
Generic Transcription Pathway	Reactome	R-HSA-212436	1.01E-11	2.24E-09
The citric acid (TCA) cycle and respiratory electron transport	Reactome	R-HSA-1428517	1.02E-11	2.24E-09
Neutrophil degranulation	Reactome	R-HSA-6798695	3.15E-11	6.44E-09
Organelle biogenesis and maintenance	Reactome	R-HSA-1852241	2.48E-10	4.79E-08
Transmembrane transport of small molecules	Reactome	R-HSA-382551	5.60E-10	1.02E-07
M Phase	Reactome	R-HSA-68886	8.45E-10	1.46E-07
miR-targeted genes in lymphocytes – TarBase	Wikipathways	WP2004	9.76E-10	1.60E-07

Table 6.5.3C: Top 20 significantly regulated pathways in Baseline – Post3 timepoints

6.5.4. Transcription Factor Profiling

Genes that were more than two-fold regulated in Yoga and Control groups were tabulated for three timepoint comparisons: BL-P1, P1-P3 & BL-P3. The differentially regulated transcription factors were determined from the PANTHER database *(Version 12.0; released on 10-07-2017).*

The list of transcription factors from three timepoint comparison is mentioned in *Appendix-12.*

Over-representation analysis of identified transcription factors was performed using PANTHER database with Bonferroni correction to understand the role of the regulated

transcription factors (*Table 6.5.4*). Over representation analysis showed similar groups of transcription factors to be overrepresented in both the groups. The differentially regulated transcription factors unique to yoga and control groups at each timepoint was tabulated using InteractiVenn. Similar to our earlier observation, the number of transcription factors regulated were less in Yoga group than in the Control group. The upregulated and downregulated transcription factors in each group for the three timepoint comparisons were viewed using ClueGo tool.

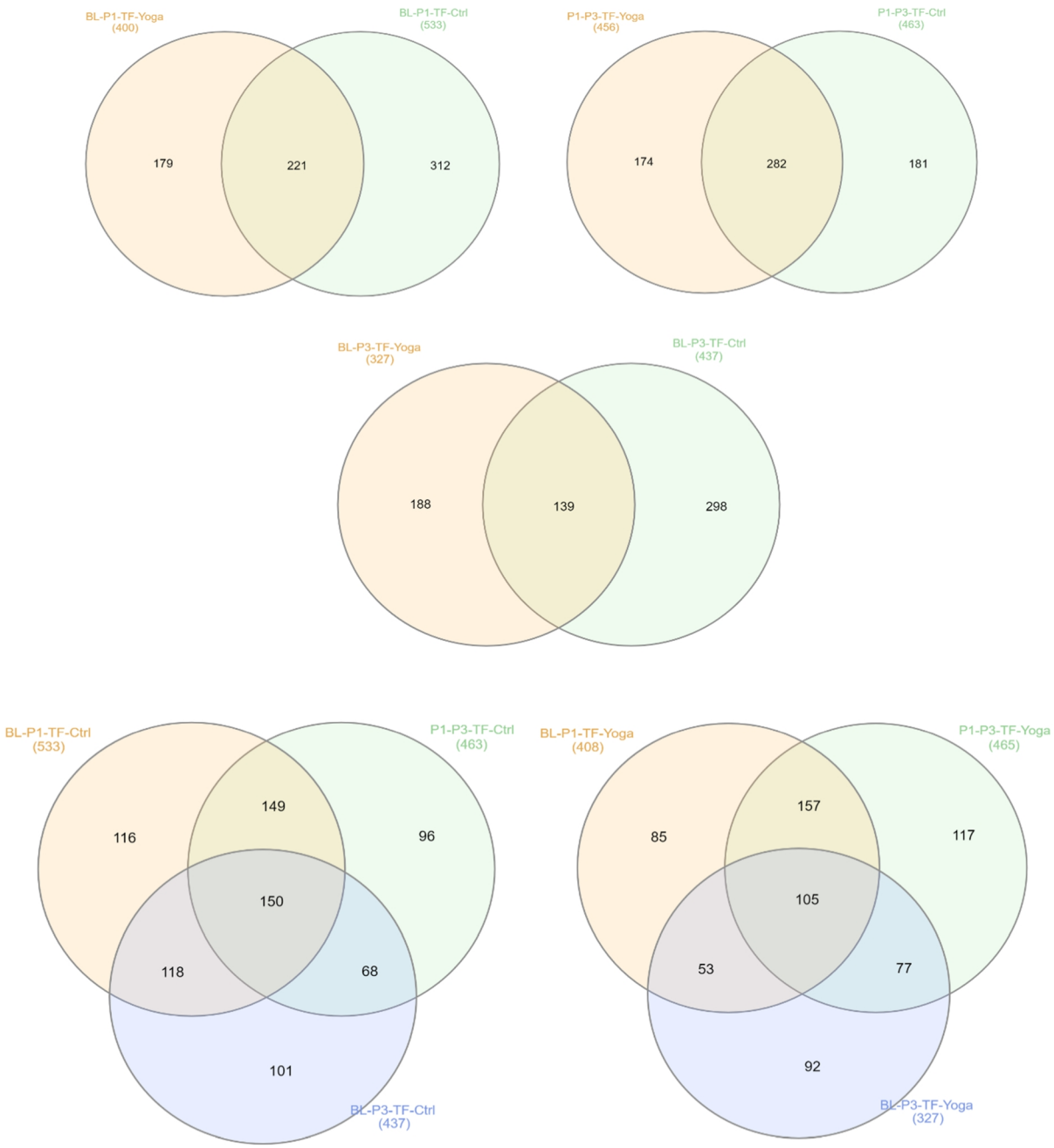


Fig 6.5.4.: Differentially expressed transcription factors in Yoga and Control groups

Over Representation Analysis of Transcription Factors

Timepoint	Molecular Function	Biological Process	Protein Class
BL-P1 C↑	ligand-activated sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0004879) sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0000981) sequence-specific DNA binding transcription factor activity (GO:0003700) protein binding transcription factor activity (GO:0000988) transcription factor binding transcription factor activity (GO:0000989) RNA polymerase II transcription factor binding transcription factor activity (GO:0001076) transcription cofactor activity (GO:0003712) DNA binding (GO:0003677) chromatin binding (GO:0003682)	transcription initiation from RNA polymerase II promoter (GO:0006367) digestive tract mesoderm development (GO:0007502) transcription elongation from RNA polymerase II promoter (GO:0006368) negative regulation of apoptotic process (GO:0043066) regulation of transcription from RNA polymerase II promoter (GO:0006357) transcription from RNA polymerase II promoter (GO:0006366) antigen processing and presentation of peptide or polysaccharide antigen via MHC class II (GO:0002504) regulation of nucleobase-containing compound metabolic process (GO:0019219) segment specification (GO:0007379) protein acetylation (GO:0006473) muscle organ development (GO:0007517) cellular defense response (GO:0006968)	basic leucine zipper transcription factor (PC00056) CREB transcription factor (PC00006) HMG box transcription factor (PC00024) nuclear hormone receptor (PC00169) zinc finger transcription factor (PC00244) transcription cofactor (PC00217) transcription factor (PC00218) KRAB box transcription factor (PC00029) basic helix-loop-helix transcription factor (PC00055) homeobox transcription factor (PC00119) helix-turn-helix transcription factor (PC00116) ATP-binding cassette (ABC) transporter (PC00003)

	ATPase activity, coupled to transmembrane movement of substances (GO:0042626) nucleic acid binding (GO:0003676) acetyltransferase activity (GO:0016407) binding (GO:0005488) protein binding (GO:0005515)	embryo development (GO:0009790) mesoderm development (GO:0007498) pattern specification process (GO:0007389) skeletal system development (GO:0001501) anatomical structure morphogenesis (GO:0009653) transcription, DNA-dependent (GO:0006351) nucleobase-containing compound metabolic process (GO:0006139) cell differentiation (GO:0030154) ectoderm development (GO:0007398) biosynthetic process (GO:0009058) developmental process (GO:0032502) gamete generation (GO:0007276) nitrogen compound metabolic process (GO:0006807) RNA metabolic process (GO:0016070) metabolic process (GO:0008152) primary metabolic process (GO:0044238) reproduction (GO:0000003) nervous system development (GO:0007399) immune system process (GO:0002376)	chromatin/chromatin-binding protein (PC00077) major histocompatibility complex antigen (PC00149) DNA binding protein (PC00009) acetyltransferase (PC00038) nucleic acid binding (PC00171) nuclease (PC00170) kinase modulator (PC00140) actin family cytoskeletal protein (PC00041)

		system development (GO:0048731) cellular process (GO:0009987)	
BL-P1 C↓	signal transducer activity (GO:0004871) transferase activity, transferring glycosyl groups (GO:0016757)	localization (GO:0051179) transport (GO:0006810) neurological system process (GO:0050877) phosphate-containing compound metabolic process (GO:0006796) Unclassified (UNCLASSIFIED) sensory perception (GO:0007600) sensory perception of smell (GO:0007608) sensory perception of chemical stimulus (GO:0007606)	
BL-P1 Y↑	sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0000981) ligand-activated sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0004879) sequence-specific DNA binding transcription factor activity (GO:0003700) protein binding transcription factor activity (GO:0000988)	transcription initiation from RNA polymerase II promoter (GO:0006367) digestive tract mesoderm development (GO:0007502) regulation of transcription from RNA polymerase II promoter (GO:0006357) transcription elongation from RNA polymerase II promoter (GO:0006368) segment specification (GO:0007379) transcription from RNA polymerase II promoter (GO:0006366)	nuclear hormone receptor (PC00169) transcription factor (PC00218) transcription cofactor (PC00217) homeobox transcription factor (PC00119) helix-turn-helix transcription factor (PC00116) HMG box transcription factor (PC00024)

	transcription factor binding transcription factor activity (GO:0000989) ATPase activity, coupled to transmembrane movement of substances (GO:0042626) transcription cofactor activity (GO:0003712) DNA binding (GO:0003677) chromatin binding (GO:0003682) nucleic acid binding (GO:0003676) binding (GO:0005488) protein binding (GO:0005515)	negative regulation of apoptotic process (GO:0043066) muscle organ development (GO:0007517) pattern specification process (GO:0007389) skeletal system development (GO:0001501) regulation of nucleobase-containing compound metabolic process (GO:0019219) mesoderm development (GO:0007498) embryo development (GO:0009790) cell differentiation (GO:0030154) heart development (GO:0007507) nucleobase-containing compound metabolic process (GO:0006139) ectoderm development (GO:0007398) cellular defense response (GO:0006968) anatomical structure morphogenesis (GO:0009653) developmental process (GO:0032502) transcription, DNA-dependent (GO:0006351) biosynthetic process (GO:0009058) nervous system development (GO:0007399) nitrogen compound metabolic process (GO:0006807)	zinc finger transcription factor (PC00244) basic helix-loop-helix transcription factor (PC00055) ATP-binding cassette (ABC) transporter (PC00003) KRAB box transcription factor (PC00029) chromatin/chromatin-binding protein (PC00077) DNA binding protein (PC00009) acetyltransferase (PC00038) nucleic acid binding (PC00171) nuclease (PC00170)

