Intranasal Light Therapy (ILIT)

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Introduction to ILIT

History of ILIT

- ILIT on local diseases such as rhinitis was put forward by Russian in 1986.
  - Filatov VF, Kalashnik MV. 1986. Microcirculation in patients with **vasomotor rhinitis** and its dynamics before and after the therapeutic use of laser irradiation. Vestn Otorinolaringol. 1986 Nov-Dec;(6):63-6.
- ILIT on systemic diseases was put forward by Chinese in 1998
  - Li Q, Guo K, Kang J and Jiang B. 1998a. Clinic analysis of endonasal low energy He-Ne laser treatment of 39 cases of **intractable headache**. **Acta Academiae medicinae Qingdao Universitatis. (1): 53**(in Chinese)**.**
  - Li Q, Guo K, Kang J, Jiang B and Wang Y. 1998b. β endorphin research for endonasal low energy He-Ne laser treatment of **ache in head or face**. **Chin J Neurol. 31(2): 91**(in Chinese)**.**

ILIT: intranasal light therapy

ILIT

- Pain
- Cerebral Palsy
- Stroke (cerebral infarction, …)
- Coronary Heart Disease
- myocardial infarction
- Inflammation
- Depression

Clinical applications

Liu CY, Zhu P (ED). 2009. Intranasal low intensity laser therapy. Beijing: People's Military Medical Press.

ILIT: intranasal light therapy

ILIT

- **Hyperlipidemia**
- Blood hyperviscosity
- Insomnia
- Mild cognitive impairment
- Alzheimer's disease
- Parkinson's disease
- **Schizophrenia**

Clinical applications

Liu CY, Zhu P (ED). 2009. Intranasal low intensity laser therapy. Beijing: People's Military Medical Press.

ILIT: intranasal light therapy

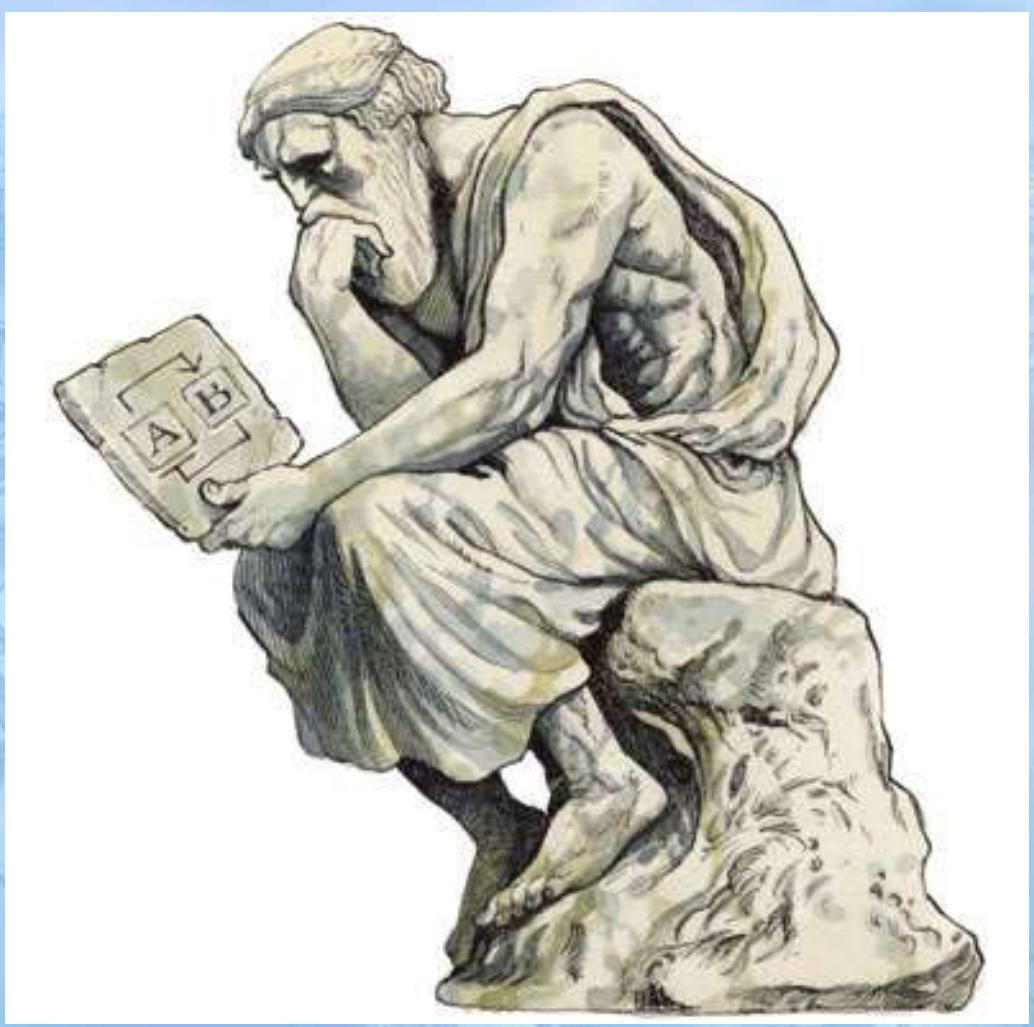
ILIT

- Asthma
- Carpal tunnel syndrome
- Epicondylitis
- Exercise-induced muscle damage
- Osteoarthritis
- Upper respiratory tract infection
- Wound

Possible applications in sports medicine

Liu TCY, Wu DF, Gu ZQ, Wu M. 2010. Applications of intranasal low intensity laser therapy in sports medicine. Journal of Innovation in Optical Health Science. 3(1): 1-16.

