The Mapping between Traditional Chinese Medicine and Signaling Molecules

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Yang Liu

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By Yang Liu

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PREFACE

Traditional Chinese Medicine (TCM) has been applied in China and east Asia Countries for thousands of years. TCM considers that there exist vital substances in human body to regulate the physiological processes, for example, Qi, Yang Qi, Yin Qi, etc. The TCM diagnosis and therapeutic strategies are all based on the functions and interrelationships of these vital substances. The fundamental doctrinal source for TCM is "Yellow Emperor's Inner Canon" (YEIC, 黄帝内经 Huangdi Neijing). YEIC consists of two medical books, i.e., Su Wen Book (SW, 素问) and Ling Shu Book (LS, 灵枢). "Su Wen (素问)" means "Basic Questions", and "Ling Shu (灵枢)" means "Miraculous Pivot". Each book consists of 81 chapters. YEIC is the conversations between Yellow Emperor and Wise Men, and cover a broad range of topics, such as causes of various diseases, functions of meridians, treatment strategies, functions of TCM vital substances, etc.

In modern medicine, signaling molecules are the fundamental substances in human body, and the cascades of molecular signaling pathways trigger a series of physiological activities of human body. TCM and modern medicine use different terms but describe the same physiological functions in human body, and there should exist mappings between TCM and modern medicine. To find the mappings, we searched each TCM vital substance in YEIC, and listed their physiological functions and interrelationships; then searched the signaling molecule that could match these physiological functions. We identified 48 mappings between TCM vital substances and signaling molecules. For each mapping, the physiological functions are the same; the interrelationships among different TCM vital substances are also the same as the signaling pathways of corresponding molecules; the specific TCM herbal medicine have the same effect on this TCM vital substance and corresponding molecule. By applying these mappings, we analysed the TCM causes of arthritis, diabetes, and constipation and their corresponding TCM treatment strategies, and

demonstrated that the causes of diseases and treatment strategies between TCM and modern medicine are the same. These mappings also enable us to understand some TCM syndromes, including "Consumptive-Thirsty Syndrome (消渴症)", "Heat Central Syndrome (热中症)", etc.

These 48 TCM substances are TCM Essence (精), TCM Mind (神), TCM Ethereal Soul (魂), TCM Corporeal Soul (魄), TCM Ideation (意), TCM Will (志), TCM Thin Fluid (津), TCM Thick Fluid (液), Qi (气), Yang Qi (阳气), Yin Qi (阴气), Zong Qi (宗气), Glory Qi (荣气), Nutrient Qi (营 气), Defending Qi (卫气), Heart Qi (心气), Spleen Qi (脾气), Lung Qi (肺 气), Kidney Qi (肾气), Liver Qi (肝气), Cold Qi (寒气), Damp Qi (湿气), Dry Qi (燥气), Heat Qi (热气), Wind Qi (风气), Summerheat Qi (暑气), Clear Qi (清气), Turbid Qi (浊气), Righteous Qi (正气), Evil Qi (邪气), Genuine Qi (真气), Blood Qi (血气), Stomach Qi (胃气), Essence Qi (精 气), Indulged Qi (淫气), Mind Qi (神气), Consumption (消), Central (中), Heart Yang (心阳), Heart Yin (心阴), Spleen Yang (脾阳), Spleen Yin (脾 阴), Lung Yang (肺阳), Lung Yin (肺阴), Kidney Yang (肾阳), Kidney Yin (肾阴), Liver Yang (肝阳), Liver Yin (肝阴). Besides these 48 TCM substances, YEIC also mentioned other TCM substances, such as Yang Essence (Yang Jing, 阳精), Yin Essence (Yin Jing, 阴精), Shape Qi (形气), etc. However, the physiological functions of these TCM vital substances are not sufficient to identify their mappings.

As YEIC was written in ancient Chinese, we need dual translations to prepare this book, i.e., one from ancient Chinese to modern Chinese, and the other from modern Chinese to English. For ease reference and check, we keep the original ancient Chinese sentences in the text, and try our best to translate them into English as the original meaning, therefore, some translated English sentence may not form a complete sentence.

YEIC covers a broad range of topics. This book is only a small step for bridging TCM and modern medicines. We believe that the communication and mutual support between eastern and western medicines would provide a thorough understanding of human physiology and enable more effective treatment of abnormal or disease states.

xvi Preface

Thanks to Professor Jian Lu for his encouragement. Thanks also go to Professor Weiwei Yan for her kind help to find out many Chinese articles and theses.

