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About OMICS International Conferences

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Metabolomics Approach to Understanding the Metabolic Regulatory Effects on Rats under Several Kinds of Stresses



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About stress

is an organism's response to a stressor such as an environmental condition or a stimulus

Body's
method of
reacting to
challenge



FIGHT OR FLIGHT RESPONSE

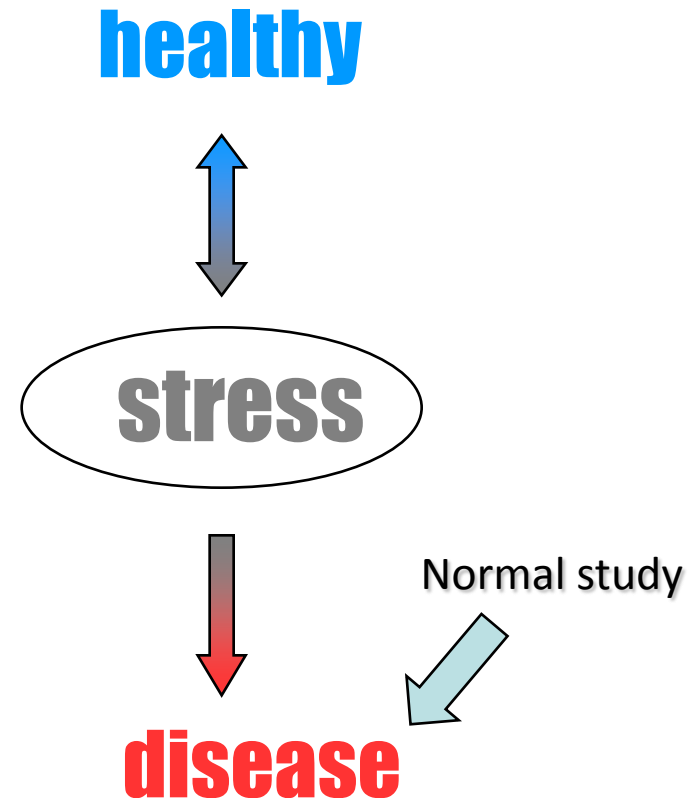
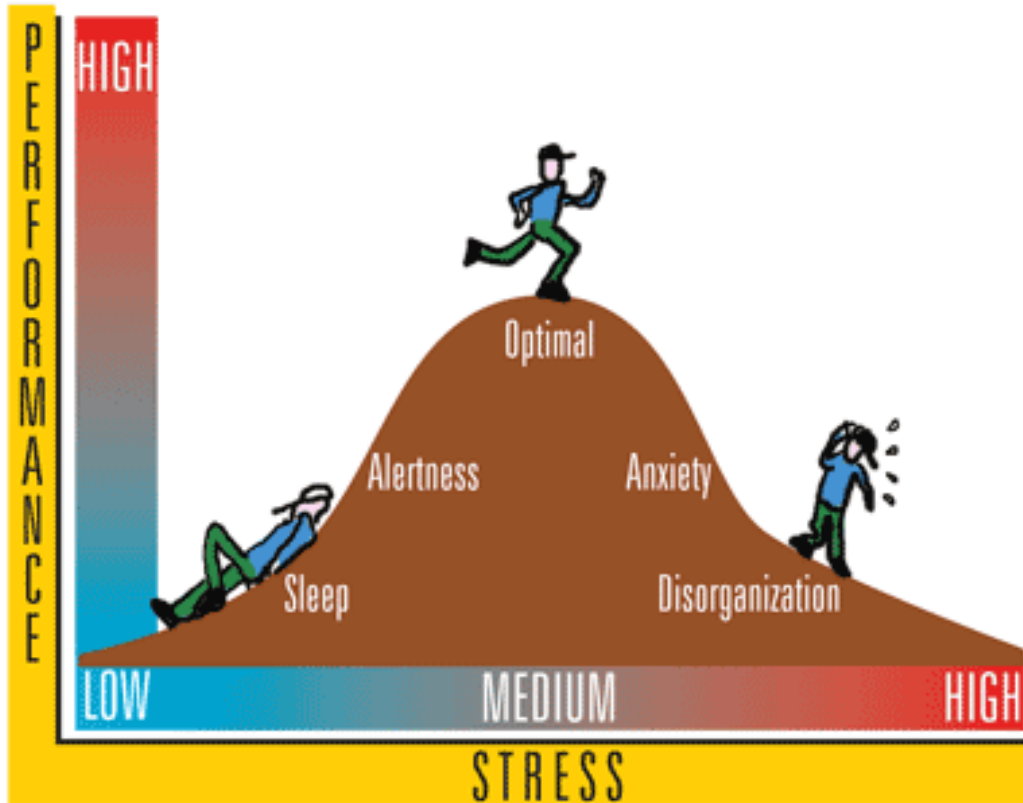
All too common in the modern workplace



STRESS

About stress

typically describes **a negative or a positive condition** that can have an impact on a person's mental and physical well-being.



Disadvantages of previous study

- ④ **Study subjects:** Diseases associated with stress response, such as chronic stress depression, stress ulcer, hypertension induced by stress
- ④ **Methods:** Molecular biology and classic medicine method on neuroendocrine, immune response, inflammatory response, biochemical and gene, protein and signal transduction

Problems:

- I. Collecting blood samples may lead to agitation, which may cause another stress
- II. Poor dynamic observation of the same objects
- III. Lack of global or systemic research methods



Our solution: Metabolomics study on stress



Acute cold stress



Acute forced swimming



Acute heat stress



Chronic stress (Chronic Unpredicted Mild Stress)



INSTRUMENTS



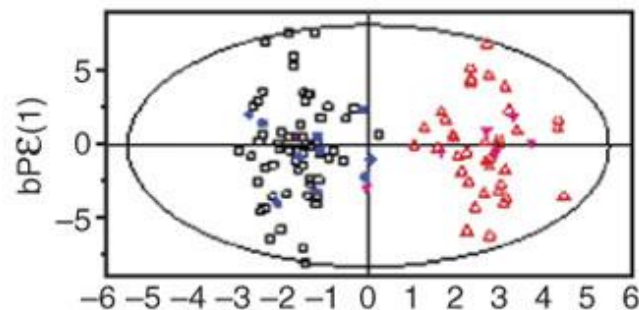
- Perkin-Elmer[®] GC and TurboMass-Autosystem XL MS(Perkin-Elmer Inc.)
- Agilent 6890N GC/5975B inert MSD (Agilent Technologies)
- Ethyl chloroformate(ECF) derivatization
- Pegasus[®] HT GC-TOFMS(LECO Inc.)
- Si(CH₃)₃ (TMS) derivatization



