"Scientific Integrative Medicine."

-a brief history &beyond

Chapter One

–National Institutes of Health (NIH)

Implications of
My Scientific Research Program

Dec.1, 1995 to September 30, 2005

Implications of my research findings (I)

- Redefine health and diseases
- Elucidate the complexity of system-level integration
- Evidence-based rational drug design

- Why do we have diseases?
- Why is the rate of cancer and chronic diseases reaching epidemic high?
- What is the intimate link between aging and chronic diseases?
- What is the link between addictive behavior and chronic disease susceptibility?

Implications of my research findings (II)

• How to assess the benefit/risk ratio for hormone replacement therapy or other preventative measure to disease susceptibility and lifespan

• How to develop predictive biomarkers for sporadic cancers, cardiovascular diseases, obesity, and degenerative diseases

• How to develop evidence-based novel preventative and therapeutic strategies

• The need to develop a comprehensive ‘biopsychosocial’ model of health and disease based on individual inborn organ complement and the rate of attrition in a social environment

• How to link diverse clinical manifestations with age, race, gender, social interaction and genetic susceptibility

Implications of my research program (III)

• How to provide a sensitive and relevant biological assay: to evaluate the health benefit of diverse preventative measures, such as herb medicine, rational and new drug combinations, or to explore unexpected use of existing medicines, etc.

• Biological basis of nature/nurture integration: survival/longevity

• Biological basis of mind/body integration: system-level integration

• Redefining health and disease: health is not elimination of diseases

• How the system is built: uncovering the rules and principles of mammalian system integration

• Chronic diseases: as the disease of the system--the universality--mismatch in organ capacity of the system as the weakest link of the system--increased risk of all chronic diseases, not one specific disease

Implications of my research program (IV)

• Gene/gene interaction, and gene/environment interaction: A universal genetic mechanism that is evolutionally selected

• The system is more complex than we think, counter-intuitive

• Why and how caloric restriction works: by slowing down the aging of organ capacity. The Question: How to measure the rate of attrition?

• What are the early life stresses on the capacity of postnatal organ formation

• The internal stress could be more potent than that of external stresses: why do we have cancers? Yet, we can mostly change external environment.

• The relationship among diverse symptoms: depression, inflammation, congestive heart failure, and cardiovascular diseases, stroke, senile dementia and neurodegenerative diseases, etc.

Implications of my research program (V)

•The roles of brain, hormonal system and immune system in system-level integration: what are the sensors they respond to internal stresses and how to achieve equilibrium/homeostasis

• An animal model for sporadic Alzhemier disease, biopolar disease, major depression, and linking anxiety to major depression

• How does the system-integrate? Dynamic, incremental, time-dependent (attrition of organ capacity), etc.

• The relationship between normal aging and chronic disease susceptibility

Chapter Two

–National Cancer Institute, NIH

My Vision
for Scientific Integrative Medicine

@ NIH

Oct. 3, 2003 to September 30, 2005

Scientific integrative medicine at NIH (I)

• More effective use of genetically manipulated mice

• Translate laboratory findings to clinics: predictability, the future of molecular medicine

• Organ capacity: linear calibration, more detailed studies on diverse organs at histological level and non-invasive imaging approach; tissue density, blood flow, size, shape, color and texture, etc.

• Threshold of organ capacity: age-related disease, epidemiology, age of onset, prevalence, mysterious comorbidity; resolving the puzzles of the human chronic disease susceptibility

• Non-invasive imaging analyses: to measure the rate of organ aging; how to calibrate the organ capacity like hearts: by number of muscle fibers? Etc.

• What microarrays and proteomics are telling us…

Scientific integrative medicine at NIH (II)

• How to prove that insight generated from the mammalian models is relevant to human medicine?

• Prevention, pre-clinical diagnosis, and the dilemma of short-term gain versus long-term survival; quality of life issue; what advice we give to public… long-term consequences… risk/benefit ratio

• It is possible to demystify the stigma associated with many human diseases to the public, such as cancer, mental illness and AIDS, etc.

• How to achieve the goal of delaying the onset of chronic disease: issues of quality of life, threshold is the key word and linear calibration of the organ capacity is the answer?