CHAPTER 1

INTRODUCTION

Traditional Chinese Medicine (TCM) has been applied in China and east Asia Countries for thousands of years. TCM considers that there exist vital substances in human body to regulate the physiological processes. The TCM diagnosis and therapeutic strategies are all based on the functions and interrelationship of these vital substances. The fundamental doctrinal source for TCM is "Yellow Emperor's Inner Canon" (YEIC 黄帝内经, Huangdi Neijing). YEIC consists of two medical books, i.e., Su Wen Book (SW, 素问) and Ling Shu Book (LS, 灵枢); each book consists of 81 chapters. YEIC is the conversations between Yellow Emperor and Wise Men. During the conversations, they discussed the physiological functions of TCM vital substances, pathological reasons of various diseases, and treatment strategies. One of the conversations is as following:

Yellow Emperor asked: How to observe the victory of Six Qis? Qi Bo (Wise Man) answered: Observe it when it comes. More Clear Qi comes, it is the victory of Dry Qi, Wind Qi in liver gets evil, then induces liver disease (SW74, in Chapter 74, Su Wen Book of YEIC). 帝曰: ...六氣之勝,何以候之. 歧伯曰: 乘其至也. 清氣大來, 燥之勝也, 風木受邪, 肝病生焉 (素問—至真要大論) (Huang-Di 2005; Neijing 2021).

This conversation clearly demonstrated the pathological pathways of TCM vital substances. In modern medical science, molecular signaling is the most fundamental physiological processes. In this book, we analyzed the physiological functions and their interrelationships of the most often described TCM vital substances in YEIC, and compared them with physiological functions and pathways of signaling molecules. We tend to establish the mapping between these TCM vital substances and signaling molecules, i.e., we tend to establish the mapping between TCM and modern

medicines. According to the mappings, the TCM vital substances and signaling molecules have the same physiological functions and signaling pathways.

Yin, Yang and Qi are probably the most popular TCM words people ever heard. Before introducing the TCM vital substances and the mappings, we should first explain the meaning of Yin, Yang and Qi in TCM.

- Yin: In TCM, Yin has the cooling/astringent capacity. When used with Yang, Yin refers to the grouping of characteristics or things opposite to Yang. Depending on the context, Yin may also indicate Yin Qi, a TCM vital substance. When Yin is used together with other word, it refers to the Yin attribute, and usually the combined word represents a TCM vital substance, such as Yin Qi, Liver Yin, Heart Yin, Spleen Yin, Lung Yin, and Kidney Yin.
- Yang: In TCM, Yang has the warming/developing function. When used with Yin, Yang refers to the grouping of characteristics or things opposite to Yin. Depending on the context, Yang may also indicate Yang Qi, a TCM vital substance. When Yang is used together with other word, it refers to the Yang attribute, and usually the combined word represents a TCM vital substance, such as Yang Qi, Liver Yang, Heart Yang, Spleen Yang, Lung Yang, and Kidney Yang.
- Qi: In TCM, Qi has the actuation/regulation function. In YEIC, Qi may refer to the general term of Qi, and represent all kind of Qis. In most cases, Qi represents a TCM vital substance. When used together with other word, it refers to the Qi attribute, and usually the combined word represents a TCM vital substance. For example, Zong Qi, Glory Qi, Nutrient Qi, Defending Qi, Liver Qi, Heart Qi, Spleen Qi, Lung Qi, Kidney Qi, Cold Qi, Damp Qi, Dry Qi, Heat Qi, Wind Qi, Summerheat Qi, Yang Qi, Yin Qi, Clear Qi, Turbid Qi, Righteous Qi, Evil Qi, Stomach Qi, Genuine Qi, Blood Qi, Essence Qi, Indulged Qi, Mind Qi, etc.