		system development (GO:0048731) metabolic process (GO:0008152) apoptotic process (GO:0006915) primary metabolic process (GO:0044238) death (GO:0016265) cell death (GO:0008219) RNA metabolic process (GO:0016070) single-multicellular organism process (GO:0044707) multicellular organismal process (GO:0032501) cellular process (GO:0009987)	
BL-P1 Y↓		sensory perception of chemical stimulus (GO:0007606)	
P1-P3 C↑	sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0000981) ligand-activated sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0004879) sequence-specific DNA binding transcription factor activity (GO:0003700)	transcription initiation from RNA polymerase II promoter (GO:0006367) regulation of transcription from RNA polymerase II promoter (GO:0006357) transcription elongation from RNA polymerase II promoter (GO:0006368) transcription from RNA polymerase II promoter (GO:0006366) negative regulation of apoptotic process (GO:0043066)	zinc finger transcription factor (PC00244) transcription factor (PC00218) basic helix-loop-helix transcription factor (PC00055) transcription cofactor (PC00217) HMG box transcription factor (PC00024)

	protein binding transcription factor activity (GO:0000988) transcription factor binding transcription factor activity (GO:0000989) transcription cofactor activity (GO:0003712) DNA binding (GO:0003677) ATPase activity, coupled to transmembrane movement of substances (GO:0042626) RNA polymerase II transcription factor binding transcription factor activity (GO:0001076) nucleic acid binding (GO:0003676) chromatin binding (GO:0003682) binding (GO:0005488) protein binding (GO:0005515)	segment specification (GO:0007379) regulation of nucleobase-containing compound metabolic process (GO:0019219) lipid transport (GO:0006869) pattern specification process (GO:0007389) cellular defense response (GO:0006968) mesoderm development (GO:0007498) muscle organ development (GO:0007517) skeletal system development (GO:0001501) cell differentiation (GO:0030154) nucleobase-containing compound metabolic process (GO:0006139) transcription, DNA-dependent (GO:0006351) anatomical structure morphogenesis (GO:0009653) biosynthetic process (GO:0009058) homeostatic process (GO:0042592) ectoderm development (GO:0007398) developmental process (GO:0032502) nitrogen compound metabolic process (GO:0006807) metabolic process (GO:0008152)	nuclear hormone receptor (PC00169) KRAB box transcription factor (PC00029) guanylate cyclase (PC00114) adenylate cyclase (PC00043) homeobox transcription factor (PC00119) helix-turn-helix transcription factor (PC00116) ATP-binding cassette (ABC) transporter (PC00003) chromatin/chromatin-binding protein (PC00077) kinase activator (PC00138) DNA binding protein (PC00009) nucleic acid binding (PC00171) kinase modulator (PC00140) nuclease (PC00170)

		system development (GO:0048731) primary metabolic process (GO:0044238) RNA metabolic process (GO:0016070) nervous system development (GO:0007399) cellular process (GO:0009987)	
P1-P3 C ↓		sensory perception of chemical stimulus (GO:0007606) sensory perception of smell (GO:0007608)	G-protein modulator (PC00022)
P1-P3 Y ↑	sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0000981) RNA polymerase II transcription factor binding transcription factor activity (GO:0001076) sequence-specific DNA binding transcription factor activity (GO:0003700) ligand-activated sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0004879) protein binding transcription factor activity (GO:0000988)	transcription initiation from RNA polymerase II promoter (GO:0006367) regulation of transcription from RNA polymerase II promoter (GO:0006357) digestive tract mesoderm development (GO:0007502) negative regulation of apoptotic process (GO:0043066) transcription from RNA polymerase II promoter (GO:0006366) regulation of nucleobase-containing compound metabolic process (GO:0019219) muscle organ development (GO:0007517) segment specification (GO:0007379) mesoderm development (GO:0007498)	zinc finger transcription factor (PC00244) basic helix-loop-helix transcription factor (PC00055) transcription factor (PC00218) transcription cofactor (PC00217) KRAB box transcription factor (PC00029) HMG box transcription factor (PC00024) nuclear hormone receptor (PC00169) ATP-binding cassette (ABC) transporter (PC00003)

	transcription factor binding transcription factor activity (GO:0000989) transcription cofactor activity (GO:0003712) DNA binding (GO:0003677) ATPase activity, coupled to transmembrane movement of substances (GO:0042626) nucleic acid binding (GO:0003676) chromatin binding (GO:0003682) binding (GO:0005488) protein binding (GO:0005515)	skeletal system development (GO:0001501) pattern specification process (GO:0007389) cell differentiation (GO:0030154) anatomical structure morphogenesis (GO:0009653) nucleobase-containing compound metabolic process (GO:0006139) cellular defense response (GO:0006968) heart development (GO:0007507) biosynthetic process (GO:0009058) fatty acid metabolic process (GO:0006631) transcription, DNA-dependent (GO:0006351) homeostatic process (GO:0042592) nitrogen compound metabolic process (GO:0006807) ectoderm development (GO:0007398) developmental process (GO:0032502) nervous system development (GO:0007399) metabolic process (GO:0008152) system development (GO:0048731) primary metabolic process (GO:0044238) RNA metabolic process (GO:0016070)	homeobox transcription factor (PC00119) helix-turn-helix transcription factor (PC00116) chromatin/chromatin-binding protein (PC00077) DNA binding protein (PC00009) acetyltransferase (PC00038) nucleic acid binding (PC00171) nuclease (PC00170) actin family cytoskeletal protein (PC00041)

		cell cycle (GO:0007049) cellular process (GO:0009987) response to stimulus (GO:0050896)	
P1-P3 Y ↓	signal transducer activity (GO:0004871)	sensory perception of chemical stimulus (GO:0007606)	
BL-P3 C ↑	protein binding transcription factor activity (GO:0000988) sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0000981) transcription factor binding transcription factor activity (GO:0000989) transcription cofactor activity (GO:0003712) ligand-activated sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0004879) sequence-specific DNA binding transcription factor activity (GO:0003700) DNA binding (GO:0003677)	transcription elongation from RNA polymerase II promoter (GO:0006368) transcription initiation from RNA polymerase II promoter (GO:0006367) negative regulation of apoptotic process (GO:0043066) digestive tract mesoderm development (GO:0007502) regulation of transcription from RNA polymerase II promoter (GO:0006357) transcription from RNA polymerase II promoter (GO:0006366) antigen processing and presentation of peptide or polysaccharide antigen via MHC class II (GO:0002504) regulation of nucleobase-containing compound metabolic process (GO:0019219) cellular defense response (GO:0006968)	transcription cofactor (PC00217) transcription factor (PC00218) zinc finger transcription factor (PC00244) HMG box transcription factor (PC00024) KRAB box transcription factor (PC00029) nuclear hormone receptor (PC00169) ATP-binding cassette (ABC) transporter (PC00003) homeobox transcription factor (PC00119) helix-turn-helix transcription factor (PC00116) basic helix-loop-helix transcription factor (PC00055)

	ATPase activity, coupled to transmembrane movement of substances (GO:0042626) nucleic acid binding (GO:0003676) chromatin binding (GO:0003682) binding (GO:0005488) protein binding (GO:0005515)	segment specification (GO:0007379) anatomical structure morphogenesis (GO:0009653) mesoderm development (GO:0007498) embryo development (GO:0009790) muscle organ development (GO:0007517) pattern specification process (GO:0007389) nucleobase-containing compound metabolic process (GO:0006139) skeletal system development (GO:0001501) transcription, DNA-dependent (GO:0006351) ectoderm development (GO:0007398) cell differentiation (GO:0030154) biosynthetic process (GO:0009058) homeostatic process (GO:0042592) developmental process (GO:0032502) metabolic process (GO:0008152) immune system process (GO:0002376) primary metabolic process (GO:0044238) nitrogen compound metabolic process (GO:0006807) RNA metabolic process (GO:0016070)	chromatin/chromatin-binding protein (PC00077) DNA binding protein (PC00009) nucleic acid binding (PC00171) actin family cytoskeletal protein (PC00041)

		system development (GO:0048731) cell cycle (GO:0007049) cellular process (GO:0009987)	
BL-P3 C ↓		sensory perception of chemical stimulus (GO:0007606)	
BL-P3 Y ↑	ligand-activated sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0004879) sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0000981) sequence-specific DNA binding transcription factor activity (GO:0003700) transcription factor binding transcription factor activity (GO:0000989) protein binding transcription factor activity (GO:0000988) transcription cofactor activity (GO:0003712) DNA binding (GO:0003677) chromatin binding (GO:0003682) nucleic acid binding (GO:0003676)	transcription initiation from RNA polymerase II promoter (GO:0006367) regulation of transcription from RNA polymerase II promoter (GO:0006357) negative regulation of apoptotic process (GO:0043066) transcription from RNA polymerase II promoter (GO:0006366) regulation of nucleobase-containing compound metabolic process (GO:0019219) muscle organ development (GO:0007517) segment specification (GO:0007379) mesoderm development (GO:0007498) anatomical structure morphogenesis (GO:0009653) skeletal system development (GO:0001501) heart development (GO:0007507) cellular defense response (GO:0006968)	nuclear hormone receptor (PC00169) transcription cofactor (PC00217) transcription factor (PC00218) basic helix-loop-helix transcription factor (PC00055) KRAB box transcription factor (PC00029) zinc finger transcription factor (PC00244) HMG box transcription factor (PC00024) homeobox transcription factor (PC00119) helix-turn-helix transcription factor (PC00116) chromatin/chromatin-binding protein (PC00077) DNA binding protein (PC00009)

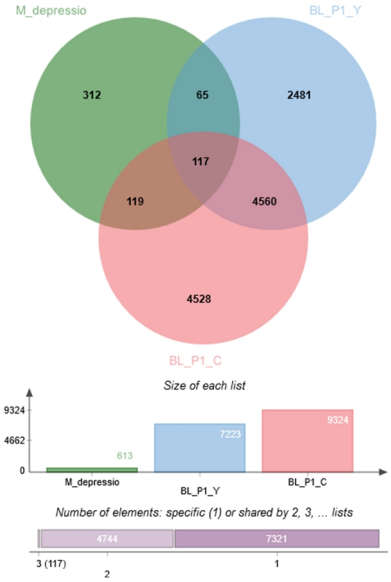
	binding (GO:0005488) protein binding (GO:0005515)	pattern specification process (GO:0007389) cell differentiation (GO:0030154) nucleobase-containing compound metabolic process (GO:0006139) ectoderm development (GO:0007398) biosynthetic process (GO:0009058) transcription, DNA-dependent (GO:0006351) developmental process (GO:0032502) nervous system development (GO:0007399) system development (GO:0048731) nitrogen compound metabolic process (GO:0006807) metabolic process (GO:0008152) primary metabolic process (GO:0044238) cell cycle (GO:0007049) RNA metabolic process (GO:0016070) cellular process (GO:0009987)	nucleic acid binding (PC00171) actin family cytoskeletal protein (PC00041)
BL-P3 Y ↓		transport (GO:0006810) sensory perception of chemical stimulus (GO:0007606)	

Tab 6.5.4: Over Representation Analysis of Differentially Regulated Transcription Factors in Yoga and Control Groups

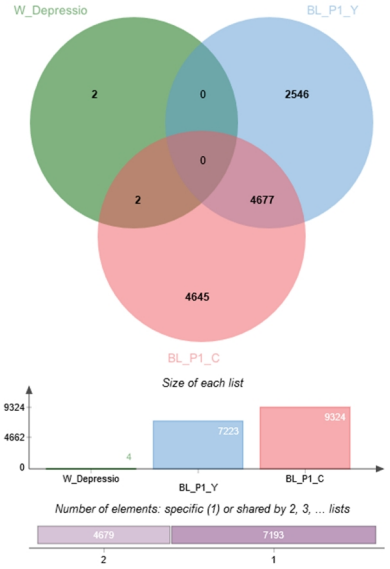
6.5.5. Common NCDs and associated gene expression in the Extreme environment

The genes are known to be involved in Type 2 Diabetes Mellitus, Obesity, Hypertension, Depression, tumour immunity, abnormal endocrine function and abnormal mental function were obtained from the "*All gene-disease association database*" from the DisGeneT database v5.0 (Piñero, Queralt-Rosinach, Bravo, & Deu-Pons, 2015). The common differentially regulated genes between disease phenotype and the Yoga and Control groups were obtained for all the three time-point comparisons: BL vs P1; P1 vs P3; BL vs P3. The results suggest that there is consistently less number of genes involved in the Yoga group as compared to the control group. The shared genes between Yoga and Control groups for the pathologies have been tabulated *(Appendix 13)*.