• It will be too late if we have the symptoms, most of time we don't even have symptom… the onset of the disease can be time of death or disability-like heart attack or stroke

Scientific integrative medicine at NIH (III)

• Alternative explanation to a large body of human epidemiological studies; Harvard Man studies; Why two cohorts of different period in human with distinctly different breast cancer incidence; what has been missed and misinterpreted by the authors: no explanation is given to the difference in slope of the age-dependent breast cancer incidence; Nun studies; longevity and AD

• Ethic issues: the dilemma of the right to know and disclosure; the genetic mechanism is quite stochastic and politically "correct"; however, the non-invasive imaging will be highly predictable to the life span and risk to disease susceptibility. We need to calibrate it on animal models with defined initial defects.

• The relationship between mind/body and emotions. Internal stresses, external stress, looks (orthodotics), habits (personal hygiene, shower, exercise), culture, values, geography, environment, prenatal and perinatal nutrition, race, ethnicity and diversity

Scientific integrative medicine at NIH (IV)

• The relationship between obesity, energy metabolism, accelerated deterioration of pancreatic functions, and obesity.

• How the body keeps balance of immunity and inflammation; compensation, regeneration and autoimmunity; exhaustion of organ capacity, and aberrant repair attempt (cancer formation).

• Understanding gender bias, disease associated with ethnic groups

• Similar calibration is needed in humans; to facilitate comparative studies between model organism and humans; more autopsy is needed: autopsied cadavers at histological level or with fresh tissues on people died of accidents

• The relationship between mitochondria function, energy metabolism, replicative senescence, telomere shortening and the free radical theory of aging.

Scientific integrative medicine at NIH (VI)

• Why NIH is the best place to do integrative research: NIH resource, there is no simple answer to all of the questions raised, but the current study, as proof of principle, has provided the 'insight' for the future

• The roadmap of NIH: resolving the complex biological systems with multidisciplinary approaches. The integrated research is made possible by integrative synthesis of researchers who develop an effective experimental system to address issues that are not readily apparent via other system. It required well-trained experimentalists, persistence and lots of sleepless nights and many waking hours.

Scientific integrative medicine at NIH (V)

How to delay aging and reduce the risk of age-related chronic diseases:

- Linkage analysis to speed up the process of more frequently linked the polymorphism in the population associated with diverse strains
- Slight changes in the genetic background will eschew the pattern of aging and mortality and morbidity
- Slight change in the social environment
- Medical advance in organ replacement and stem cell technology
- When and how to give the drugs
- Revaluate the impact of drug on the systems as a whole and improve organ functions: what is the most effective way
- Incorporation of and beyond the caloric restriction for life extension
- Pills and alternative medicines
- Intervention via organ repairs- matching the lifespan of organ parts of the whole system by stem cell research

Chapter Three

– National Cancer Institute, NIH

Build a Platform for Personal & Professional Growth for All?

From Good to Great-Jim Collins
8th Habits-Stephen Covey

October 1, 1999- September 30, 2005

Timeline for Building a Research Program on System-level Integration in Mammals at LCCTP, NCI

Year 1--Oct. 1, 1999-Oct. 1, 2000

Re-derivation of mouse strains: one full year/ASP submissions to Bethesda and Frederick ACUCs,
Set up Germline Mutation Core Facility and personnel training.

Year 2--Oct., 2001

Started expansion of mouse colonies to holding capacity, starting from Nov. , 2000, one full year delay
Genetic manipulation of mouse strains @ *Gdnf/c-ret, Telomerase, Survivin, Nicastrin* loci (7 constructs total, 6 succeeded). A total of 30 projects between 2001-2003 (Core closed by Dec. 2003).

Year 3--Oct., 2002

Setup quantitative analysis by real time RT-PCR
Kidney MRI Imaging/*in vitro/in vivo*
Behavioral Analysis (set up experimental paradigm to monitor cognitive, motor and emotional Functionality of mice over life course).
Animal Database/Comprehensive Necropsy/Histology
Kidney/EPO/Mitochondria Link over life course
Characterization of Survivin-DsRed and Telomerase-GFP K/in mice as generic stem cell marker.