In LS30, Chapter 30, Ling Shu Book: Yellow Emperor said, "I heard that human have Essence of Life (Jing, 精), Qi (气), TCM thin fluid (Jin, 津), TCM thick fluid (Ye, 液), Blood, and Pulse (脈); I thought they were a kind of Qi only; now I understand they are categorized into six aspects. (黃帝曰: 余聞人有精、氣、津、液、血、脈,余意以為一氣耳,今乃辨為六名)"(Huang-Di 2005; Neijing 2021). This statement indicates that Essence

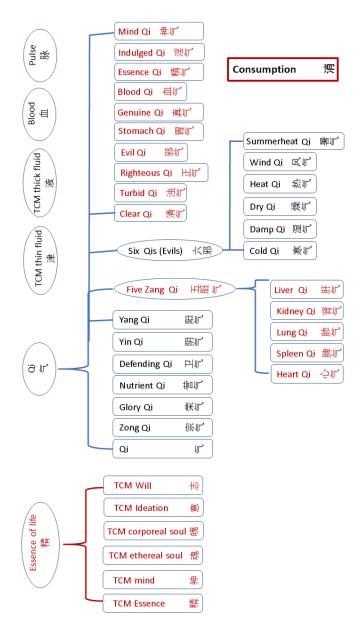


Fig. 1-1 TCM vital substances described in YEIC.

of Life (Jing, 精), Qi (气), TCM thin fluid (Jin, 津), TCM thick fluid (Ye, 液), Blood, and Pulse are important aspects of TCM. In this book, we do not introduce Pulse, but discuss the mappings of TCM vital substances that are most often discussed in YEIC. Fig. 1-1 shows the categories of TCM vital substances described in YEIC. We categorize these TCM vital substances into five parts, and introduce the mappings as following order.

1.1 TCM vital substances related to mood, TCM thin fluid, and TCM thick fluid

In TCM, the Essence of Life (Jing, 精) are vital substances relate to mood, including TCM Essence (Jing, 精), TCM Mind (Shen, 神), TCM Ethereal Soul (Hun, 魂), TCM Corporeal Soul (Po, 魄), TCM Ideation (Yi, 意), and TCM Will (Zhi, 志). TCM considers that these vital substances are responsible for mood regulation, and they are stored in five organs, respectively, as shown in Fig. 1-2. That is, heart containing TCM Mind (心藏神), lung containing TCM Corporeal Soul (肺藏魄), liver containing TCM Ethereal Soul (肝藏魂), spleen containing TCM Ideation (脾藏意), kidney containing TCM Will (腎藏志), and kidney containing TCM Essence (腎藏精) (Huang-Di 2005). TCM names heart, lung, spleen, kidney, and liver collectively as Five Zang-Organs. TCM considers there also exist vital substances related to these Five Zang-Organs and divides these vital substances into five groups according to their physiological functions.

TCM also considers that TCM thin fluid (Jin, 津) and TCM thick fluid (Ye, 液) are important aspects in human body.

The mappings are tabulated in table 1-1, and the details are discussed in Chapter 2.

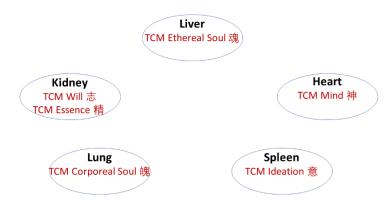


Fig.1-2 Heart containing TCM Mind (心藏神), lung containing TCM Corporeal Soul (肺藏魄), liver containing TCM Ethereal Soul (肝藏魂), spleen containing TCM Ideation (脾藏意), kidney containing TCM Will (腎藏志), and kidney containing TCM Essence (腎藏精).

Table 1-1 The mappings between TCM vital substances of mood and molecules

TCM vital substances	Corresponding molecule
TCM Essence (Jing, 精)	Tyrosine
TCM Mind (Shen, 神)	Melatonin
TCM Ethereal Soul (Hun, 魂)	Serotonin
TCM Corporeal Soul (Po, 魄)	Cysteine
TCM Ideation (Yi, 意)	Tryptophan
TCM Will (Zhi, 志)	Arginine
TCM Thin Fluid (Jin, 津)	Proteins
TCM Thick Fluid (Ye, 液)	Lipids

1.2 Qi, Zong Qi, Glory Qi, Nutrient Qi, Defending Qi, Yin Qi and Yang Qi

In YEIC, the general term of Qi may indicate all kinds of Qis; when discussed a specific physiological function, the Qi may represent the TCM

substance, Qi. Qi is the TCM substance most often discussed in YEIC. Zong Qi (宗气), Glory Qi (荣气), Nutrient Qi (营气), Defending Qi (卫气), Yin Qi (阴气), and Yang Qi (阳气) are also TCM vital substances.

The mappings are tabulated in Table 1-2, and the details are discussed in Chapter 3.