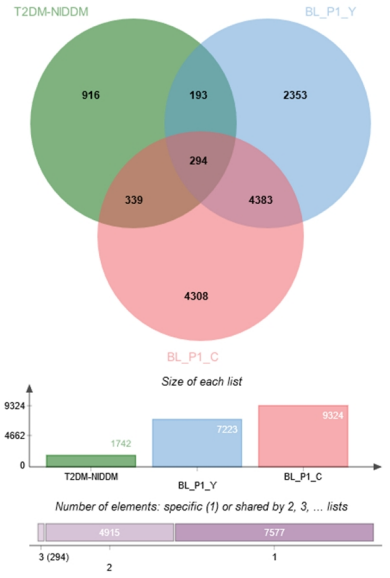
Mental Depression



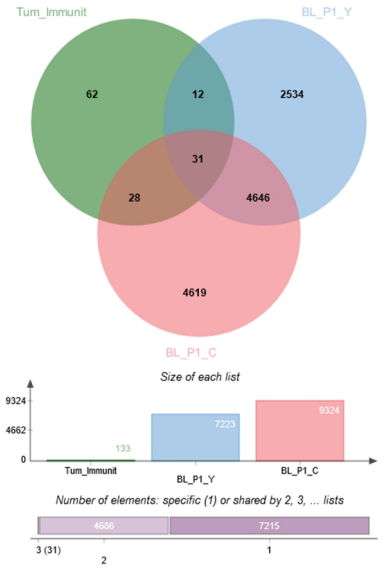
Winter Depression



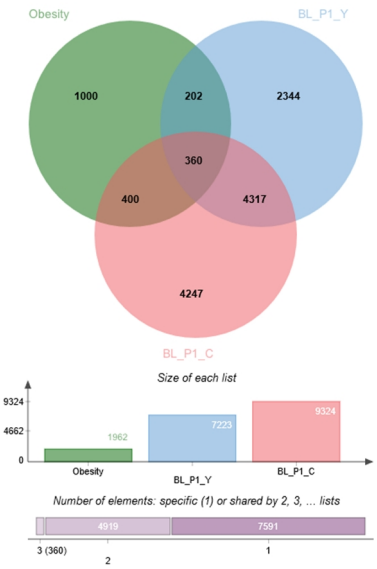
T2 Diabetes Mellitus



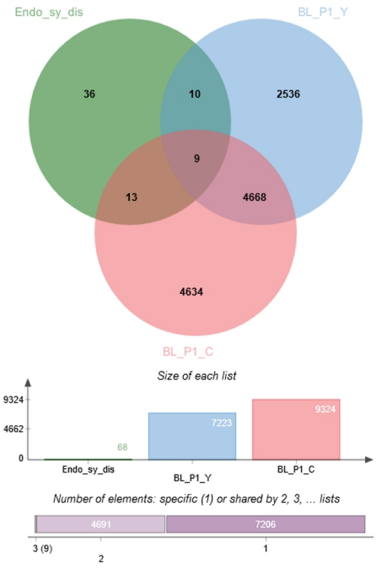
Tumour Immunity



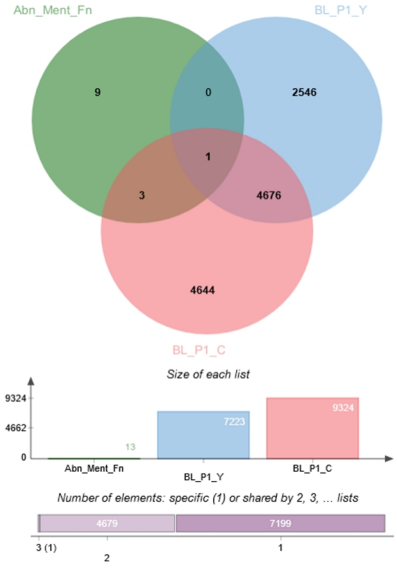
Obesity



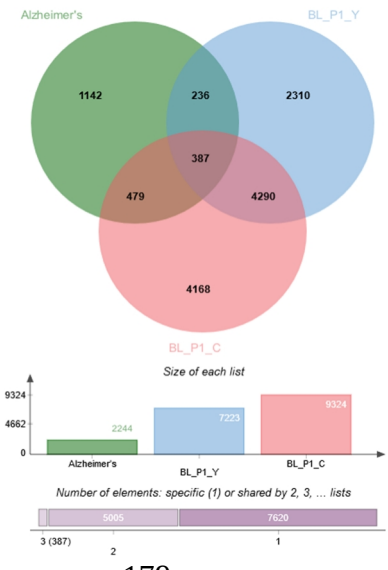
Endocrine System Disorders



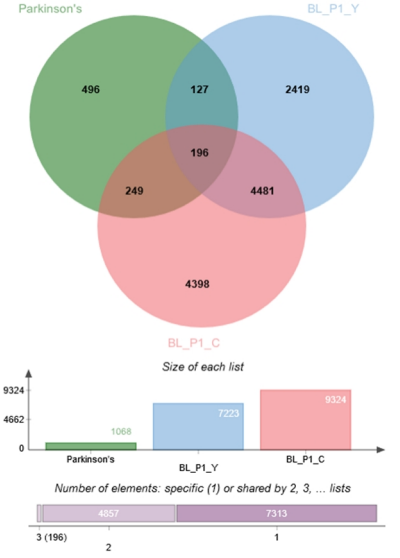
Abnormal Mental Function



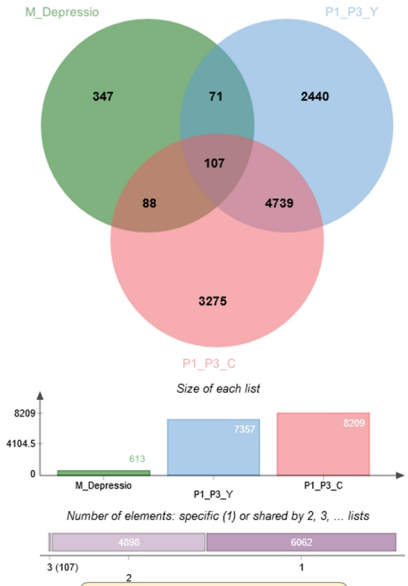
Alzheimer's Disease



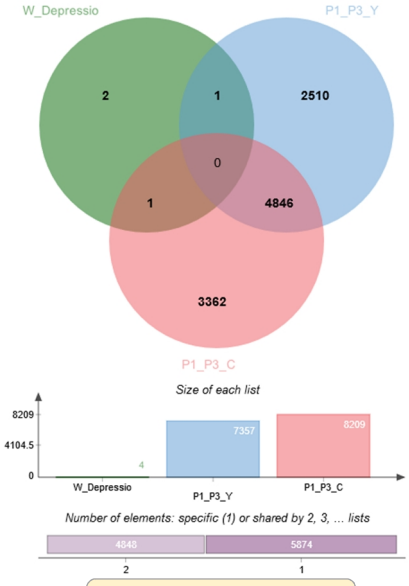
Parkinson's Disease



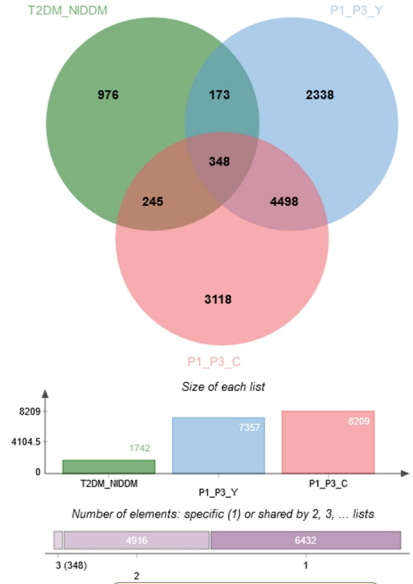
Mental Depression



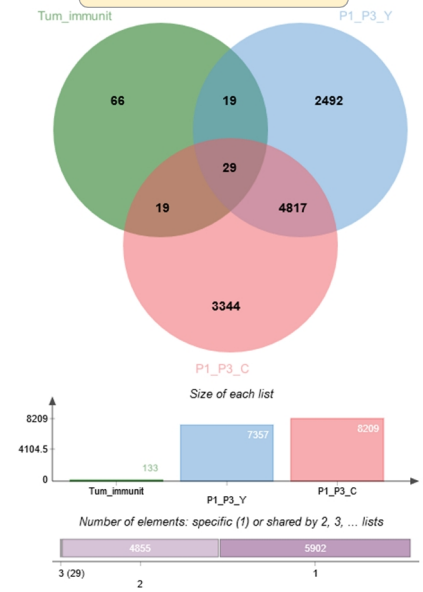
Winter Depression



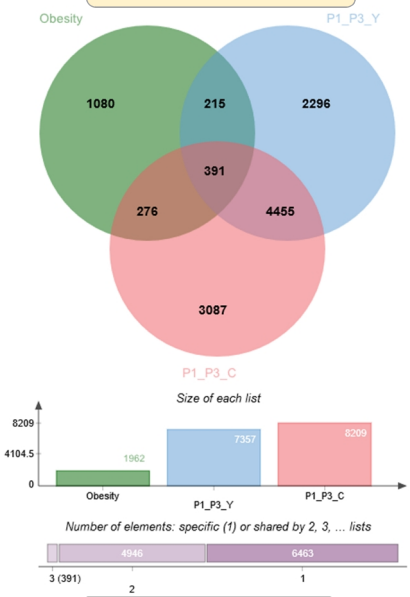
T2 Diabetes Mellitus



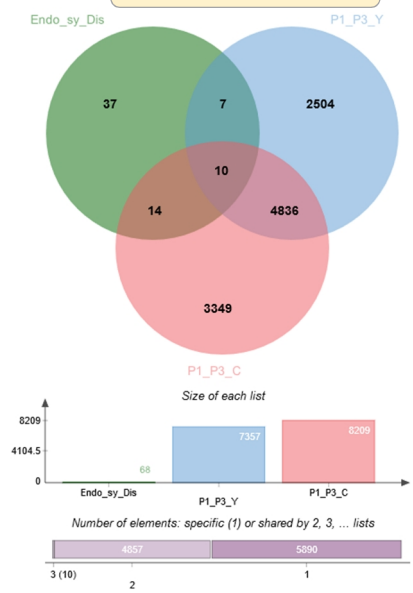
Tumour Immunity



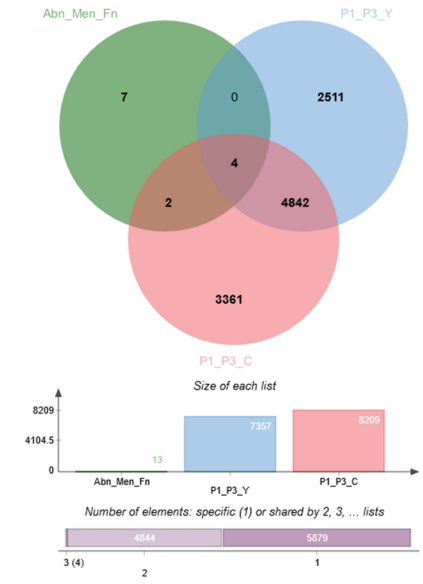
Obesity



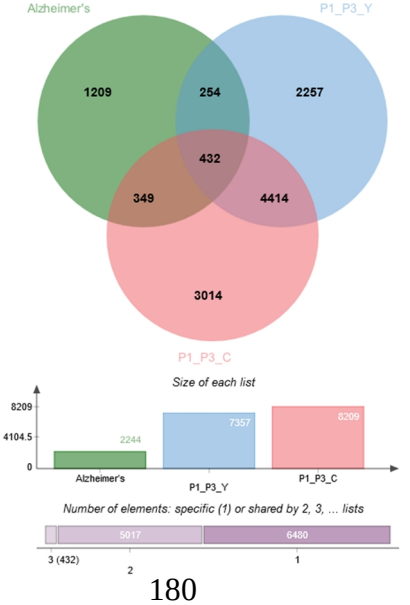
Endocrine System Disorders



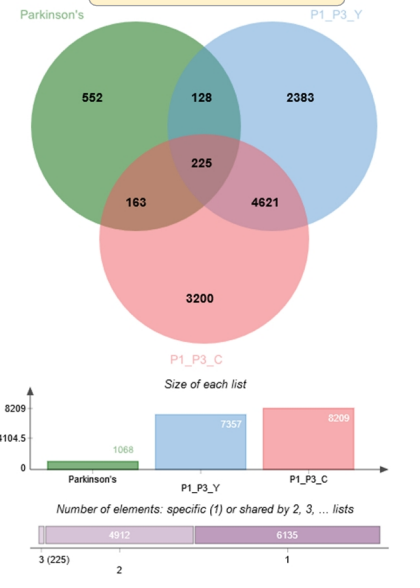
Abnormal Mental Function



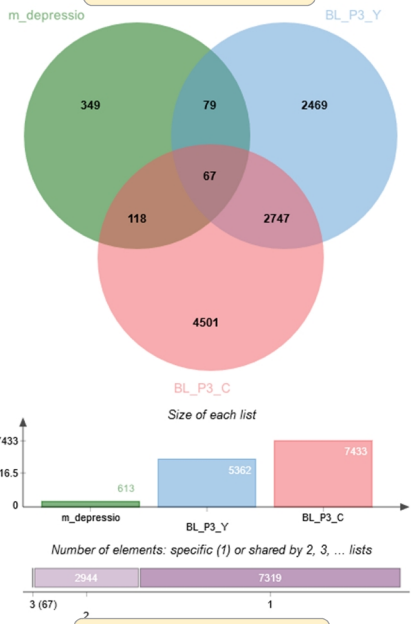
Alzheimer's Disease



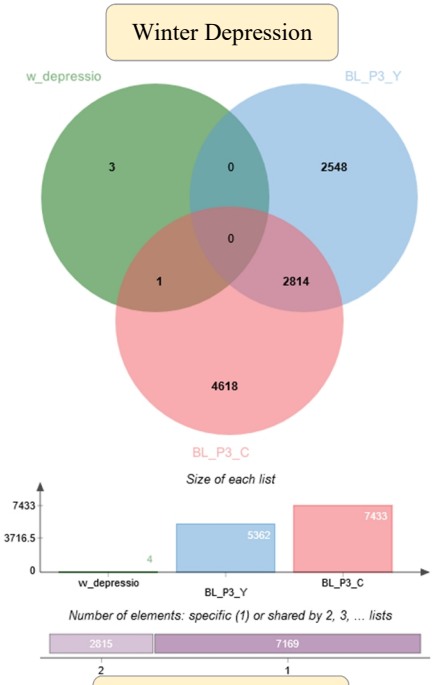
Parkinson's Disease



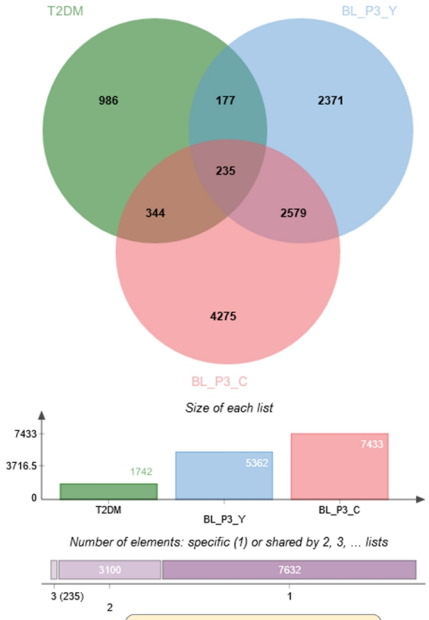