Year 4--Oct., 2003

Survival Analysis/Congestive Heart Failure/Hyperglycemia and Type II Diabetes/Cancer
Systematic Dissection/Tissue Array

Year 3-5, Constant Interruptions of Experimental Flow, Aug., 2002-March, 2004, Animal Study Protocol Suspensions due to misunderstanding of my research needs. Loss of competitions on two Publications in 2003 and 2004. Preparation for my first site visit, April -Oct. 2003. Core closure end of Dec. 2003
May, 2004, Memo for closure of my research program by BSC, CCR, NCI. Denial of two year extension request

Year 6--Oct. 2004, Cohort data verification, survival analysis, developmental origin of aging. An ongoing process
Subtle link between aging and chronic disease susceptibility, observation on gender bias, ethnicity.
Oct. and Dec., 2004, loss of two postdoc fellows. One postdoc remained, left July, 2005.
January 2005, Active job hunting (NIA, NIMH, and SIMIG), talks, data analyses, and problem-solving.
Hantaar Virus infection and loss of 500 cages of mice 3/30/05, 2,000 mice loss

September 30, 2005, Frederick mice kept alive?? Expansion of my cohort to restore my program of research??

My PI responsibilities

• Lab setup: major equipment purchase and setup
• Comprehensive program of research: molecular biology, imaging (in vitro and in vivo), behavioral phenotyping, clinical and pathological analyses, etc.
• Large animal cohort management: database, breeding and health monitoring, etc.
• Administrative responsibilities: hiring, training and promotion of students and postdoc.
• Technical trainings: fellows, staff and core members, assay development, and trouble shootings.
• Animal Study Protocols: working with 3 ACUC committees and ASP for both Core and lab. *Constant* updates for new procedures, addition and deletion of new members of the lab.
• Credit card reconciliation: Monthly, and controlled substance, etc.
• 30 or so short-term students: interviewing, training, paper work for project and for mouse work, data analysis, discussion and presentation.
• Collaborative research: animal transportations.
• Space renovations: for animal facilities and my lab, in basement, at second floor and fourth floor (core and my lab).
• Community services: Grant reviews, journal review, FARE award judge, and others.
• Seminars, meetings and workshops: Talks and presentations at various places.
• Readings and writings: Lots of readings. Communications with experts on diverse areas.
• Site visit, April-Oct. 2003: First time to synthesize my work, directed and coordinated a small research group.
• Core responsibility: 30% of my total activities. Technical support to core users with my lab resources and manpower.

People are the most important asset

• Breaking the vicious cycle of low trust and low morale is in the hands of policy makers: to promote excellence, creativity, tolerance, but not to perpetuate mediocrity

• Breaking the vicious cycle of woman and minority career development barrier is in the hands of policy makers: to level the ground and to revise the rule of game for scientific excellence, creativity and productivity for women and minority who are in a more vulnerable and disadvantaged position

• The survival of my research program is in the hands of directors and lab chiefs who control resources, my performance evaluation and my paycheck

Good Attitude Matters

No one is Perfect and unlikely to be.

Do everything within one's control.

Be comfortable with oneself and one's past performance.

There is always room to improve.

Give people plenty of 'benefit of doubt'.

Learn on the job while doing it.

Be assertive, protecting one's best interest without hurting others.

Be honest and speaks the truth.

Live a principled life.

Make contribution to society

Make self and one's family happy.

Use one's strength.

Time is the most precious commodity in one's life

- Donate my leave to people who need them, I don’t have time to take time off
- Rarely take time off
- Minimize extra activities, such as seeing shows, play, and others.
- Stay up late and come to work early
- Get things done by managing my energy
- Budget time well
- Focus, focus and focus
- Priorities: my value, principle and best interest (family, kids, fairness, and career development of myself and my spouse)
- Plan for the future, act on now
- Do not dwell on the past, not to worry about the future, but focus on today
- Focus on long-term benefit, not short-term gain
- Do things efficiently
- Do things effectively (within my control)
- Win cooperation of others I have in direct contact with
- Recognize my reality and act accordingly
- Believe in the power of logic and reasoning, not give up hope
- Patient, attention to details and thorough
- Multi-tasking…..