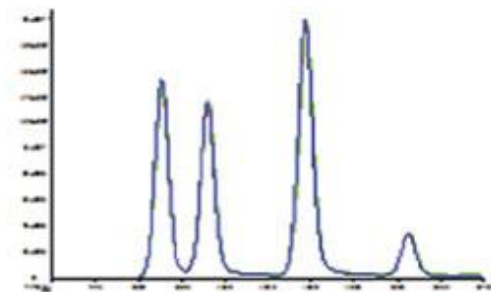
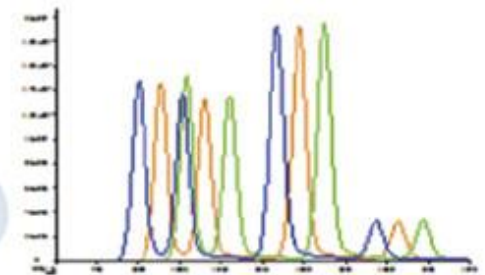
Metabolomics Study Flow Chart



Identification of
metabolites and
metabolic pathway
interpretation



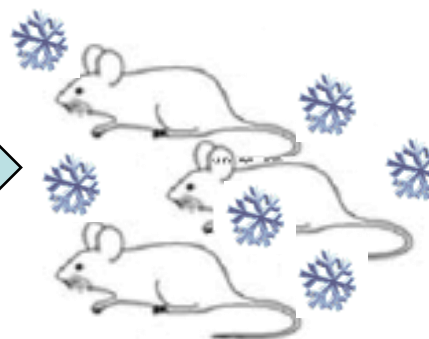
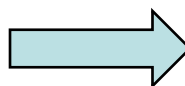
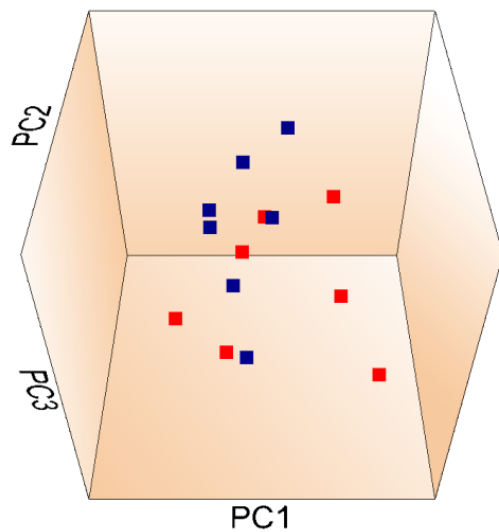
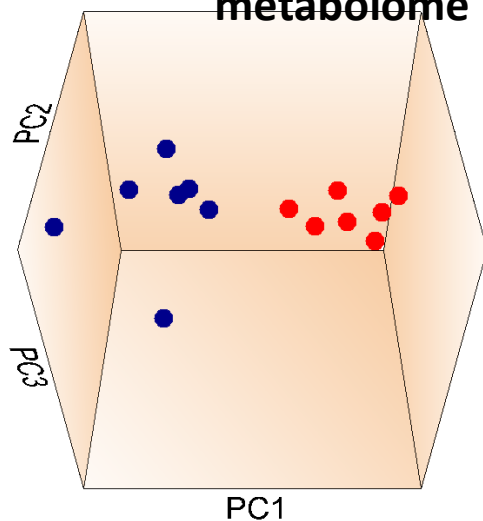
Chemometric data analysis