Mental Depression



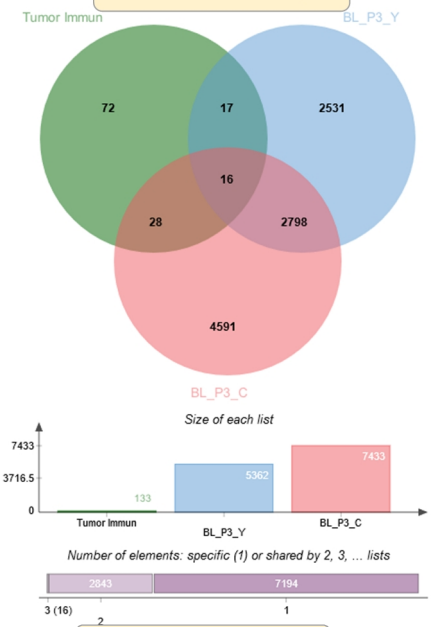
Winter Depression



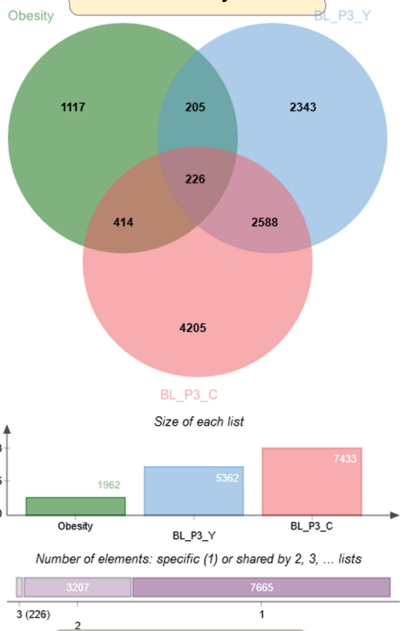
T2 Diabetes Mellitus



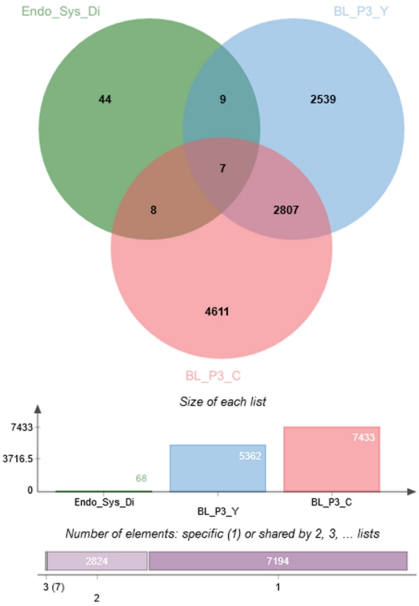
Tumour Immunity



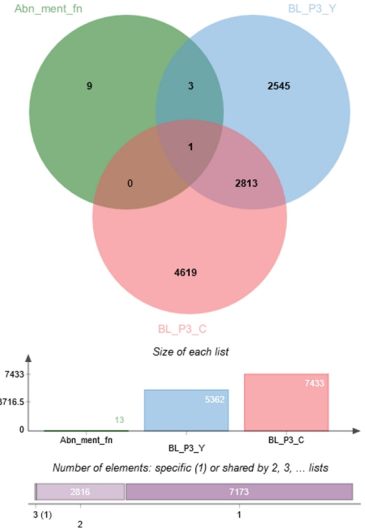
Obesity



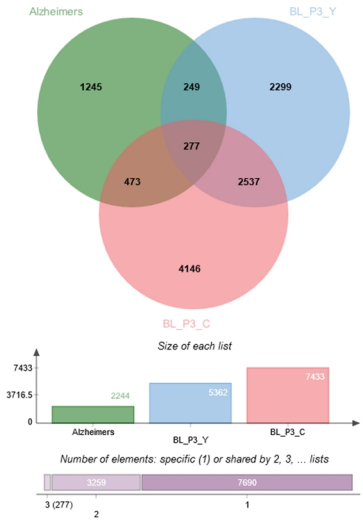
Endocrine System Disorders



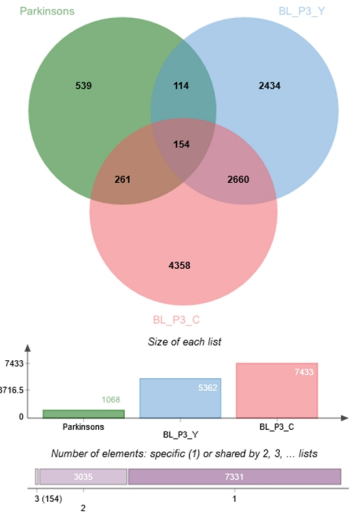
Abnormal Mental Function



Alzheimer's Disease



Parkinson's Disease



6.6. Gene Expression – Conventional Analysis (Stringent Protocol)

6.6.1. Gene ontology Analysis

The Differentially Expressed Genes (DEG) were analysed under three conditions for both Yoga and Control Groups:

a. Baseline Vs Post 1

b. Post 1 Vs Post 3

c. Baseline Vs Post 3

Database for Annotation, Visualization and Integrated Discovery (DAVID) version 6.8 was used for computing gene ontology classes for the differentially regulated genes for each time point comparisons. Fischer Exact's test for multiple testing correction was used to identify the significantly regulated gene ontologies. GOTERM_BP_Direct; GOTERM_CC_Direct and GOTERM_MF_Direct were considered for reporting the direct ontology classes.