Table 1-2 The mappings between TCM Qis and molecules

TCM Qis	Corresponding molecule
Qi (气)	Sodium
Zong Qi (宗气)	Dopamine
Nutrient Qi (营气)	cyclic Adenosine Monophosphate (cAMP)
Glory Qi (荣气)	Adenosine Triphosphate (ATP)
Defending Qi (卫气)	Chloride
Yin Qi	Potassium
Yang Qi	Calcium

1.3 Yin, Yang, Qi in Five Zang-Organs (Five Groups, 五行)

As mentioned in Section 1.1, YEIC named heart, spleen, lung, kidney and liver as Five Zang-Organs. TCM categorized the vital substances related to Five Zang-Organs into five groups according to their physiological functions, i.e., heart group, spleen group, lung group, kidney group and liver group, the so-called "Five Groups (五行)." In each group, TCM further divided the vital substances into specific Yang, Yin, and Qi. As shown in Fig. 1-3, heart group consists of "Heart Yin, Heart Yang, and Heart Qi", spleen group consists of "Spleen Yin, Spleen Yang, and Spleen Qi", lung group consists of "Lung Yin, Lung Yang, and Lung Qi", kidney group consists of "Kidney Yin, Kidney Yang, and Kidney Qi", and liver group consists of "Liver Yin, Liver Yang, and Liver Qi".

The mappings are tabulated in Table 1-3, and the details are discussed in Chapter 4.

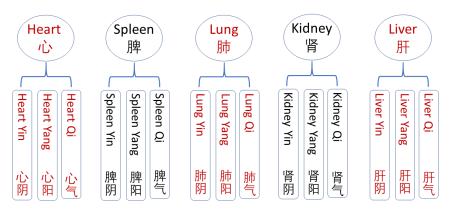


Fig. 1-3 TCM Yin-Yang-Qi in Five Groups

Table 1-3 The Mappings between TCM Five Groups and signaling molecules

	Yang 阳	Yin 阴	Qi 气
Heart group 心	Insulin Growth	Angiotensin	Magnesium (Mg)
	Factor (IGF)		
Spleen group 脾	Atrial Natriuretic	Aldosterone,	Ghrelin
	Peptide (ANP)	Retinoic Acid	
Lung group 肺	Vascular	Ascorbic Acid	Hypoxia-
	Endothelial		Inducible Factor
	Growth Factor		(HIF)
	(VEGF)		
	Fibroblast		
	Growth Factor 7		
	(FGF7)		
Kidney group 肾	Calcitonin	Wnt	Nitric Oxide
	Parathyroid		(NO)
	hormone-related		
	protein (PTHrP)		
Liver group 肝	Hepatocyte	Superoxide	Glutathione
	Growth Factor	Dismutase (SOD)	(GSH)
	(HGF)	Renin	
	Erythropoietin		
	(EPO)		

1.4 Six Qis (Six Evils, 六邪): TCM vital substances related to environment

YEIC named the TCM vital substances related to environment as Six Qis (Six Evils 六邪), such as "Wind Qi" (风), "Cold Qi (寒),", "Damp Qi (湿)", "Heat (fire) Qi (热/火)", "Summerheat Qi (暑)", and "Dry Qi (燥)". In ordinary conditions, these Six Qis regulate the human body to adapt to the variation of environment. When these Six Qis change abnormally, they would cause illness and various clinical manifestations, and they are called "Six Evils", as shown in Fig. 1-4. These "Six Evils" can be induced by external factors, i.e., "Wind Evil" can be induced by wind, "Cold Evil" can be induced by cold environment, "Damp Evil" can be induced by humid environment, "Heat (Fire) Evil" can be induced by heat, "Summerheat Evil" can be induced by summer heat stress, and "Dry Evil" can be induced by dry environment. These TCM "Six Evils" may cause pain, fever and inflammation, and TCM has identified various herbal medicines to treat these "Six Evils", respectively (赵.C. Zhao and Li 2000). Moreover, TCM considers that, among these Six Evils, "Wind Evil" affects the liver organ, "Summerheat Evil" affects the heart organ, "Damp Evil" affects the spleen organ, "Dry Evil" affects the lung organ, and "Cold Evil" affects the kidney organ, as shown in Fig. 1-5.

The mappings are tabulated in Table 1-4, and the details are discussed in Chapter 5.

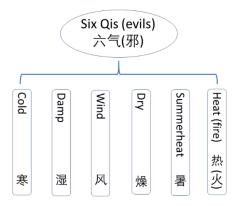


Fig. 1-4 TCM "Six Evils".