RT alignment

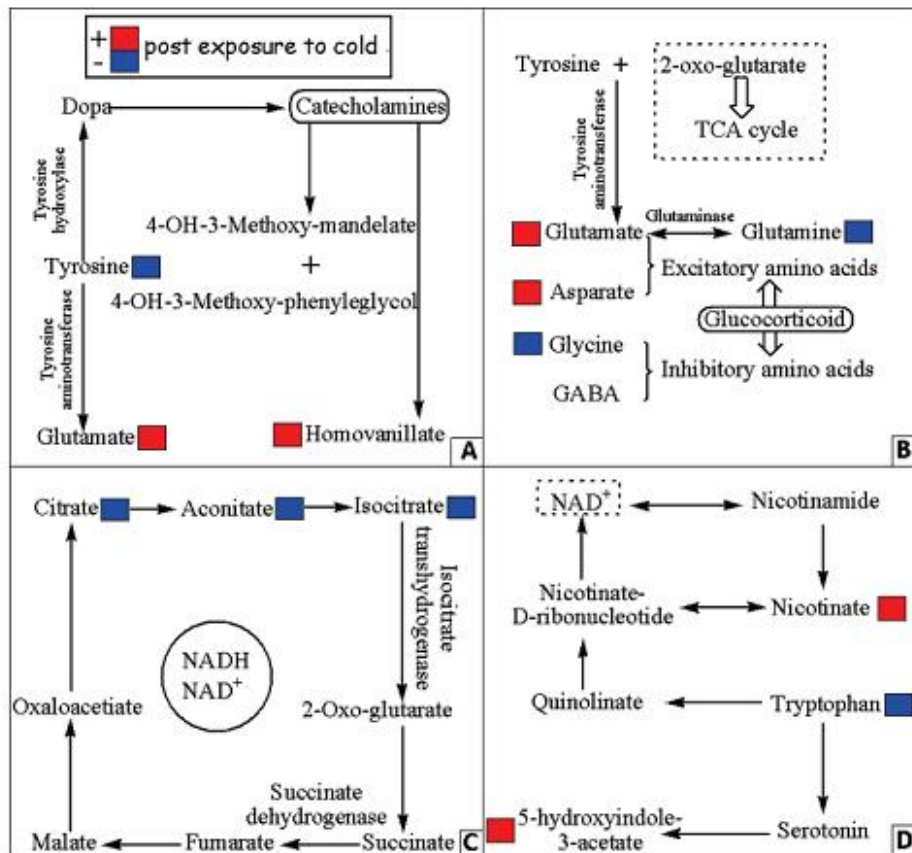
Acute Cold Stress:2 hours

PCA : Pre and post-cold stress of urine
metabolome

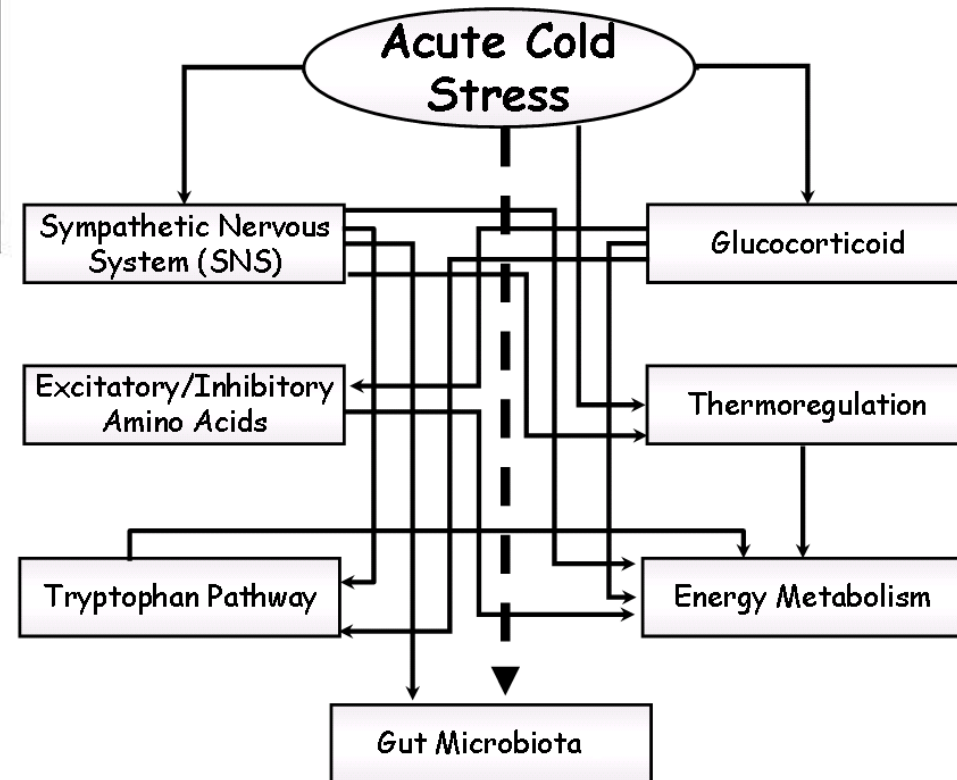


2 weeks Ginsenosides



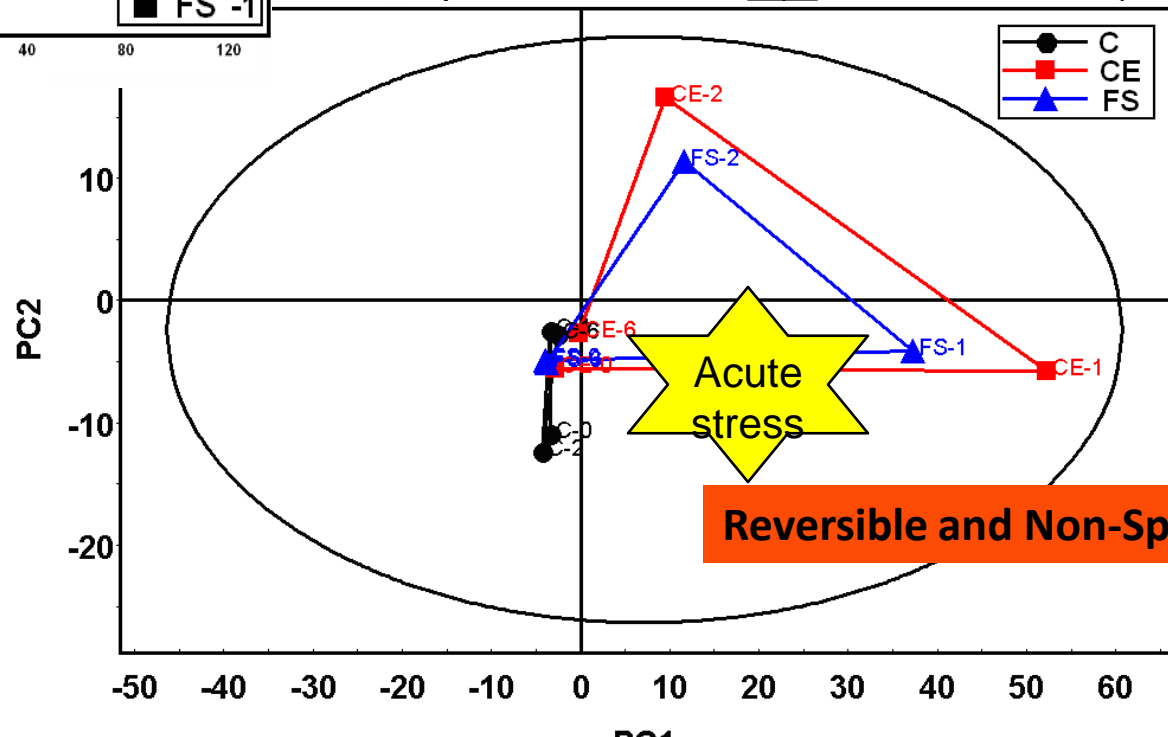
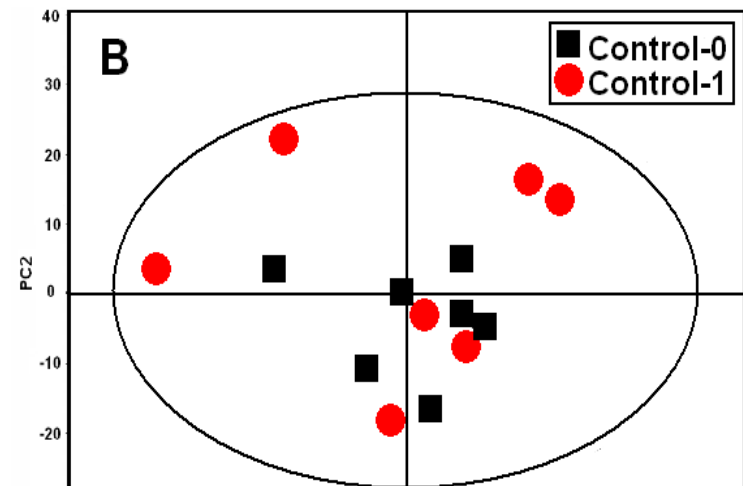
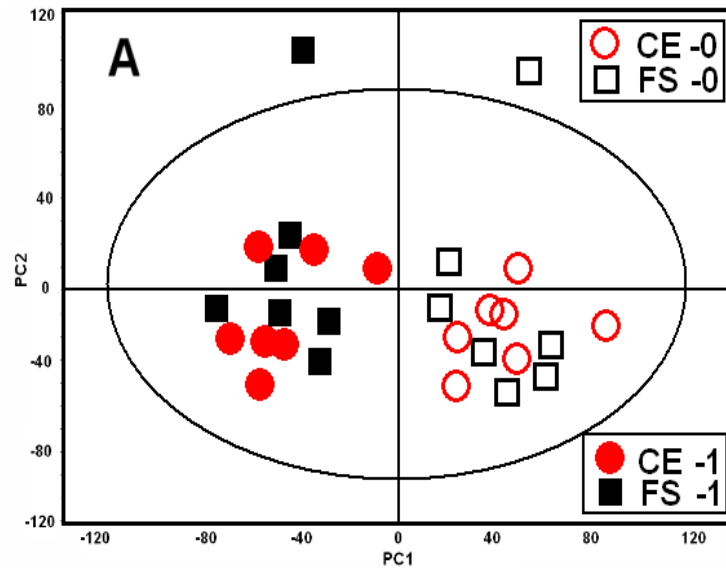