GO	Biological Process BL-P1 Yoga	%	PValue	Genes	Fold Enrichment	Fisher Exact
GO:0007613	Memory	0.828729	0.002	9	3.875276	0.000
GO:0030154	cell differentiation	2.762431	0.005	30	1.733529	0.003
GO:0032094	response to food	0.460405	0.007	5	6.356272	0.001
GO:0030216	keratinocyte differentiation	0.828729	0.007	9	3.161409	0.002
GO:0007010	cytoskeleton organization	1.289134	0.008	14	2.321421	0.003
GO:0031424	Keratinization	0.644567	0.009	7	3.893217	0.002
GO:0010524	positive regulation of calcium ion transport into cytosol	0.368324	0.009	4	8.898781	0.001
GO:0030277	maintenance of gastrointestinal epithelium	0.368324	0.009	4	8.898781	0.001
GO:0007165	signal transduction	5.524862	0.010	60	1.379656	0.007
GO:0018149	peptide cross-linking	0.644567	0.010	7	3.737488	0.003
GO:0031641	regulation of myelination	0.368324	0.011	4	8.21426	0.001
GO:0051602	response to electrical stimulus	0.460405	0.011	5	5.561738	0.002
GO:0045542	positive regulation of cholesterol biosynthetic process	0.276243	0.013	3	16.01781	0.000
GO:0008544	epidermis development	0.828729	0.014	9	2.826672	0.005
GO:0046426	negative regulation of JAK-STAT cascade	0.552486	0.016	6	4.004452	0.004
GO:0042493	response to drug	1.841621	0.020	20	1.756338	0.011
GO:0007281	germ cell development	0.460405	0.025	5	4.449391	0.005
GO:0030432	Peristalsis	0.276243	0.026	3	11.44129	0.002
GO:0045747	positive regulation of Notch signaling pathway	0.460405	0.034	5	4.044901	0.007
GO:0007275	multicellular organism development	2.67035	0.035	29	1.485977	0.022
GO:0002028	regulation of sodium ion transport	0.368324	0.042	4	5.085018	0.007
GO:0042147	retrograde transport, endosome to Golgi	0.644567	0.044	7	2.708325	0.015
GO:0048015	phosphatidylinositol-mediated signaling	0.828729	0.045	9	2.266671	0.018
GO:0033138	positive regulation of peptidyl-serine phosphorylation	0.644567	0.047	7	2.669634	0.016
GO:0032570	response to progesterone	0.460405	0.057	5	3.422608	0.015

GO:0001666	response to hypoxia	1.104972	0.059	12	1.862536	0.029
GO:0009743	response to carbohydrate	0.276243	0.061	3	7.280821	0.007
GO:0043249	erythrocyte maturation	0.276243	0.061	3	7.280821	0.007
GO:0007155	cell adhesion	2.302026	0.062	25	1.454049	0.040
GO:0051056	regulation of small GTPase mediated signal transduction	0.92081	0.064	10	1.992264	0.029
GO:0030198	extracellular matrix organization	1.197053	0.065	13	1.770676	0.033
GO:0000188	inactivation of MAPK activity	0.368324	0.065	4	4.271415	0.013
GO:0002181	cytoplasmic translation	0.368324	0.065	4	4.271415	0.013
GO:0032526	response to retinoic acid	0.460405	0.066	5	3.255652	0.018
GO:0007268	chemical synaptic transmission	1.381215	0.067	15	1.668521	0.037
GO:0051496	positive regulation of stress fiber assembly	0.460405	0.071	5	3.178136	0.020
GO:0031295	T cell costimulation	0.644567	0.072	7	2.395826	0.027
GO:0045666	positive regulation of neuron differentiation	0.644567	0.072	7	2.395826	0.027
GO:0050999	regulation of nitric-oxide synthase activity	0.368324	0.072	4	4.10713	0.015
GO:0043206	extracellular fibril organization	0.276243	0.072	3	6.674086	0.009
GO:0045086	positive regulation of interleukin-2 biosynthetic process	0.276243	0.072	3	6.674086	0.009
GO:0042136	neurotransmitter biosynthetic process	0.276243	0.072	3	6.674086	0.009
GO:0007567	Parturition	0.276243	0.072	3	6.674086	0.009
GO:0003420	regulation of growth plate cartilage chondrocyte proliferation	0.184162	0.073	2	26.69634	0.001
GO:1902952	positive regulation of dendritic spine maintenance	0.184162	0.073	2	26.69634	0.001
GO:0003057	regulation of the force of heart contraction by chemical signal	0.184162	0.073	2	26.69634	0.001
GO:0034342	response to type III interferon	0.184162	0.073	2	26.69634	0.001
GO:0021681	cerebellar granular layer development	0.184162	0.073	2	26.69634	0.001
GO:0006469	negative regulation of protein kinase activity	0.736648	0.078	8	2.15728	0.032
GO:0035335	peptidyl-tyrosine dephosphorylation	0.736648	0.078	8	2.15728	0.032
GO:0048678	response to axon injury	0.368324	0.078	4	3.955014	0.017

GO:0048712	negative regulation of astrocyte differentiation	0.276243	0.083	3	6.160695	0.011
GO:0030308	negative regulation of cell growth	0.828729	0.084	9	1.985678	0.038
GO:0061337	cardiac conduction	0.460405	0.087	5	2.96626	0.026
GO:0051591	response to cAMP	0.460405	0.092	5	2.901776	0.028
GO:0050885	neuromuscular process controlling balance	0.460405	0.092	5	2.901776	0.028
GO:0042113	B cell activation	0.368324	0.093	4	3.682254	0.022
GO-CC	**Cellular Component BL-P1 Yoga**	**%**	**PValue**	**Genes**	**Fold Enrichment**	**Fisher Exact**
GO:0045095	keratin filament	1.657459	0.000	18	4.692876	0.000
GO:0042383	Sarcolemma	1.012891	0.001	11	3.373963	0.000
GO:0005578	proteinaceous extracellular matrix	2.025783	0.002	22	2.1402	0.001
GO:0001533	cornified envelope	0.644567	0.008	7	3.967407	0.002
GO:0005856	Cytoskeleton	2.302026	0.009	25	1.756842	0.005
GO:0005796	Golgi lumen	0.92081	0.011	10	2.715784	0.004
GO:0043186	P granule	0.368324	0.012	4	8.022009	0.001
GO:0071682	endocytic vesicle lumen	0.368324	0.022	4	6.517883	0.003
GO:0043235	receptor complex	1.012891	0.024	11	2.258164	0.010
GO:0005882	intermediate filament	0.92081	0.030	10	2.307215	0.012
GO:0043195	terminal bouton	0.644567	0.031	7	2.94356	0.009
GO:0043198	dendritic shaft	0.460405	0.033	5	4.073677	0.007
GO:0005615	extracellular space	5.893186	0.057	64	1.238736	0.043
GO:0031594	neuromuscular junction	0.552486	0.059	6	2.844167	0.018
GO:0005833	hemoglobin complex	0.276243	0.075	3	6.517883	0.010
GO:0033270	paranode region of axon	0.276243	0.075	3	6.517883	0.010
GO:0070701	mucus layer	0.184162	0.075	2	26.07153	0.002
GO:0005886	plasma membrane	16.11418	0.077	175	1.107139	0.067
GO:0005604	basement membrane	0.644567	0.082	7	2.310136	0.032
GO:0030018	Z disc	0.828729	0.083	9	1.988507	0.038

GO:0030027	lamellipodium	1.012891	0.088	11	1.792418	0.044
GO:0045202	synapse	1.104972	0.089	12	1.728499	0.047
GO_MF	**Molecular function BL-P1 Yoga**	**%**	**PValue**	**Genes**	**Fold Enrichment**	**Fisher Exact**
GO:0005198	structural molecule activity	2.117864	0.000	23	2.515064	0.000
GO:0005201	extracellular matrix structural constituent	0.92081	0.001	10	4.031284	0.000
GO:0019210	kinase inhibitor activity	0.276243	0.008	3	20.2572	0.000
GO:0030197	extracellular matrix constituent, lubricant activity	0.276243	0.019	3	13.5048	0.001
GO:0005200	structural constituent of cytoskeleton	0.92081	0.021	10	2.455418	0.008
GO:0046983	protein dimerization activity	1.104972	0.024	12	2.160768	0.010
GO:0001540	beta-amyloid binding	0.460405	0.036	5	3.972	0.008
GO:0030506	ankyrin binding	0.368324	0.036	4	5.40192	0.006
GO:0001972	retinoic acid binding	0.368324	0.051	4	4.697322	0.009
GO:0016791	phosphatase activity	0.460405	0.059	5	3.3762	0.015
GO:0005249	voltage-gated potassium channel activity	0.552486	0.063	6	2.794097	0.020
GO:0001106	RNA polymerase II transcription corepressor activity	0.368324	0.070	4	4.155323	0.015
GO:0071633	dihydroceramidase activity	0.184162	0.073	2	27.0096	0.001
GO:0004725	protein tyrosine phosphatase activity	0.736648	0.077	8	2.160768	0.032
GO:0017017	MAP kinase tyrosine/serine/threonine phosphatase activity	0.276243	0.081	3	6.232985	0.011
GO:0019902	phosphatase binding	0.460405	0.084	5	3.001067	0.025
GO:0005344	oxygen transporter activity	0.276243	0.093	3	5.787771	0.014
GO:0019825	oxygen binding	0.460405	0.095	5	2.873362	0.029
GO:0005543	phospholipid binding	0.644567	0.099	7	2.198456	0.040

GO	BL-P3 Yoga Molecular Functions	%	PValue	Genes	Fold Enrichment	Fisher Exact
GO:0002039	p53 binding	11.11111	0.038998	2	45.81004	8.30E-04

BP	P1-P3 Yoga Biological Process	%	PValue	Genes	Fold Enrichment	Fisher Exact
GO:0007165	signal transduction	6.695464	0.009	31	1.618647	5.60E-03
GO:0009743	response to carbohydrate	0.647948	0.013	3	16.53298	6.60E-04
GO:0010524	positive regulation of calcium ion transport into cytosol	0.647948	0.016	3	15.15523	8.70E-04
GO:0045086	positive regulation of interleukin-2 biosynthetic process	0.647948	0.016	3	15.15523	8.70E-04
GO:0006839	mitochondrial transport	0.647948	0.025	3	12.12419	1.70E-03
GO:0021681	cerebellar granular layer development	0.431965	0.033	2	60.62094	2.70E-04
GO:0031295	T cell costimulation	1.079914	0.040	5	3.885958	9.30E-03
GO:0045666	positive regulation of neuron differentiation	1.079914	0.040	5	3.885958	9.30E-03
GO:0042326	negative regulation of phosphorylation	0.647948	0.042	3	9.093141	4.10E-03
GO:0044267	cellular protein metabolic process	1.295896	0.045	6	3.082421	1.40E-02
GO:0032094	response to food	0.647948	0.046	3	8.660134	4.70E-03
GO:0007565	female pregnancy	1.079914	0.059	5	3.405671	1.60E-02
GO:0000188	inactivation of MAPK activity	0.647948	0.063	3	7.274513	7.80E-03
GO:0032355	response to estradiol	1.079914	0.063	5	3.330821	1.70E-02
GO:0032507	maintenance of protein location in cell	0.431965	0.064	2	30.31047	1.60E-03
GO:0006997	nucleus organization	0.647948	0.068	3	6.994724	8.70E-03
GO:0051260	protein homooligomerization	1.511879	0.072	7	2.397438	2.80E-02
GO:0032689	negative regulation of interferon-gamma production	0.647948	0.077	3	6.495101	1.10E-02
GO:0007155	cell adhesion	2.807775	0.077	13	1.716933	4.20E-02
GO:0019217	regulation of fatty acid metabolic process	0.431965	0.080	2	24.24838	2.60E-03
GO:0006701	progesterone biosynthetic process	0.431965	0.080	2	24.24838	2.60E-03
GO:0030154	cell differentiation	2.807775	0.080	13	1.705784	4.40E-02