Things I cannot control…when it involved others (humans or animals)

- To shorten the time course of the life course study
- To decrease the sample size, if not big enough, no statistical significance (I do interim analyses whenever possible, to design breeding strategies to get mice ready for specific data collection.)
- The initial 14 month delay in Animal Study Protocol approval
- Frequent inaccessibility of my animal cohort between 8/2002-4/2004
- Not to do Core set up, equipment purchase, hiring, training and promotion, survey, committee, webpage design and problem-solving, satisfy customer's needs, etc.
- How did other perceive me, not listen to my messages, misinterpreting my behaviors, high expectations, false belief or ignoring me, or withdrawal, or preventing people taking things personally, etc……
- Not problem-solving with me……

Culture, Value and Habits- Know Myself

- Uncomfortable to blow one's own trumpet
- Uneasy to ask for help
- Uneasy to get ahead of myself , before the readiness of the program
- Unwilling to do things I don’t feel right, even others have harmed me
- Do want to make things better, stick to the facts, truth (even people want to deny, or rather not to hear).
- Self-reliant, independent and intuitive, rational thinker
- Extremely tolerant, without knowing, yet hard to avoid unintended consequences for misinterpretations.
- Not fearful, peace of mind and self-assured, optimistic and future-minded
- Attention to detail, patient, fast decision, action-oriented, emotional control, self-discipline

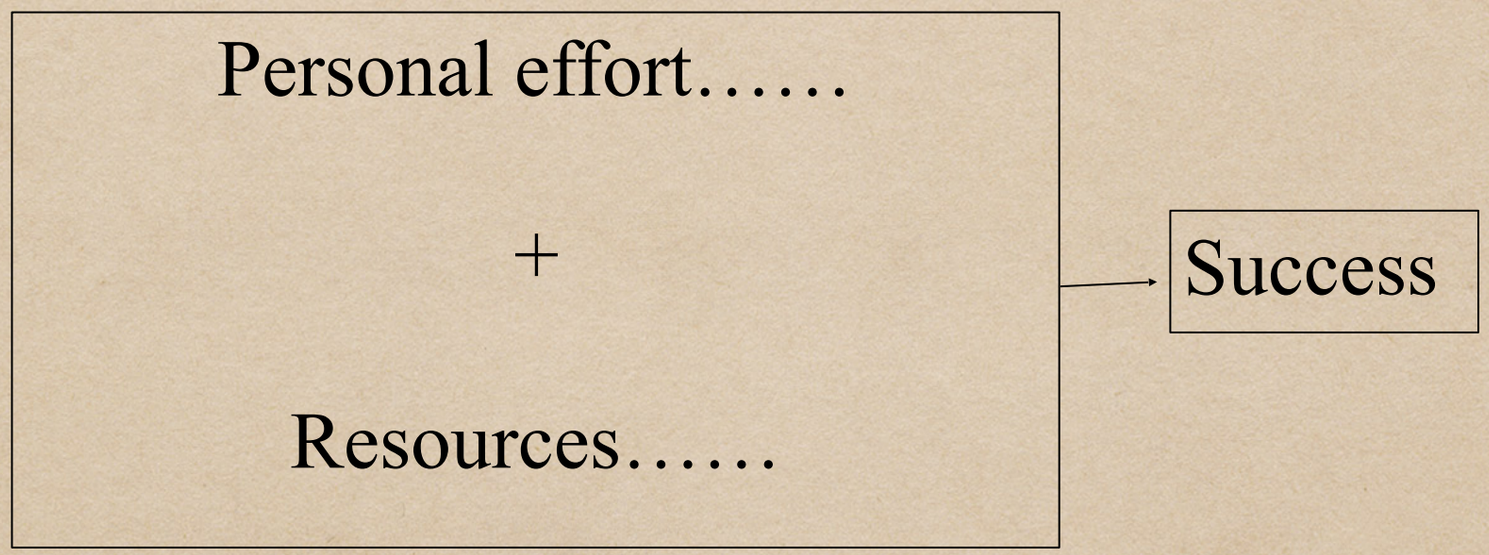
Bamboo ceiling for Asian

Asian Professional Americans are disproportionally missing in senior executive level position relative to number of professional pool, in both government and private sector.