Catecholamines, glucocorticoids, the tricarboxylic acid (TCA) cycle, tryptophan (nicotinate), and gut microbiota metabolites



Metabolic regulation and compensation required to restore homeostasis

Acute stress comparison: Acute Cold & forced swimming



Chronic Unpredicted Mild Stress(CUMS)

CUMS for 27 days

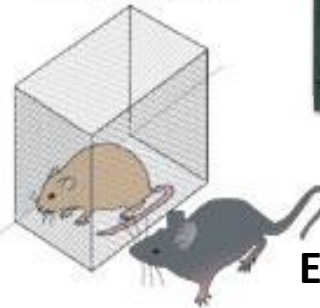
Forced swim test



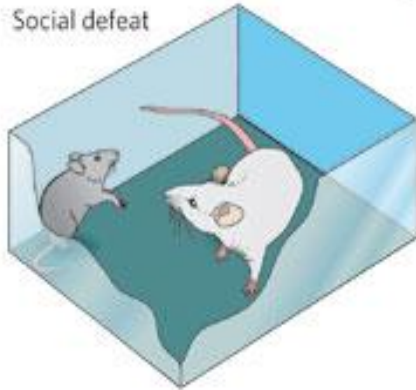
Learned helplessness



Social interaction



Social defeat



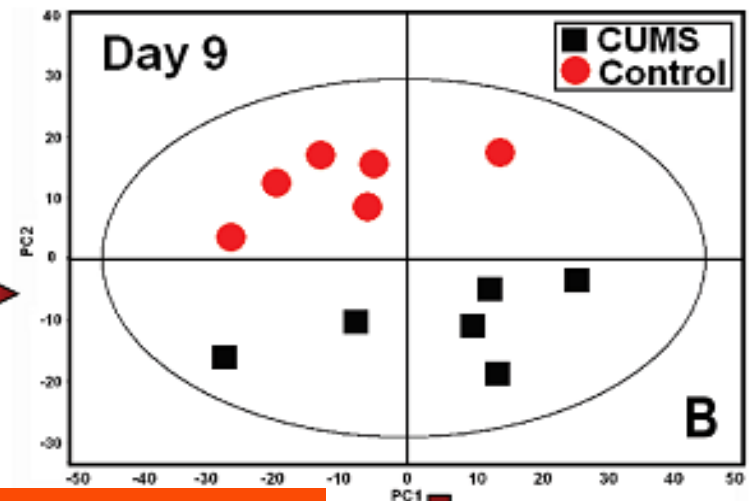
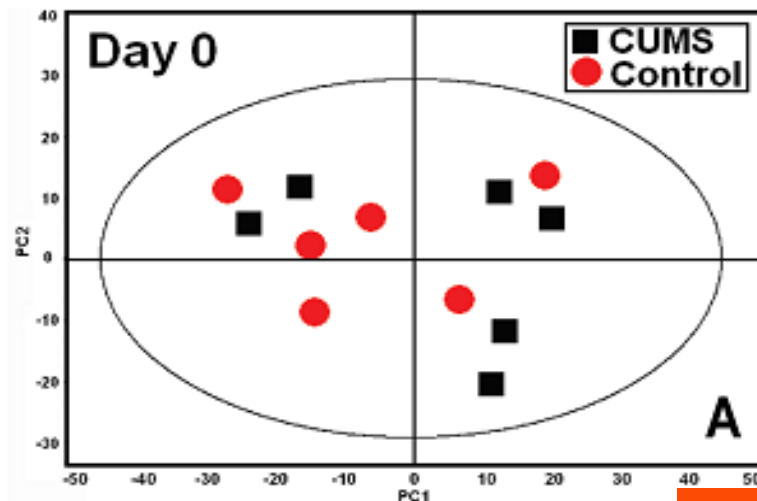
Intracranial self-stimulation