GO:0007596	blood coagulation	1.511879	0.083	7	2.306231	3.30E-02
GO:0007586	Digestion	0.863931	0.085	4	3.848948	2.00E-02
GO:0006348	chromatin silencing at telomere	0.431965	0.095	2	20.20698	3.90E-03
GO:0001764	neuron migration	1.079914	0.095	5	2.886711	3.00E-02
GO:0045595	regulation of cell differentiation	0.647948	0.097	3	5.683213	1.50E-02
GO:0042220	response to cocaine	0.647948	0.097	3	5.683213	1.50E-02
CC	**P1-P3 Yoga Cellular Component**	**%**	**PValue**	**Genes**	**Fold Enrichment**	**Fisher Exact**
GO:0030659	cytoplasmic vesicle membrane	1.727862	0.005	8	3.806182	1.30E-03
GO:0045095	keratin filament	1.511879	0.006	7	4.196316	1.40E-03
GO:0005856	Cytoskeleton	3.023758	0.010	14	2.262165	4.00E-03
GO:0031225	anchored component of membrane	1.511879	0.012	7	3.713554	2.90E-03
GO:0005578	proteinaceous extracellular matrix	2.159827	0.036	10	2.236842	1.50E-02
GO:0048471	perinuclear region of cytoplasm	3.671706	0.057	17	1.641071	3.20E-02
GO:0045121	membrane raft	1.727862	0.057	8	2.328053	2.30E-02
GO:0008076	voltage-gated potassium channel complex	1.079914	0.059	5	3.4061	1.60E-02
GO:0016363	nuclear matrix	1.079914	0.078	5	3.090071	2.30E-02
GO:0005615	extracellular space	6.479482	0.089	30	1.335131	6.40E-02
MF	**P1-P3 Yoga Molecular Function**	**%**	**PValue**	**Genes**	**Fold Enrichment**	**Fisher Exact**
GO:0005198	structural molecule activity	3.023758	0.000	14	3.479338	0.000056
GO:0005201	extracellular matrix structural constituent	1.079914	0.023	5	4.581004	0.0047
GO:0005521	lamin binding	0.647948	0.024	3	12.27709	0.0017
GO:0044325	ion channel binding	1.295896	0.037	6	3.259405	0.01
GO:0005249	voltage-gated potassium channel activity	0.863931	0.068	4	4.23348	0.015
GO:0031490	chromatin DNA binding	0.863931	0.068	4	4.23348	0.015
GO:0008134	transcription factor binding	1.943844	0.092	9	1.945314	0.044
GO:1990782	protein tyrosine kinase binding	0.431965	0.094	2	20.46182	0.0038
GO:0010485	H4 histone acetyltransferase activity	0.431965	0.094	2	20.46182	0.0038

BP	BL-P1 Control Biological Process	%	PValue	Genes	Fold Enrichment	Fisher Exact
GO:0015701	bicarbonate transport	1.069519	0.002	6	7.045594	1.90E-04
GO:0001666	response to hypoxia	1.960784	0.002	11	3.304329	5.30E-04
GO:0042493	response to drug	2.673797	0.002	15	2.549393	9.00E-04
GO:0015671	oxygen transport	0.713012	0.003	4	13.77805	1.60E-04
GO:0046426	negative regulation of JAK-STAT cascade	0.891266	0.007	5	6.458462	9.90E-04
GO:0007155	cell adhesion	3.208556	0.008	18	2.026184	3.80E-03
GO:0007165	signal transduction	6.238859	0.010	35	1.557596	6.10E-03
GO:0002181	cytoplasmic translation	0.713012	0.012	4	8.266831	1.30E-03
GO:0071897	DNA biosynthetic process	0.713012	0.013	4	7.948876	1.50E-03
GO:0018149	peptide cross-linking	0.891266	0.016	5	5.166769	2.70E-03
GO:0010763	positive regulation of fibroblast migration	0.534759	0.018	3	14.09119	1.10E-03
GO:0048266	behavioral response to pain	0.534759	0.018	3	14.09119	1.10E-03
GO:0009743	response to carbohydrate	0.534759	0.018	3	14.09119	1.10E-03
GO:0042136	neurotransmitter biosynthetic process	0.534759	0.022	3	12.91692	1.40E-03
GO:0010524	positive regulation of calcium ion transport into cytosol	0.534759	0.022	3	12.91692	1.40E-03
GO:0030728	ovulation	0.534759	0.022	3	12.91692	1.40E-03
GO:0051693	actin filament capping	0.534759	0.025	3	11.92331	1.80E-03
GO:0050900	leukocyte migration	1.247772	0.031	7	2.96454	9.60E-03
GO:0032355	response to estradiol	1.069519	0.031	6	3.406661	8.50E-03
GO:0042026	protein refolding	0.534759	0.033	3	10.33354	2.70E-03
GO:0006614	SRP-dependent cotranslational protein targeting to membrane	1.069519	0.035	6	3.297938	9.80E-03
GO:0030198	extracellular matrix organization	1.604278	0.036	9	2.372496	1.40E-02
GO:0006182	cGMP biosynthetic process	0.534759	0.037	3	9.687692	3.30E-03
GO:0006810	transport	2.317291	0.038	13	1.930115	1.80E-02
GO:0030199	collagen fibril organization	0.713012	0.039	4	5.29925	6.60E-03

GO:0032570	response to progesterone	0.713012	0.039	4	5.29925	6.60E-03
GO:1901741	positive regulation of myoblast fusion	0.534759	0.042	3	9.117828	4.00E-03
GO:0032526	response to retinoic acid	0.713012	0.044	4	5.04075	7.90E-03
GO:0071300	cellular response to retinoic acid	0.891266	0.046	5	3.690549	1.10E-02
GO:0001764	neuron migration	1.069519	0.053	6	2.95244	1.60E-02
GO:0050850	positive regulation of calcium-mediated signaling	0.534759	0.056	3	7.750154	6.40E-03
GO:0006364	rRNA processing	1.604278	0.056	9	2.17294	2.40E-02
GO:1901857	positive regulation of cellular respiration	0.356506	0.057	2	34.44513	1.10E-03
GO:0061684	chaperone-mediated autophagy	0.356506	0.057	2	34.44513	1.10E-03
GO:0051591	response to cAMP	0.713012	0.059	4	4.492843	1.20E-02
GO:0033198	response to ATP	0.534759	0.061	3	7.381099	7.40E-03
GO:0045666	positive regulation of neuron differentiation	0.891266	0.064	5	3.312032	1.80E-02
GO:0030154	cell differentiation	2.673797	0.065	15	1.677522	3.60E-02
GO:0009408	response to heat	0.713012	0.065	4	4.305641	1.40E-02
GO:0019083	viral transcription	1.069519	0.066	6	2.767912	2.20E-02
GO:0001503	ossification	0.891266	0.069	5	3.229231	1.90E-02
GO:0008284	positive regulation of cell proliferation	2.673797	0.069	15	1.663123	3.90E-02
GO:0045472	response to ether	0.356506	0.075	2	25.83385	2.20E-03
GO:0014832	urinary bladder smooth muscle contraction	0.356506	0.075	2	25.83385	2.20E-03
GO:0007269	neurotransmitter secretion	0.713012	0.075	4	4.052368	1.70E-02
GO:0044267	cellular protein metabolic process	1.069519	0.078	6	2.627171	2.70E-02
GO:0006631	fatty acid metabolic process	0.713012	0.079	4	3.974438	1.80E-02
GO:0071320	cellular response to cAMP	0.713012	0.079	4	3.974438	1.80E-02
GO:0000184	nuclear-transcribed mRNA catabolic process, nonsense-mediated decay	1.069519	0.081	6	2.605094	2.80E-02
GO:0008544	epidermis development	0.891266	0.082	5	3.039276	2.50E-02
GO:0000188	inactivation of MAPK activity	0.534759	0.083	3	6.200123	1.20E-02
GO:0007411	axon guidance	1.247772	0.088	7	2.274678	3.50E-02

GO:0006997	nucleus organization	0.534759	0.089	3	5.961657	1.30E-02
GO:0006027	glycosaminoglycan catabolic process	0.534759	0.089	3	5.961657	1.30E-02
GO:0006873	cellular ion homeostasis	0.356506	0.093	2	20.66708	3.60E-03
GO:1903862	positive regulation of oxidative phosphorylation	0.356506	0.093	2	20.66708	3.60E-03
GO:0019217	regulation of fatty acid metabolic process	0.356506	0.093	2	20.66708	3.60E-03
GO:0060591	chondroblast differentiation	0.356506	0.093	2	20.66708	3.60E-03
GO:0007565	female pregnancy	0.891266	0.093	5	2.902679	2.90E-02
CC	**BL-P1 Control Cellular Component**	**%**	**PValue**	**Genes**	**Fold Enrichment**	**Fisher Exact**
GO:0045095	keratin filament	1.782531	0.000	10	5.062222	0.000029
GO:0005615	extracellular space	8.02139	0.001	45	1.691166	0.00037
GO:0031012	extracellular matrix	2.85205	0.001	16	2.736336	0.00028
GO:0071682	endocytic vesicle lumen	0.713012	0.004	4	12.65556	0.00023
GO:0031225	anchored component of membrane	1.426025	0.007	8	3.583874	0.0018
GO:0070062	extracellular exosome	13.19073	0.007	74	1.332638	0.0052
GO:0030863	cortical cytoskeleton	0.713012	0.009	4	9.20404	0.00083
GO:0022625	cytosolic large ribosomal subunit	1.069519	0.011	6	4.466667	0.0022
GO:0042470	melanosome	1.247772	0.015	7	3.508471	0.0039
GO:0033270	paranode region of axon	0.534759	0.022	3	12.65556	0.0015
GO:0005833	hemoglobin complex	0.534759	0.022	3	12.65556	0.0015
GO:0005925	focal adhesion	2.673797	0.023	15	1.942029	0.011
GO:0015934	large ribosomal subunit	0.534759	0.030	3	10.84762	0.0024
GO:0043195	terminal bouton	0.891266	0.034	5	4.082437	0.0075
GO:0005576	extracellular region	7.664884	0.037	43	1.352022	0.026
GO:0005578	proteinaceous extracellular matrix	1.960784	0.040	11	2.077778	0.018
GO:0005796	Golgi lumen	1.069519	0.041	6	3.163889	0.012
GO:0005604	basement membrane	0.891266	0.071	5	3.203938	0.02
GO:0032587	ruffle membrane	0.891266	0.079	5	3.086721	0.023
GO:0031526	brush border membrane	0.713012	0.079	4	3.97037	0.018