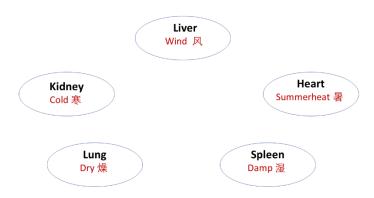


Fig. 1-5 Wind Evil affects liver, Summerheat Evil affects heart, Damp Evil affects spleen, Dry Evil affects lung, and Cold Evil affects kidney.

Table 1-4 The mappings between TCM "Six Qis (Evils)" and molecules

TCM "Six Qis" (Six evils)	Corresponding cytokine
Cold Qi (cold evil 寒)	Interleukin-1 (IL-1)
Damp Qi (damp evil 湿)	Interleukin-6 (IL-6)
Wind Qi (wind evil 风)	Nuclear Factor-κB (NF-κB)
Heat (fire) Qi (heat evil 热)	Tumor Necrosis Factor alpha
	(TNF-α)
Dry Qi (dry evil 燥)	Interleukin-8 (IL-8)
Summerheat Qi (summerheat	Cyclooxygenase-2 (COX-2)
evil 暑)	

1.5 Clear Qi, Turbid Qi, Righteous Qi, Evil Qi, Stomach Qi, Genuine Qi, Blood Qi, Essence Qi, Indulged Qi, and Mind Qi

In the conversation of YEIC, it also described the physiological functions and interrelationships of Clear Qi (清气), Turbid Qi (浊气), Righteous Qi (正气), Evil Qi (邪气), Stomach Qi (胃气), Genuine Qi (真气), Blood Qi (血气). Essence Qi (精气), Indulged Qi (淫气), and Mind Qi (神气).

The mappings are tabulated in Table 1-5, and the details are discussed in Chapter 6.

Table 1-5 The mappings of other Qis, Consumption and Central

TCM vital substance	Molecule
Clear Qi (清气)	Toll-like receptor 4 (TLR4)
Turbid Qi (浊气)	Leptin
Righteous Qi (正气)	Immunoglobulin G (IgG)
Evil Qi (邪气)	Lipopolysaccharide (LPS)
Stomach Qi (胃气)	Amylase
Genuine Qi (真气)	Phosphorus
Blood Qi (血气)	Iron
Essence Qi (精气)	Zinc
Indulged Qi (淫气)	Gonadotropin-releasing hormone
	(GnRH)
Mind Qi (神气)	Thyroid Hormone (TH)
Consumption (消)	Forkhead Box O1 (FoxO1)
Central (中)	Aldosterone

1.6 Consumption (消) and Central (中)

In YEIC, the "Consumption (消)" is a TCM vital substance. The "Consumption" may represent various syndromes, such as "Wind Consumption 風消" syndrome, "Lung Consumption 肺消" syndrome, "Consumption Central 消中" syndrome, and "Consumptive-Thirsty" Syndrome (消渴症). Where "Consumptive-Thirsty" (消渴) corresponds to diabetes. The mapping is tabulated in Table 1-5, and the details are discussed in Chapter 10.

The "Central" is also a TCM vital substance. The mapping is tabulated in Table 1-5, and the details are discussed in Section 4.2.5 and Chapter 11.

1.7 The methods to identify the mapping between signaling molecule and TCM vital substance

In physiological reality, molecular signaling is the most fundamental physiological processes. Signaling pathway is a series of chemical reactions that occur within a biological cell when initiated by a stimulus. This stimulus, known as a first messenger, acts on a receptor that is transduced to the cell interior through second messengers which amplify the signal and transfer it to effector molecules, causing the cell to respond to the initial stimulus. Most biochemical cascades are series of events, in which one event triggers the next, in a linear fashion. At each step of the signaling cascade, various controlling factors are involved to regulate cellular actions, in order to respond effectively to cues about their changing internal and external environments (Gomperts et al. 2002). The transduction pathways of signaling molecules are important to understanding how signaling molecules regulate the physiological function and in predicting the pathological development which is important to therapeutic strategy. However, despite the documented importance of signaling molecules to human life, we still lack thorough knowledge of transduction pathways of signaling molecules.