Experimental depression model

**Chronic mild stress
occurs more frequently**

The Process of Chronic stress

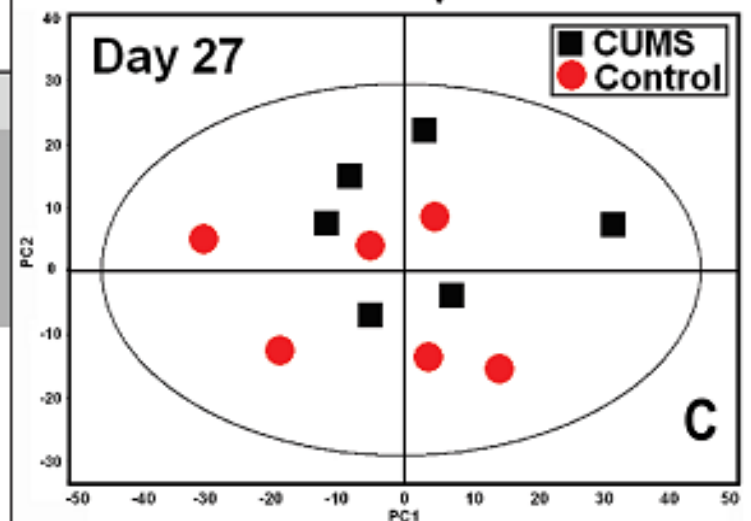


Reversible and Non-Specific

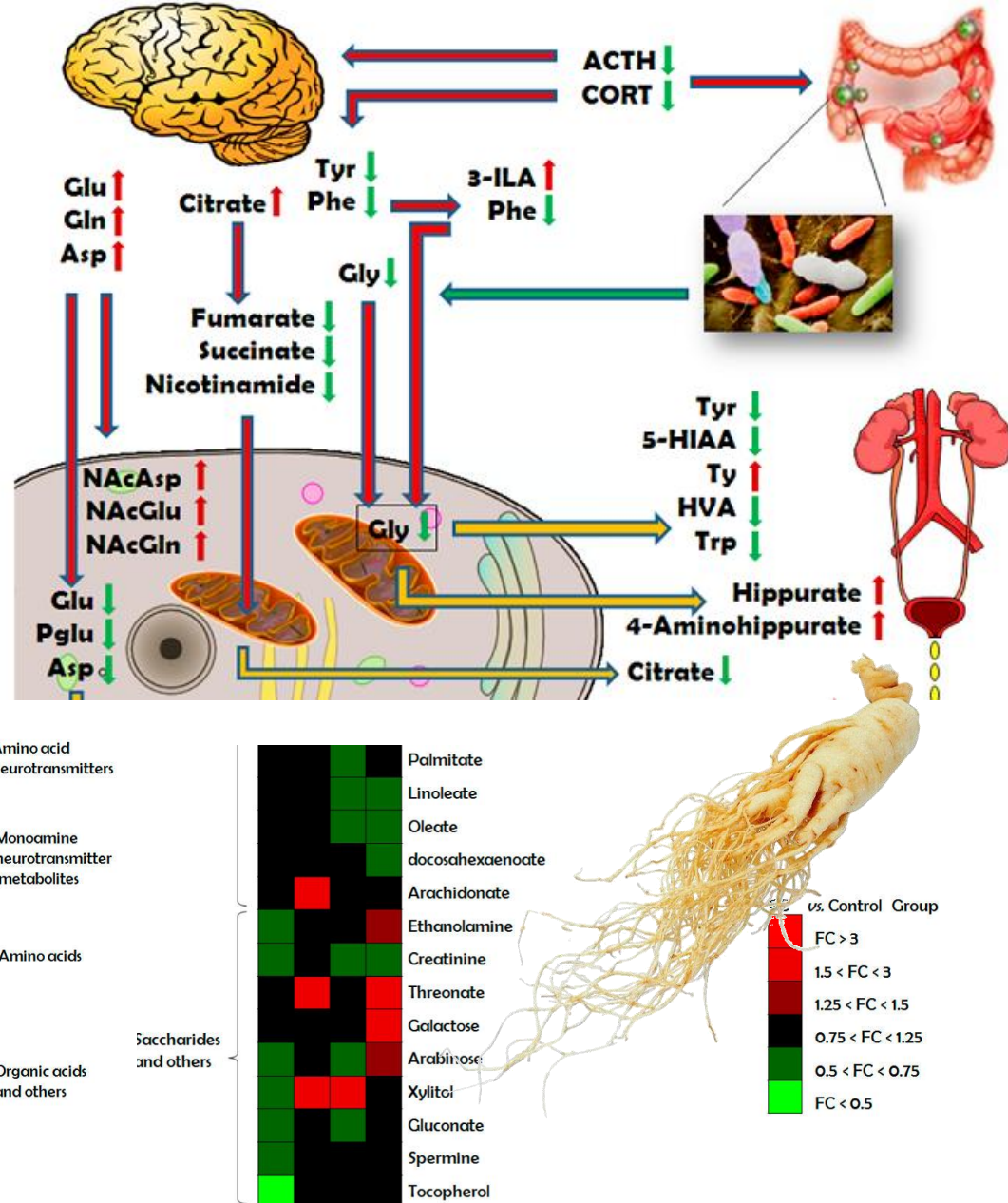