GO:0043202	lysosomal lumen	0.891266	0.087	5	2.977778	0.027
GO:0031410	cytoplasmic vesicle	1.604278	0.094	9	1.938723	0.044
GO:0005887	integral component of plasma membrane	6.417112	0.096	36	1.287915	0.071
MF	**BL-P1 Control Molecular Functions**	**%**	**PValue**	**Genes**	**Fold Enrichment**	**Fisher Exact**
GO:0030506	ankyrin binding	0.891266	0.001	5	12.98538	3.10E-05
GO:0022857	transmembrane transporter activity	1.069519	0.002	6	6.360188	3.40E-04
GO:0019825	oxygen binding	0.891266	0.012	5	5.525696	2.00E-03
GO:0005344	oxygen transporter activity	0.534759	0.029	3	11.13033	2.20E-03
GO:0071633	dihydroceramidase activity	0.356506	0.038	2	51.94154	3.70E-04
GO:0051082	unfolded protein binding	1.069519	0.061	6	2.833175	2.00E-02
GO:0046983	protein dimerization activity	1.247772	0.069	7	2.423938	2.60E-02
GO:0017040	ceramidase activity	0.356506	0.075	2	25.97077	2.20E-03
GO:0005506	iron ion binding	1.247772	0.075	7	2.37641	2.90E-02
GO:0004860	protein kinase inhibitor activity	0.713012	0.078	4	3.995503	1.80E-02
GO:0005102	receptor binding	2.139037	0.079	12	1.765718	4.10E-02
GO:0043236	laminin binding	0.534759	0.083	3	6.232985	1.20E-02
GO:0001205	transcriptional activator activity, RNA polymerase II distal enhancer sequence-specific binding	0.534759	0.083	3	6.232985	1.20E-02
GO:0050840	extracellular matrix binding	0.534759	0.088	3	5.993254	1.30E-02

BP	**BL-P3 Control Biological Processess**	**%**	**PValue**	**Genes**	**Fold Enrichment**	**Fisher Exact**
GO:0016486	peptide hormone processing	7.407407	0.0180	2	104.95	1.60E-04
GO:0006337	nucleosome disassembly	7.407407	0.0191	2	98.77647	1.80E-04
GO:0043044	ATP-dependent chromatin remodeling	7.407407	0.0257	2	73.0087	3.40E-04
GO:0016485	protein processing	7.407407	0.0784	2	23.32222	3.30E-03
GO:0001843	neural tube closure	7.407407	0.0837	2	21.80779	3.70E-03

GO:0006338	chromatin remodeling	7.407407	0.0930	2	19.52558	4.60E-03
CC	**BL-P3 Control Cellular Component**	**%**	**PValue**	**Count**	**Fold Enrichment**	**Fisher Exact**
GO:0090544	BAF-type complex	7.407407	0.0066	2	289.2698	1.90E-05
GO:0071564	npBAF complex	7.407407	0.0131	2	144.6349	8.30E-05
GO:0071565	nBAF complex	7.407407	0.0153	2	123.9728	1.10E-04
GO:0016514	SWI/SNF complex	7.407407	0.0163	2	115.7079	1.30E-04
MF	**BL-P3 Control Molecular Function**	**%**	**PValue**	**Genes**	**Fold Enrichment**	**Fisher Exact**
GO:0002039	p53 binding	7.407407	0.0728	2	25.19552	2.80E-03

BP	P1-P3 Control Biological Process	%	PValue	Genes	Fold Enrichment	Fisher Exact
GO:0001503	Ossification	2.1021	4.7E-04	7	7.03014354	6.20E-05
GO:0030154	cell differentiation	4.2042	5.1E-03	14	2.43468175	2.00E-03
GO:0050727	regulation of inflammatory response	1.5015	7.7E-03	5	6.37654743	1.10E-03
GO:0007596	blood coagulation	2.4024	8.1E-03	8	3.49323903	2.20E-03
GO:0030168	platelet activation	1.8018	1.4E-02	6	4.19188683	3.20E-03
GO:0006839	mitochondrial transport	0.9009	1.4E-02	3	16.0688995	7.70E-04
GO:0044267	cellular protein metabolic process	1.8018	1.6E-02	6	4.08531344	3.60E-03
GO:0045666	positive regulation of neuron differentiation	1.5015	1.6E-02	5	5.15028831	2.90E-03
GO:0006182	cGMP biosynthetic process	0.9009	1.6E-02	3	15.0645933	9.40E-04
GO:0032094	response to food	0.9009	2.7E-02	3	11.4777854	2.10E-03
GO:0003342	proepicardium development	0.6006	3.7E-02	2	53.5629984	4.60E-04
GO:0046686	response to cadmium ion	0.9009	3.8E-02	3	9.64133971	3.60E-03
GO:0002181	cytoplasmic translation	0.9009	3.8E-02	3	9.64133971	3.60E-03
GO:0002576	platelet degranulation	1.5015	3.9E-02	5	3.90021833	9.30E-03
GO:0071248	cellular response to metal ion	0.6006	4.9E-02	2	40.1722488	9.10E-04

GO:0045472	response to ether	0.6006	4.9E-02	2	40.1722488	9.10E-04
GO:0032496	response to lipopolysaccharide	1.8018	5.3E-02	6	2.93943284	1.70E-02
GO:0035811	negative regulation of urine volume	0.6006	6.0E-02	2	32.137799	1.50E-03
GO:1902261	positive regulation of delayed rectifier potassium channel activity	0.6006	6.0E-02	2	32.137799	1.50E-03
GO:0006348	chromatin silencing at telomere	0.6006	7.2E-02	2	26.7814992	2.20E-03
GO:0043410	positive regulation of MAPK cascade	1.2012	7.9E-02	4	3.96762951	1.80E-02
GO:0042127	regulation of cell proliferation	1.8018	8.0E-02	6	2.60576749	2.80E-02
GO:0007617	mating behavior	0.6006	8.4E-02	2	22.9555707	3.10E-03
GO:0007204	positive regulation of cytosolic calcium ion concentration	1.5015	8.5E-02	5	2.99792902	2.60E-02
GO:0007566	embryo implantation	0.9009	9.5E-02	3	5.73889269	1.50E-02
CC	**P1-P3 Control Cellular Component**	**%**	**PValue**	**Count**	**Fold Enrichment**	**Fisher Exact**
GO:0031092	platelet alpha granule membrane	0.9009	1.2E-02	3	17.9723866	5.40E-04
GO:0009898	cytoplasmic side of plasma membrane	1.2012	1.6E-02	4	7.41717542	2.00E-03
GO:0000781	chromosome, telomeric region	1.2012	2.1E-02	4	6.77220364	2.80E-03
GO:0031966	mitochondrial membrane	1.5015	3.3E-02	5	4.14257138	7.30E-03
GO:0045095	keratin filament	1.5015	3.9E-02	5	3.89401709	9.40E-03
GO:0009986	cell surface	3.9039	4.7E-02	13	1.86797868	2.30E-02
GO:0043292	contractile fiber	0.6006	8.6E-02	2	22.2515263	3.30E-03
GO:0070062	extracellular exosome	13.5135	8.6E-02	45	1.2467504	6.60E-02
GO:0005634	Nucleus	24.024	9.2E-02	80	1.15058677	7.70E-02
GO:0044327	dendritic spine head	0.6006	9.8E-02	2	19.4700855	4.40E-03
MF	**P1-P3 Control Molecular Functions**	**%**	**PValue**	**Count**	**Fold Enrichment**	**Fisher Exact**
GO:0030506	ankyrin binding	0.9009	2.5E-02	3	11.9441038	1.90E-03
GO:0003756	protein disulfide isomerase activity	0.9009	3.0E-02	3	10.8582762	2.50E-03

GO:0003723	RNA binding	3.9039	4.3E-02	13	1.89242351	2.10E-02
GO:0044822	poly(A) RNA binding	6.60661	4.4E-02	22	1.55164029	2.70E-02
GO:0015026	coreceptor activity	0.9009	5.4E-02	3	7.96273585	6.20E-03
GO:0019960	C-X3-C chemokine binding	0.6006	6.1E-02	2	31.8509434	1.50E-03
GO:0010485	H4 histone acetyltransferase activity	0.6006	7.3E-02	2	26.5424528	2.30E-03
GO:0005251	delayed rectifier potassium channel activity	0.9009	7.4E-02	3	6.63561321	1.00E-02
GO:0051087	chaperone binding	1.2012	8.1E-02	4	3.93221523	1.90E-02

Table 6.6.1.: Significantly regulated gene ontologies in stringent protocol using DAVID database tested for multiple corrections with level of significance fixed at $p<0.05$

6.6.2. Over representation Analysis

The genes that are found to be detected in all the 36 conditions (12 samples across 3 timepoints) alone were filtered out and processed for obtaining differentially regulated genes making a stringent condition. Over-representation analysis was performed using PANTHER database to understand the processes regulated in the Yoga group and Control group.

Timepoint	Molecular Function	Biological Process	Protein Class
BL-P1 Yoga ↑	sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0000981) transcription cofactor activity (GO:0003712) transcription factor binding transcription factor activity (GO:0000989) protein binding transcription factor activity (GO:0000988)	segment specification (GO:0007379) skeletal system development (GO:0001501) muscle organ development (GO:0007517) regulation of transcription from RNA polymerase II promoter (GO:0006357) mesoderm development (GO:0007498)	basic helix-loop-helix transcription factor (PC00055) transcription cofactor (PC00217) homeobox transcription factor (PC00119) helix-turn-helix transcription factor (PC00116) transcription factor (PC00218) zinc finger transcription factor (PC00244)

	sequence-specific DNA binding transcription factor activity (GO:0003700) DNA binding (GO:0003677) nucleic acid binding (GO:0003676) binding (GO:0005488)	regulation of nucleobase-containing compound metabolic process (GO:0019219) nervous system development (GO:0007399) developmental process (GO:0032502) system development (GO:0048731) nucleobase-containing compound metabolic process (GO:0006139) biosynthetic process (GO:0009058) nitrogen compound metabolic process (GO:0006807) metabolic process (GO:0008152) primary metabolic process (GO:0044238)	DNA binding protein (PC00009) nucleic acid binding (PC00171)
BL-P1 Control ↑	transcriptional activator activity, RNA polymerase II core promoter proximal region sequence-specific binding (GO:0001077) transcriptional activator activity, RNA polymerase II transcription regulatory region sequence-specific binding (GO:0001228)	regulation of transcription from RNA polymerase II promoter (GO:0006357) regulation of nucleobase-containing compound metabolic process (GO:0019219) developmental process (GO:0032502) metabolic process (GO:0008152)	basic helix-loop-helix transcription factor (PC00055) homeobox transcription factor (PC00119) helix-turn-helix transcription factor (PC00116) transcription factor (PC00218)

	transcription factor activity, RNA polymerase II core promoter proximal region sequence-specific binding (GO:0000982) RNA polymerase II core promoter proximal region sequence-specific DNA binding (GO:0000978) core promoter proximal region sequence-specific DNA binding (GO:0000987) core promoter proximal region DNA binding (GO:0001159) RNA polymerase II regulatory region sequence-specific DNA binding (GO:0000977) RNA polymerase II regulatory region DNA binding (GO:0001012) transcription regulatory region sequence-specific DNA binding (GO:0000976) RNA polymerase II transcription factor activity, sequence-specific DNA binding (GO:0000981) sequence-specific double-stranded DNA binding (GO:1990837)		DNA binding protein (PC00009) nucleic acid binding (PC00171)

	transcription factor binding (GO:0008134) sequence-specific DNA binding (GO:0043565) transcription regulatory region DNA binding (GO:0044212) regulatory region DNA binding (GO:0000975) regulatory region nucleic acid binding (GO:0001067) double-stranded DNA binding (GO:0003690) transcription factor activity, sequence-specific DNA binding (GO:0003700) nucleic acid binding transcription factor activity (GO:0001071) transcription regulator activity (GO:0140110) DNA binding (GO:0003677) protein dimerization activity (GO:0046983) nucleic acid binding (GO:0003676)		

	heterocyclic compound binding (GO:1901363) organic cyclic compound binding (GO:0097159)		
P1-P3 Yoga ↑	sequence-specific DNA binding RNA polymerase II transcription factor activity (GO:0000981) sequence-specific DNA binding transcription factor activity (GO:0003700) DNA binding (GO:0003677) nucleic acid binding (GO:0003676) binding (GO:0005488)	regulation of transcription from RNA polymerase II promoter (GO:0006357) regulation of nucleobase-containing compound metabolic process (GO:0019219) developmental process (GO:0032502) nucleobase-containing compound metabolic process (GO:0006139) metabolic process (GO:0008152)	transcription factor (PC00218) homeobox transcription factor (PC00119) helix-turn-helix transcription factor (PC00116) zinc finger transcription factor (PC00244) DNA binding protein (PC00009) nucleic acid binding (PC00171)
P1-P3 Control ↑	sequence-specific DNA binding transcription factor activity (GO:0003700) DNA binding (GO:0003677) nucleic acid binding (GO:0003676)	regulation of transcription from RNA polymerase II promoter (GO:0006357) regulation of nucleobase-containing compound metabolic process (GO:0019219) nucleobase-containing compound metabolic process (GO:0006139) metabolic process (GO:0008152)	basic helix-loop-helix transcription factor (PC00055) homeobox transcription factor (PC00119) helix-turn-helix transcription factor (PC00116) transcription factor (PC00218) DNA binding protein (PC00009) nucleic acid binding (PC00171)