Traditional Asia culture values can be in conflict with dominant corporate culture, resulting costly gap that to be bridged by both the individuals and the employers.

The unconscious behavioral differences exhibited by Asia are often misinterpreted by their non-Asia counterparts, resulting in lost career opportunities and untapped talent.

Career advancement is never easy



Chapter Four

–Research Institute for Optimal Health? 2005~2012
Center for Applied System Biology, Inc. 2013~present

Building on My Own Signature Strength

The Need to Create

'a novel professional practice sector'

Oct. 1, 2005 into 2030 &beyond

The Need to Create

'a novel professional practice sector'

创造一个新兴预防医学产业

'From Discovery to Invention'
2003~2012

'From Innovation to Commercialization' 2013~2023

未来16年，建立行业标准，
资格考试，准入门槛。。。

My Signature Strength

Creativity, ingenuity, and originality Thinking of new ways to do things is a crucial part of who you are. You are never content with doing something the conventional way if a better way is possible.

Curiosity and interest in the world You are curious about everything. You are always asking questions, and you find all subjects and topics fascinating. You like exploration and discovery.

Forgiveness and mercy You forgive those who have done you wrong. You always give people a second chance. Your guiding principle is mercy and not revenge.

Hope, optimism, and future-mindedness You expect the best in the future, and you work to achieve it. You believe that the future is something that you can control.

Love of learning You love learning new things, whether in a class or on your own. You have always loved school, reading, and museums-anywhere and everywhere there is an opportunity to learn.

Center for Applied System Biology, Inc. (CASB)

应用系统生物学研究中心

Since 2013

"Predictive, Preventive, Personalized Medicine"

"Whole Person Development"

"Complex Knowledge & Skill Transfer Platform"

"Wellness Economy"

"Habits of Excellence"

Reward 奖励丨Promotion 进阶丨Build up 建树丨Career Advancement 职业进程

- **Excellence 卓越**
- **Trust 信任**
- **Nurturance 培育**
- **Guidance 引导**
- **Moral Courage 道德勇气**
- **Voice 醒世警言**
- **Conscience 良知**
- **Value 价值**