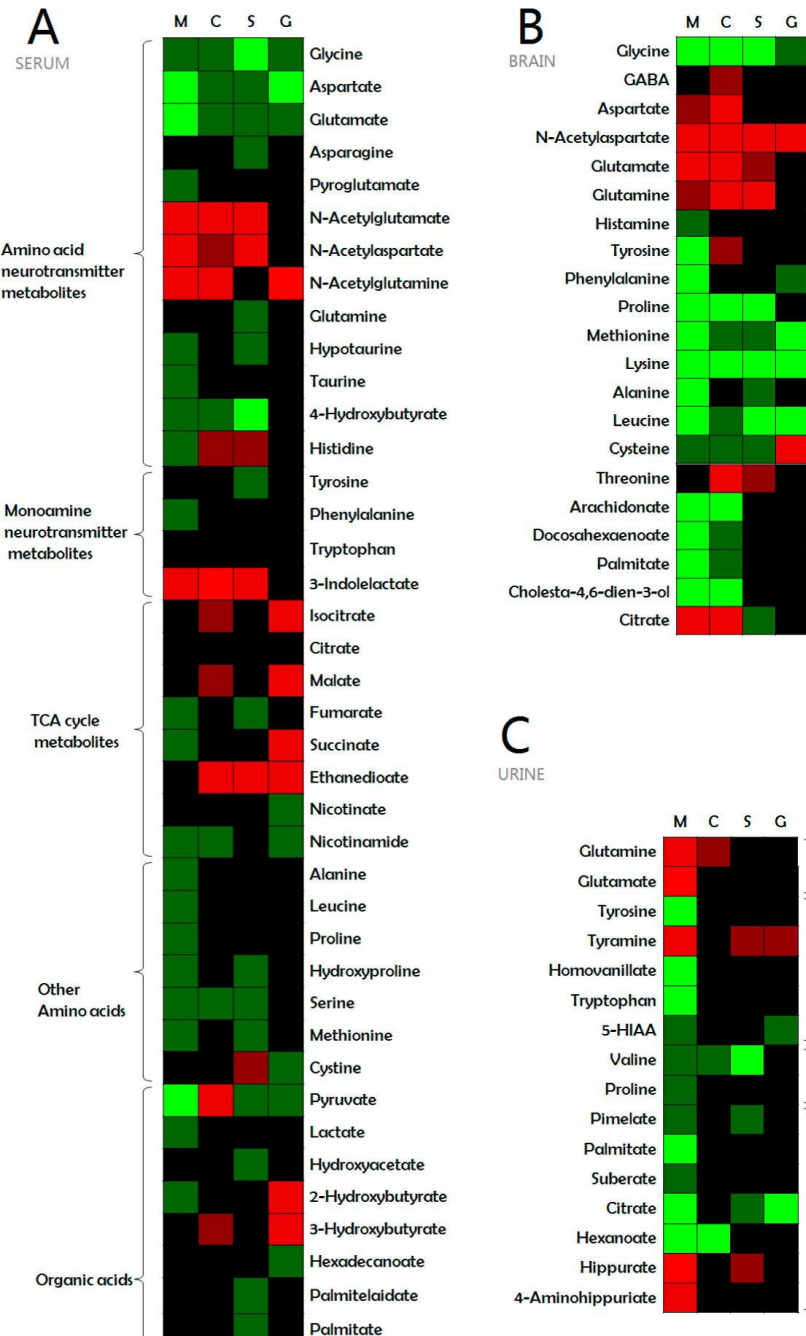
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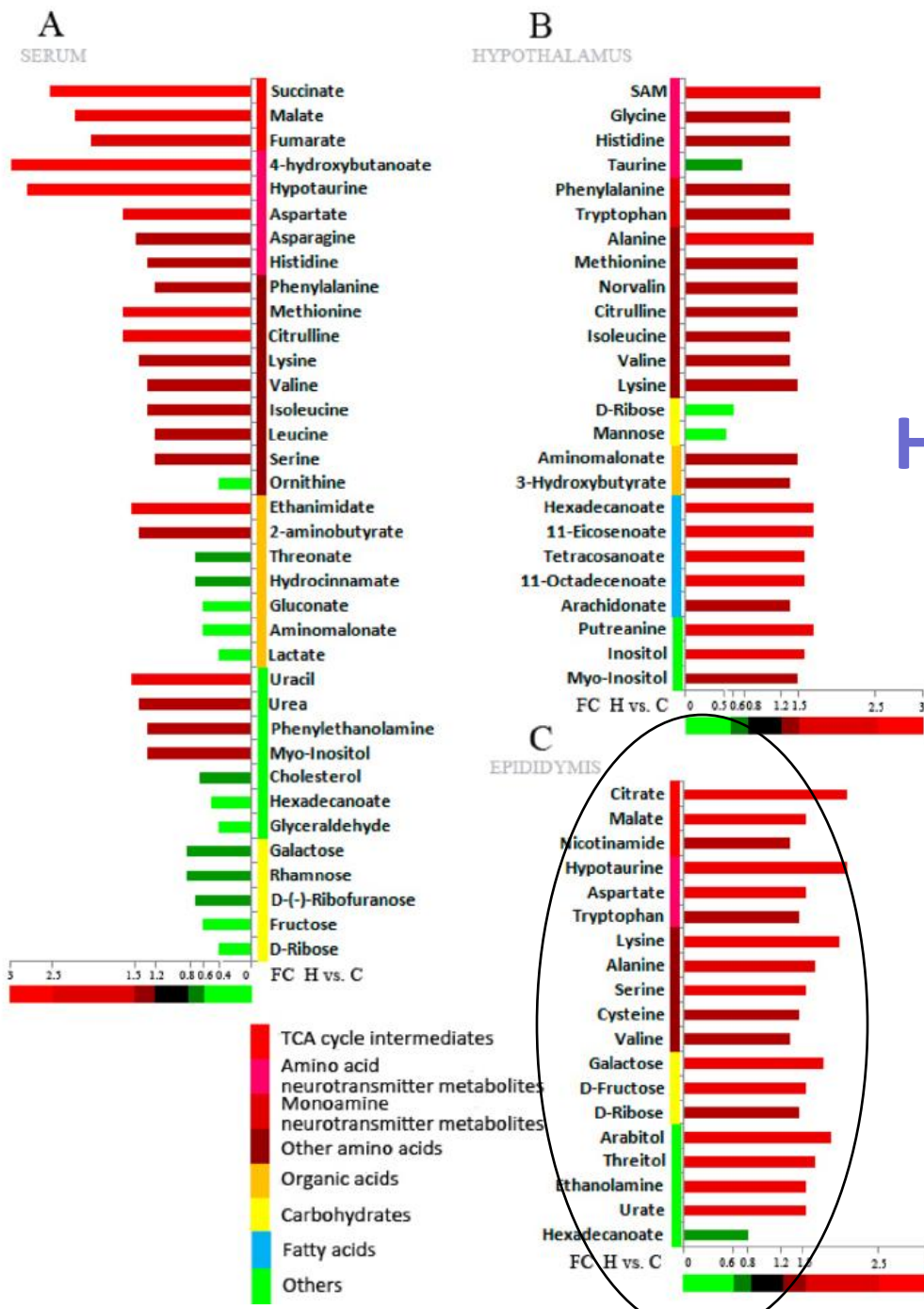
A list of the most significant metabolites relevant to CUMS