Table 6.6.2: Over-Representation analysis of over(+) and under(-) represented gene ontologies for DEGs across timepoints in Yoga and Control groups

6.6.3.Statistical Enrichment Analysis of DEG from Stringent protocol

The DEGs obtained for each time-point comparison for Yoga and control groups were tabulated with both genes common and unique to either of the groups. Consensus database was used for Gene Set Enrichment Analysis and the pathways for each time-point comparison was determined [*table 6.5.6B*] . Surprisingly, no significant pathways for the comparison BL-P3 were found.

BL-P1 pathways	**source**	**external_id**	**p-value**	**q-value**
Signal Transduction	Reactome	R-HSA-162582	1.36E-10	9.25E-08
Gene Expression	Reactome	R-HSA-74160	1.07E-06	0.000231
Metabolism	Reactome	R-HSA-1430728	1.31E-06	0.000231
GPCR downstream signalling	Reactome	R-HSA-388396	1.35E-06	0.000231
Generic Transcription Pathway	Reactome	R-HSA-212436	2.38E-06	0.000325
Metabolism of proteins	Reactome	R-HSA-392499	6.04E-06	0.000686
Metabolism of lipids and lipoproteins	Reactome	R-HSA-556833	7.49E-06	0.000729
Developmental Biology	Reactome	R-HSA-1266738	2.46E-05	0.001927
Immune System	Reactome	R-HSA-168256	2.54E-05	0.001927
Signaling by GPCR	Reactome	R-HSA-372790	3.56E-05	0.002427
Calcium signaling pathway - Homo sapiens (human)	KEGG	path:hsa04020	0.000244	0.015137

Transcriptional Regulation by TP53	Reactome	R-HSA-3700989	0.000305	0.017344
Post-translational protein modification	Reactome	R-HSA-597592	0.000364	0.0191
Neuroactive ligand-receptor interaction - Homo sapiens (human)	KEGG	path:hsa04080	0.000488	0.022938
Signaling by Rho GTPases	Reactome	R-HSA-194315	0.000504	0.022938
Keratinization	Reactome	R-HSA-6805567	0.00061	0.026016
Innate Immune System	Reactome	R-HSA-168249	0.000695	0.027873
Hemostasis	Reactome	R-HSA-109582	0.000966	0.036591
Adaptive Immune System	Reactome	R-HSA-1280218	0.001093	0.039221
Signaling by Wnt	Reactome	R-HSA-195721	0.001526	0.051971
Membrane Trafficking	Reactome	R-HSA-199991	0.0016	0.051971
Olfactory transduction - Homo sapiens (human)	KEGG	path:hsa04740	0.001709	0.052979
Signalling by NGF	Reactome	R-HSA-166520	0.00234	0.069377
Ras signaling pathway - Homo sapiens (human)	KEGG	path:hsa04014	0.002441	0.069377
Neuronal System	Reactome	R-HSA-112316	0.002579	0.070348

GPCRs, Class A Rhodopsin-like	Wikipathways	WP455	0.00293	0.076848
Olfactory Signaling Pathway	Reactome	R-HSA-381753	0.003418	0.086335
Metabolism of carbohydrates	Reactome	R-HSA-71387	0.003906	0.091864
G alpha (s) signalling events	Reactome	R-HSA-418555	0.003906	0.091864
cAMP signaling pathway - Homo sapiens (human)	KEGG	path:hsa04024	0.004745	0.107422
Rho GTPase cycle	Reactome	R-HSA-194840	0.004883	0.107422
p75 NTR receptor-mediated signalling	Reactome	R-HSA-193704	0.007813	0.166504
MAPK signaling pathway - Homo sapiens (human)	KEGG	path:hsa04010	0.008545	0.173201
Vesicle-mediated transport	Reactome	R-HSA-5653656	0.008635	0.173201
Metabolism of vitamins and cofactors	Reactome	R-HSA-196854	0.009277	0.180776
Olfactory receptor activity	Wikipathways	WP3608	0.009766	0.185004

P1_P3 pathway	**source**	**external_id**	**p-value**	**q-value**
Gene Expression	Reactome	R-HSA-74160	4.01E-05	0.007284
Metabolism	Reactome	R-HSA-1430728	5.83E-05	0.007284

Metabolism of proteins	Reactome	R-HSA-392499	0.000113	0.009454
GPCR downstream signalling	Reactome	R-HSA-388396	0.00051	0.022802
Generic Transcription Pathway	Reactome	R-HSA-212436	0.00061	0.022802
Post-translational protein modification	Reactome	R-HSA-597592	0.000631	0.022802
Immune System	Reactome	R-HSA-168256	0.000638	0.022802
Signal Transduction	Reactome	R-HSA-162582	0.003041	0.095031
Transcriptional Regulation by TP53	Reactome	R-HSA-3700989	0.003906	0.108507
Neuronal System	Reactome	R-HSA-112316	0.006836	0.170898

Table 6.6.3: Significantly regulated pathways from stringent gene list analysis for timepoints BL-P1 and P1-P3

6.6.4. Transcription factor Profiling

Genes that were more than two-fold regulated in Yoga and Control groups were tabulated for three timepoint comparisons: BL-P1, P1-P3 & BL-P3. The differentially regulated transcription factors were determined from the PANTHER database (Version 12.0; released on 10-07-2017).

The list of transcription factors from three timepoint comparison is mentioned in Appendix-13.

Over-representation analysis of identified transcription factors was performed using PANTHER database with Bonferroni correction to understand the role of the regulated transcription factors (Annexure 13). The differentially regulated transcription factors unique to yoga

and control groups at each timepoint was tabulated using InteractiVenn (Fig. 6.6.4). Unlike our earlier observation, the number of transcription factors regulated were more in Yoga group in the initial and last phase of expedition.

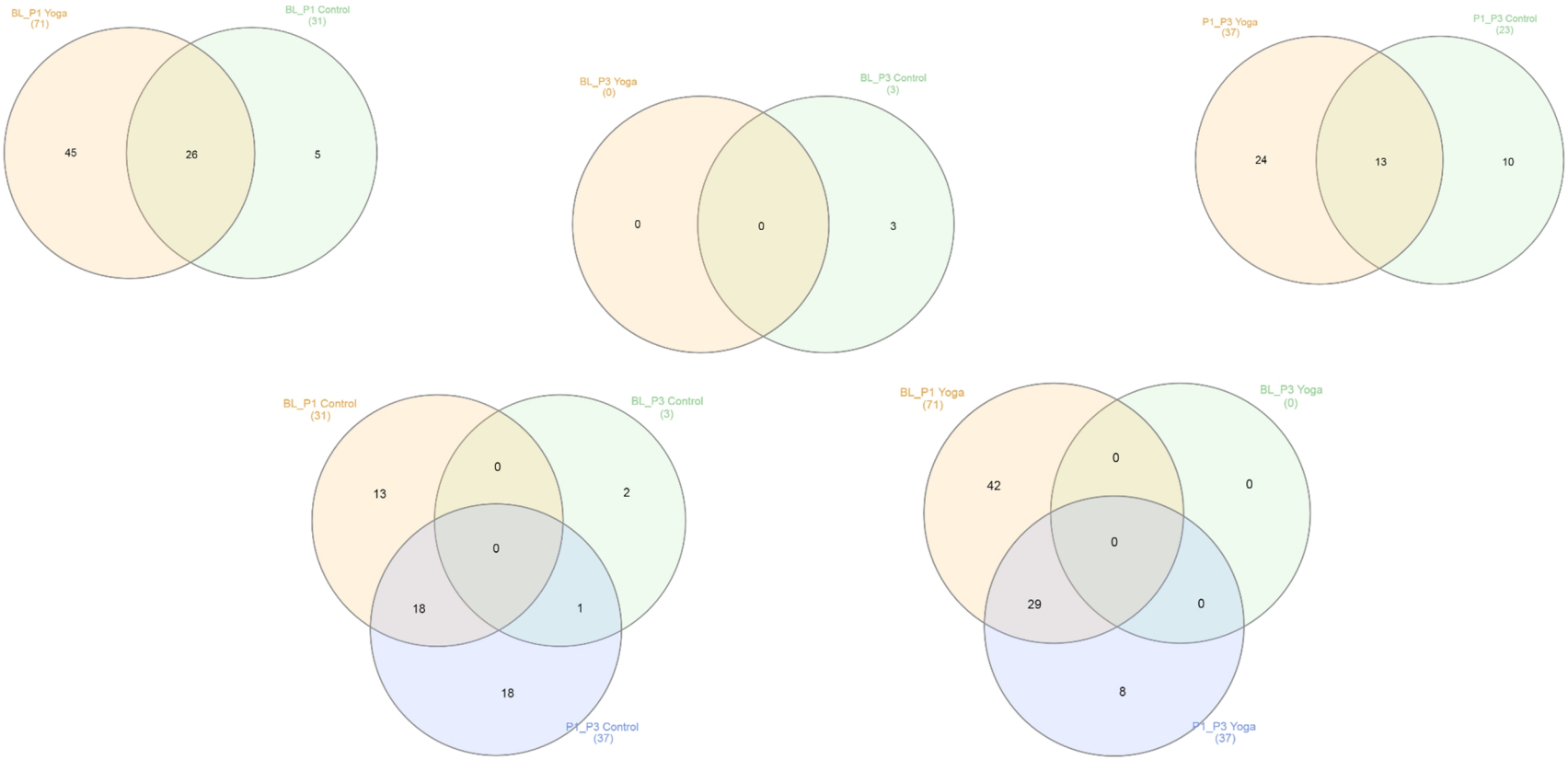


Fig 6.6.4: Differentially expressed transcription factors in Conventional analysis (Stringent protocol)