In YEIC, the TCM vital substances are usually discussed in two conditions, i.e., the "static" and the "dynamic" conditions. The examples of these two conditions are as following:

- "Static" Condition: The physiological functions of TCM vital substances do not change with time or the TCM vital substances are not specified at a certain location. For example, in Chapter 01, Su Wen Book: At age of 48, Yang Qi exhausts, the skin becomes withered and dark, hairs become white (素問-上古天真論: 六八, 陽氣衰竭於上, 面焦, 髮鬢頭白). This statement described the Static Effect of Yang Qi. There have been abundant experimental and clinical references for the "Static" Conditions.
- "Dynamic" Condition: TCM vital substances change with time and location. For example, in Chapter 29, Su Wen Book: Yang Qi travels up from hands to head, then travels down to feet (素問-太陰陽明論: 陽氣從手上行至頭,而下行至足). This statement described the "dynamic" state of Yang Qi. However, the current techniques cannot measure this kind of "dynamic" process yet.

TCM and modern medicine should describe the same physiological processes in the human body but using different terminology. There must be some links between the TCM vital substances and the signaling molecules. In this book, we have established the mapping between these TCM vital substances and the signaling molecules. To identify each mapping, we have applied the following procedures.

- In YEIC, the functions of TCM vital substances are discussed in the conversations in various chapters. For each TCM vital substance, we summarize all the "static" conditions and take them as the constraint conditions to search for the corresponding molecule that could match these "static" conditions. These constraint conditions include not only the physiological functions but also the interrelationships among different TCM vital substances.
- 2. If the corresponding molecule satisfies the constraint conditions, the identified corresponding molecule should have the same physiological functions as those of the TCM vital substance. Moreover, the interrelationships among the TCM vital substances should be consistent with the signaling pathways of the corresponding molecules as well. This indicates that the pathways of the TCM vital substances are the same as the pathways of the signaling molecules.
- TCM uses herbal medicine to regulate each vital substance. We have validated each mapping by comparing the effect of the same herbal medicine on the TCM vital substance and the corresponding molecule, and the effects are the same.

YEIC also discussed the pathways of the TCM vital substances. As an example, by applying the mappings, we have analyzed some of the TCM pathways, and found that the TCM pathways are consistent with the molecular signaling pathways. Moreover, we have applied the mappings to analyze the molecular mechanism of constipation, arthritis and diabetes, and shown that the TCM causes of these diseases and TCM therapeutic strategies are the same as those of modern medicines. Further, these mappings also enable us to understand some TCM syndromes, including "Consumptive-Thirsty Syndrome (消渴症)", "Heat Central Syndrome (热中症)", etc.

The mappings for 48 TCM vital substances are shown in Fig. 1-6. We explain the mappings in detail in the following chapters.

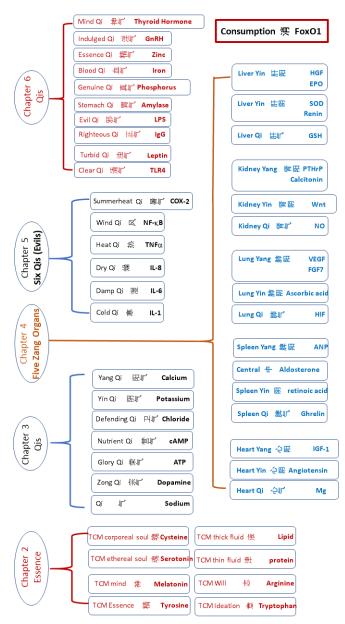


Fig. 1-6 Mappings between molecules and TCM vital substances.

CHAPTER 2

THE MAPPINGS OF TCM VITAL SUBSTANCES RELATED TO MOOD, TCM THIN FLUID, AND TCM THICK FLUID

The TCM vital substances relate to mood are TCM Essence (Jing, 精), TCM Mind (Shen, 神), TCM Ethereal Soul (Hun, 魂), TCM Corporeal Soul (Po, 魄), TCM Ideation (Yi, 意), and TCM Will (Zhi, 志). TCM also considers that TCM thin fluid (Jin, 津) and TCM thick fluid (Ye, 液) are important aspects in the human body. To establish the mapping between the TCM vital substance and the molecule, for each vital substance, we summarize its physiological functions and compare with those of corresponding molecule. For ease reference, we list the chapter number and the original statement in ancient Chinese as well.

2.1 TCM Essence (Jing, 精) corresponds to tyrosine

2.1.1 Comparison between TCM Essence and Tyrosine

The physiological functions of TCM Essence described in YEIC are tabulated and compared with tyrosine in Table 2-1, where SW indicates Su Wen Book (素问), LS indicates Ling Shu Book (灵枢), and NJ indicates Yellow Emperor Nan Jing (黄帝难经).