CUMS and Control on day 9 (n=6)				CUMS and Control on day 27 (n=6)			
Metabolites	P (one-way ANOVA)	P (Kruskal-Wallis)	Fold Change	Metabolites	P (one-way ANOVA)	P (Kruskal-Wallis)	Fold Change
Glutamine*	0.0298	0.0112	-2.6	Glutamine	0.0298	0.0268	2.7
Homovanillate*	0.0169	0.0027	2.5	Homovanillate	0.0006	0.0005	-3.0
Pimelate#	0.0054	0.0127	-2.4	Pimelate	0.0456	0.0330	-2.0
Proline*	0.0283	0.0550	-1.7	Proline	1.9E-05	0.0105	-2.0
Citrate*	0.0039	0.0105	-2.5	Citrate	1.4E-06	0.0105	-2.4
Glutamate*	0.0089	0.0105	2.1	Glutamate	0.0341	0.0330	3.6
Hippurate#	0.0323	0.0105	2.0	Hippurate	0.0015	0.0105	5.6
Tyramine	0.0001	0.0230	3.0	Tyramine	0.0334	0.0153	2.4
Hexadecanoate	0.0033	0.0190	-1.8	Hexadecanoate	0.0020	0.0190	-4.6
Methionine	0.0671	0.0330	2.8	Hexanoate	0.0017	0.0015	-2.4
Threonine	0.0122	0.0373	-2.1	Valine	0.0081	0.1052	-1.6
Succinate*	0.0090	0.0163	-2.3	Suberate	0.0034	0.0010	-1.5
Hexanedioate	0.0125	0.0039	2.7	Tyrosine	0.0007	0.0105	-2.4
Phenylalanine	0.0009	0.0105	3.0	5-Hydroxyindoleacetate	0.0019	0.0108	-2.0
Metabolites with the same trend(*), the opposite trend(#), of variation as acute stress				Tryptophan	0.0153	0.0242	-2.4
				4-Aminohippurate	0.0136	0.0105	2.7

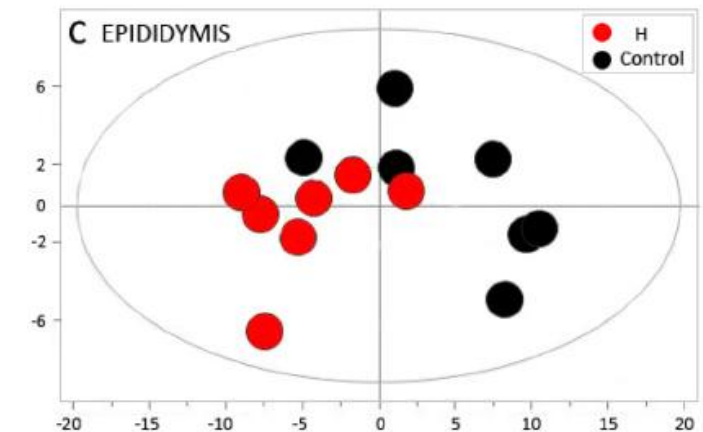
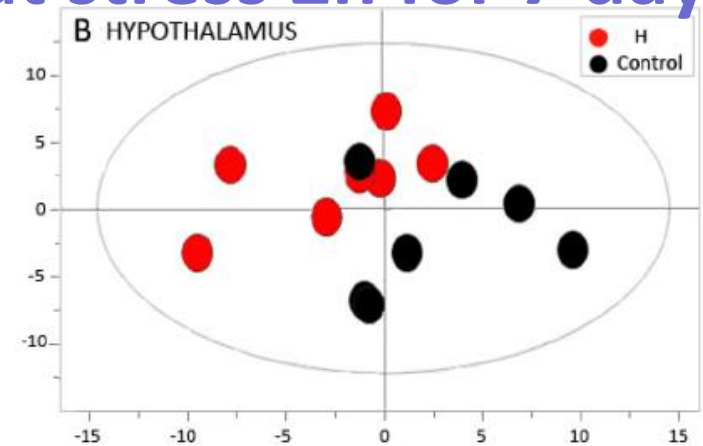
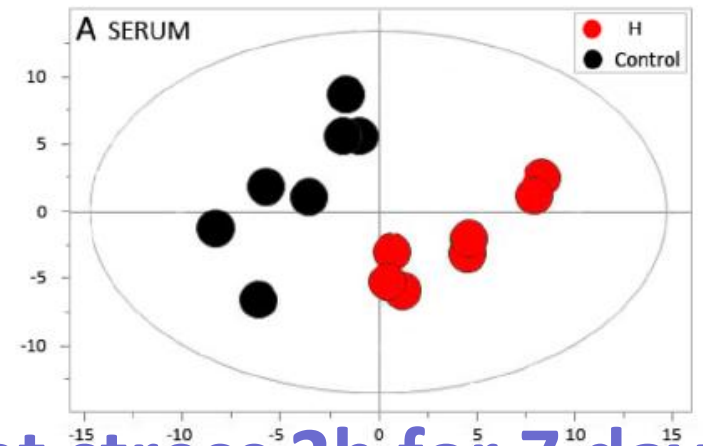