Culture 文化。Value 价值 。Attitude 态度。Habits 习惯 。

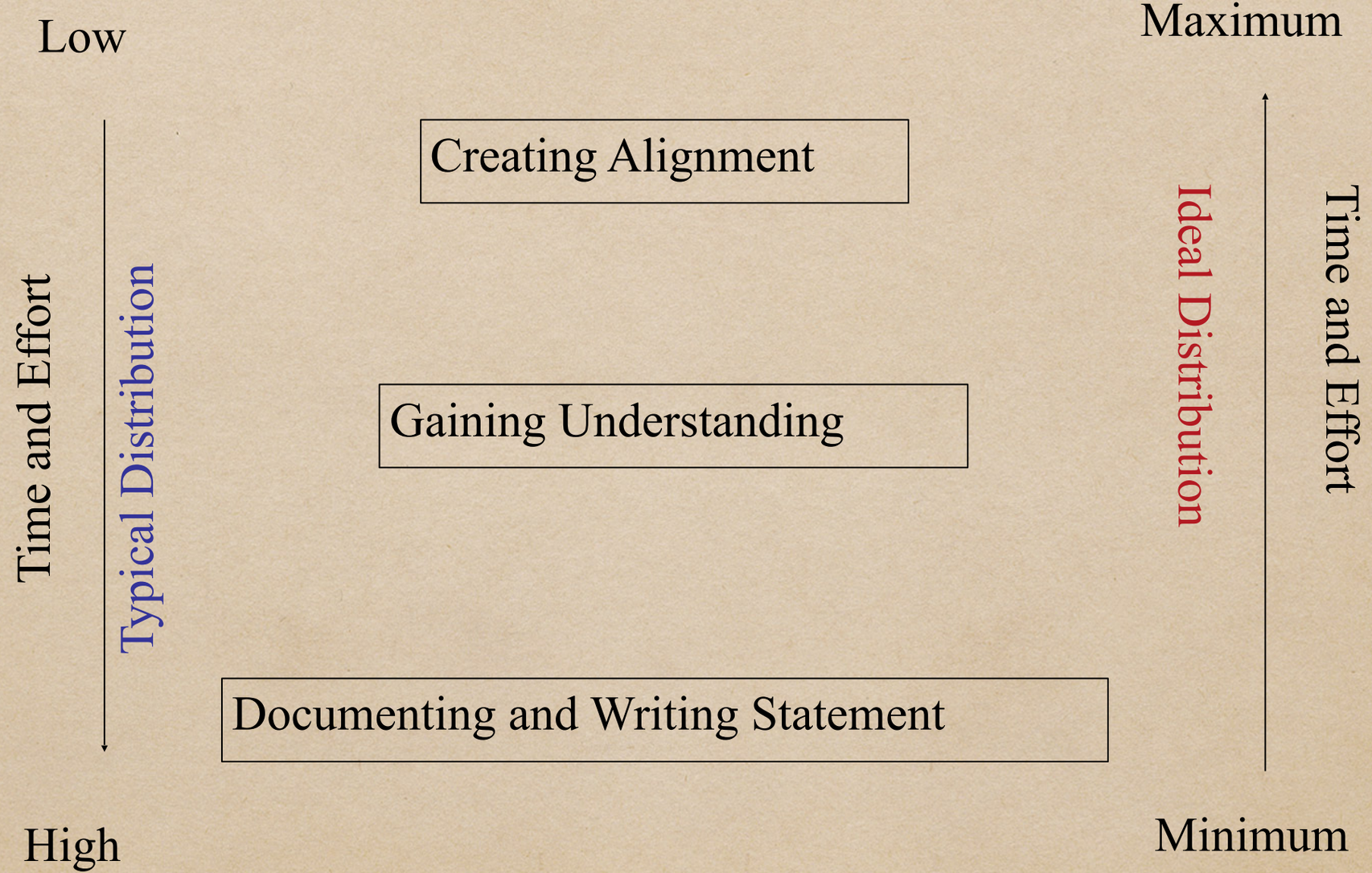
- Time Management (时间管理)
- Effort (努力)
- Resources (资源)
- Knowledge (知识)
- Skills (技能)
- Wisdom (智慧)
- Priority (优先考虑)
- Productivity (成效)
- Cooperation (合作)
- Responsibility (责任感)

Developing Signature Strength 真才实学—Criteria

- A sense of ownership and authenticity ("this is the real me").
- A feeling of excitement while displaying it, particularly at first.
- A rapid learning curve as the strength was first practiced.
- Continuous learning of new ways to enact the strength.
- A sense of yearning to find ways to use it.
- A feeling of inevitability in using the strength ("try and stop me").
- Invigoration rather than exhaustion while using the strength.
- The creation and pursuit of personal projects that revolve around it.
- Joy, zest, enthusiasm, even ecstasy while using it.
- The more of these that apply to any strength, the more clearly is that strength one of your SIGNATURES.

Aligning Action and Values

知行合一



Chapter Five

–Global Presence & Social Impact

从 " 0 " 到 " 千万亿 " 大健康产业

'From Discovery to Invention 2003~2012

从发现到发明

'From Creation to Innovation 2012~2017

从创造到创新

From Zero to Commercialization 2013~2050

从零到万亿级产业化

Center for Applied System Biology, Inc. (CASB)

应用系统生物学研究中心

2013年7月，美国

承诠生物科技有限公司(上海)

2015年11月

时间表：未来七年，未来十六年，未来二十三年。。。

~2017 & beyond

美国，中国，印度，非洲—10个试点,未来七年

1000中国特色小镇—扩大复制，未来十六年

2000中国生物科技创业园—产业化预防医学，未来二十三年

一路一带:“丝绸之路经济带”和“21世纪海上丝绸之路”，未来五十年

东西方文明融和，世界大同