Metabonomics study of Chronic Stress(CUMS)

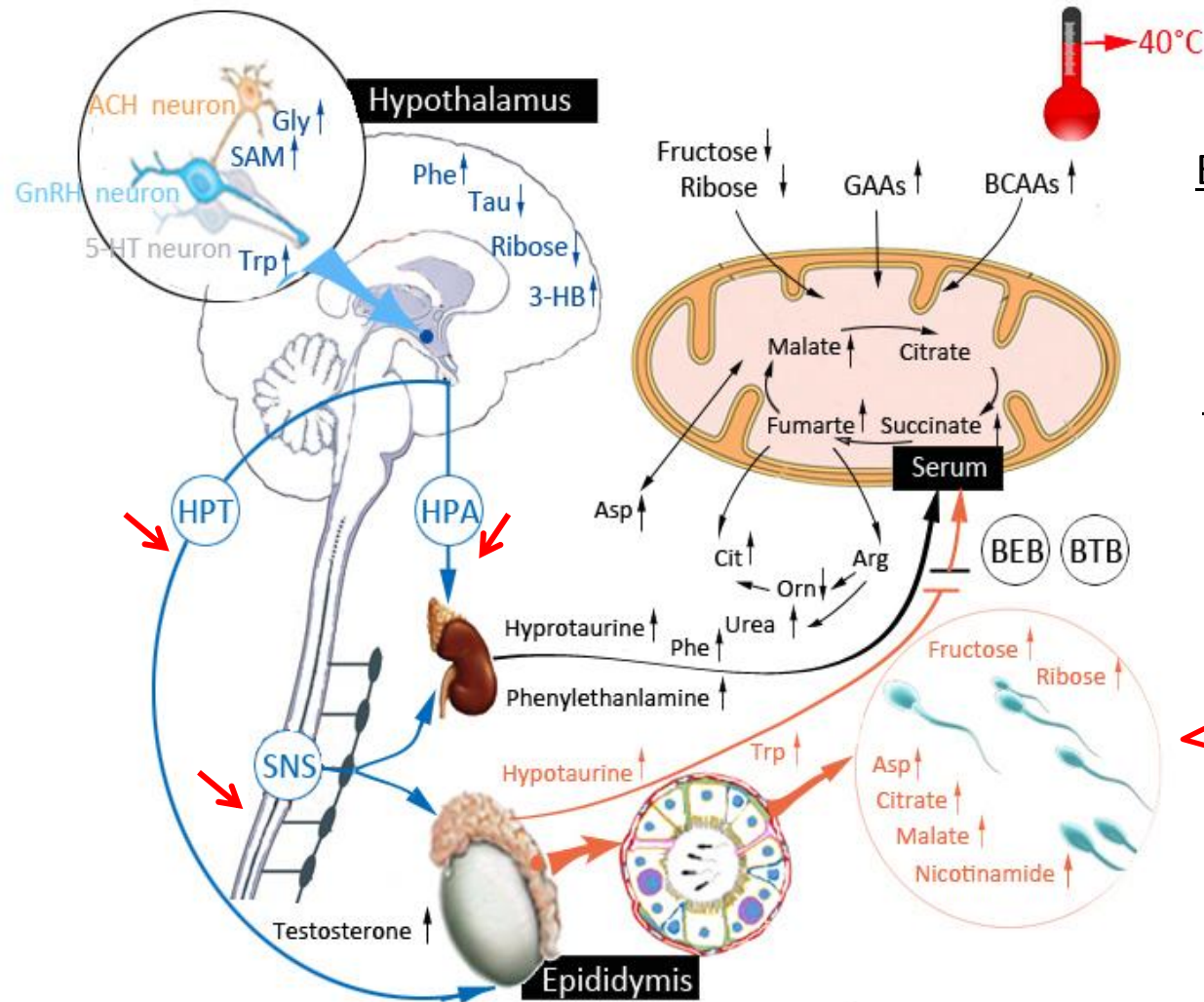




Heat stress 2h for 7 days



Heat-Stress-induced Metabolic Changes and Altered Male Reproductive Function

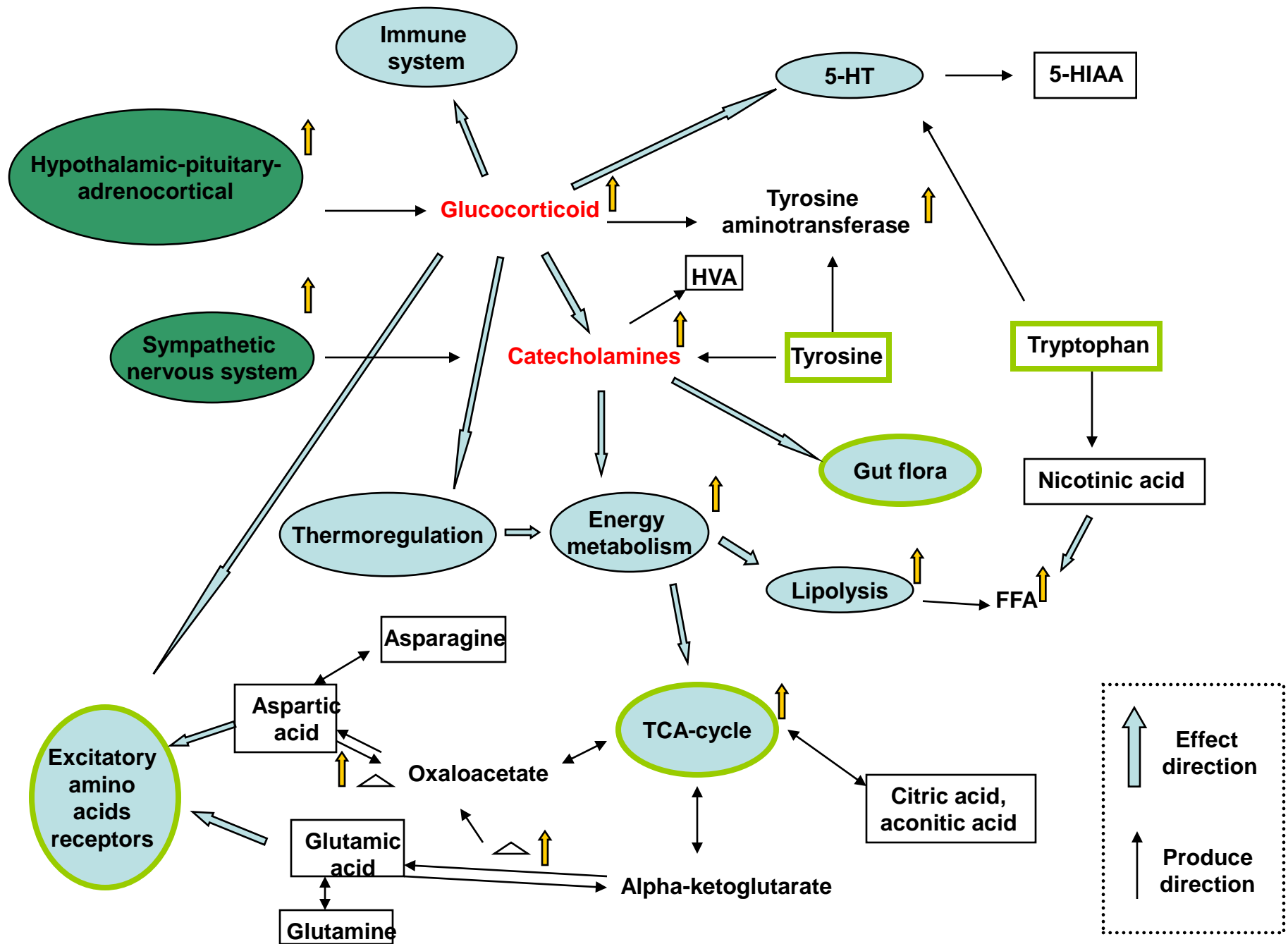


Energy metabolism metabolites

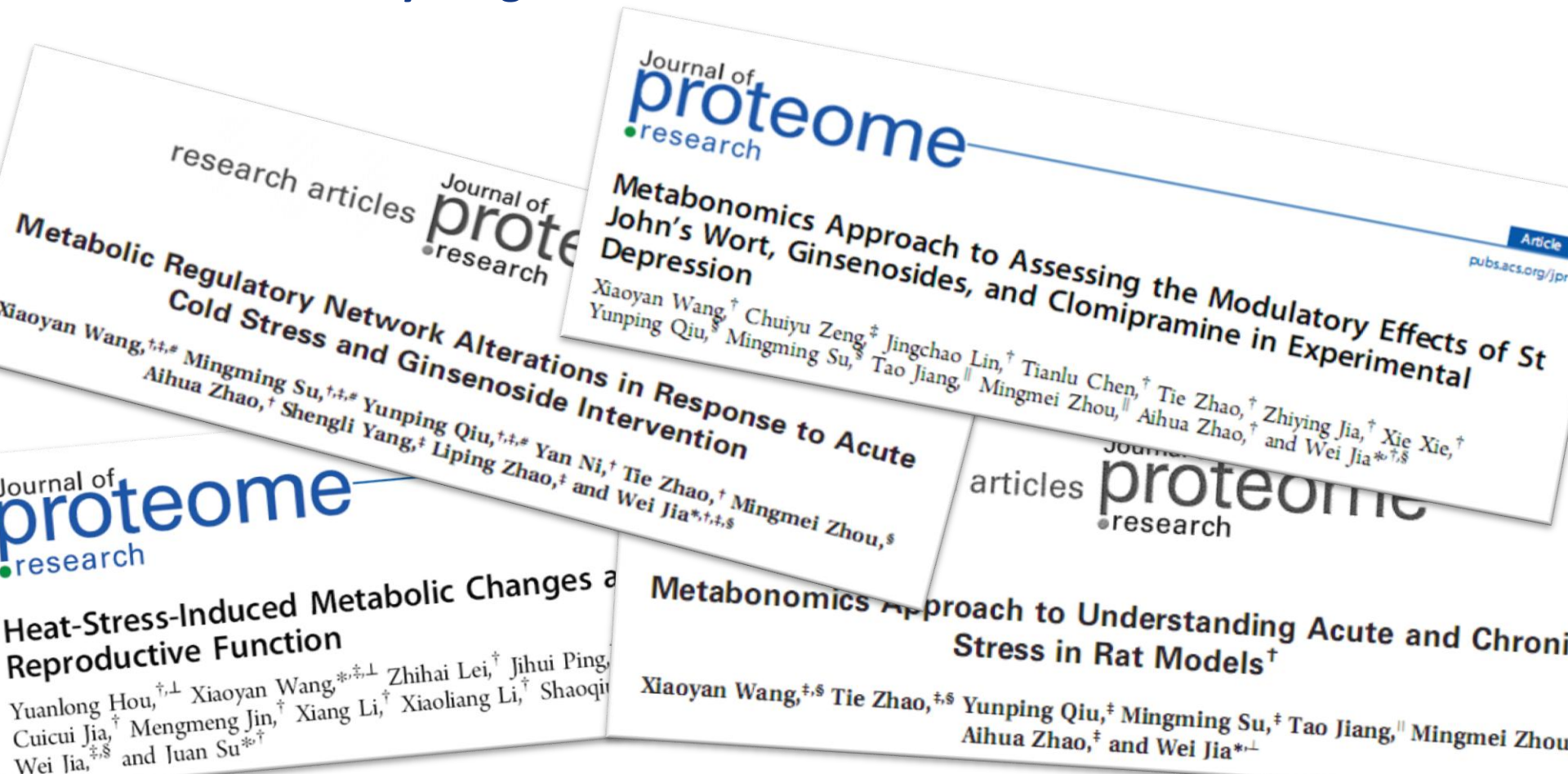
Amino acid neurotransmitters

Monoamine neurotransmitters

Self-preserving
action



- The metabolic variation were reversible and non-specific.
- Body has self-preserving and compensation functions required to restore homeostasis.
- Both of the metabolic variation and the side-effects could be alleviated by drug or medicine.





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Mingming Su
Yunping Qiu
Yuanlong Hou

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THANKS !



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