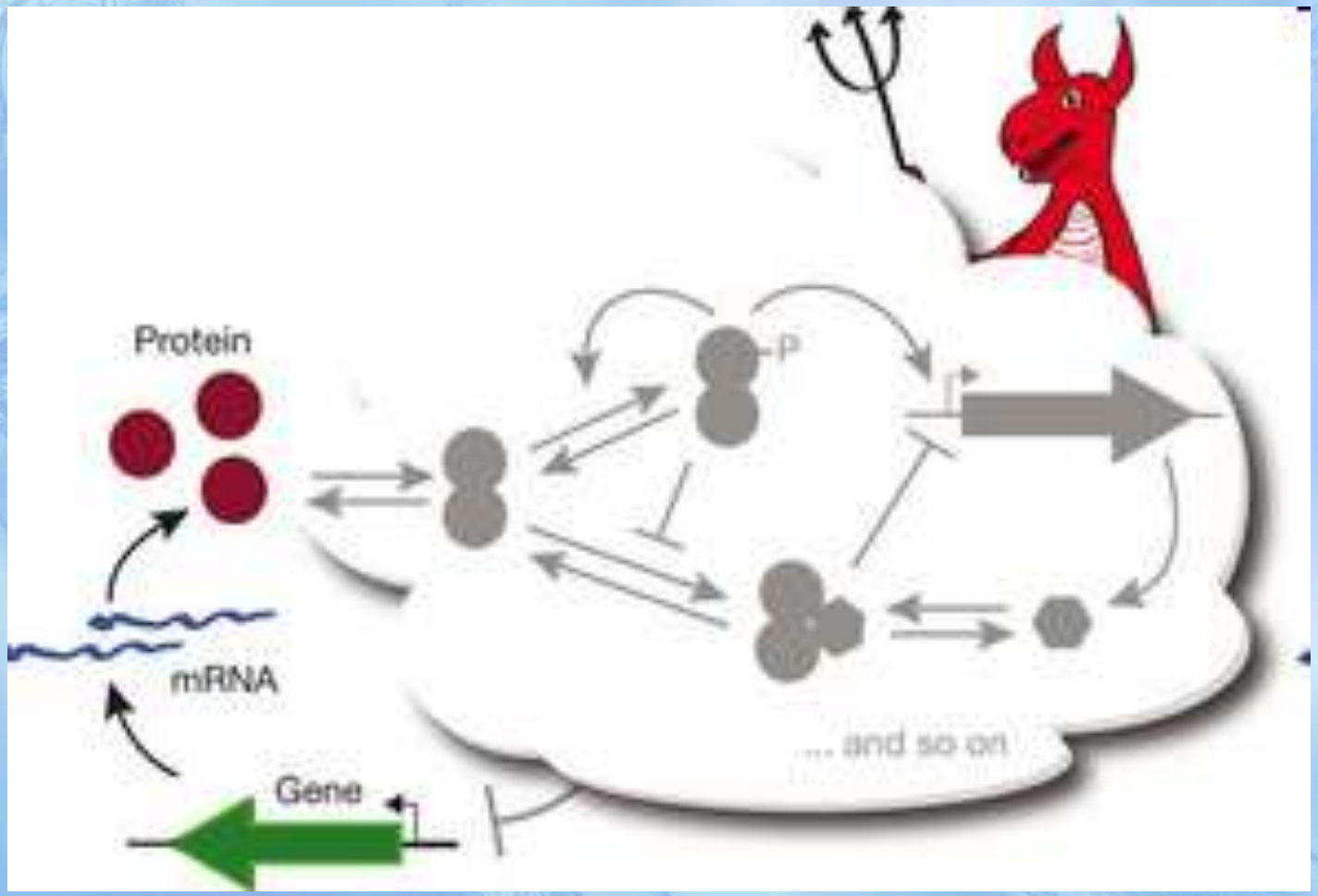
Negative feedback



A makes *B*; *B* inhibits *A*

http://www.nature.com/nature/journal/v458/n7241/full/458969a.html

Negative Feedback on Proteins



Lestas I, Vinnicombe G and Paulsson J. 2010. Fundamental limits on the suppression of molecular fluctuations. Nature 467, 174–178. http://www.nature.com/nature/journal/v467/n7312/full/nature09333.html

Negative feedback on functions

PBM Biomechanism: FSH

Photobiomodulation(PBM)
Function-specific homeostasis (**FSH**)

Photobiomodulation (PBM) is a modulation of low intensity laser irradiation or monochromatic light (LIL) on biosystems, which stimulates or inhibits biological functions but does not result in irreducible damage

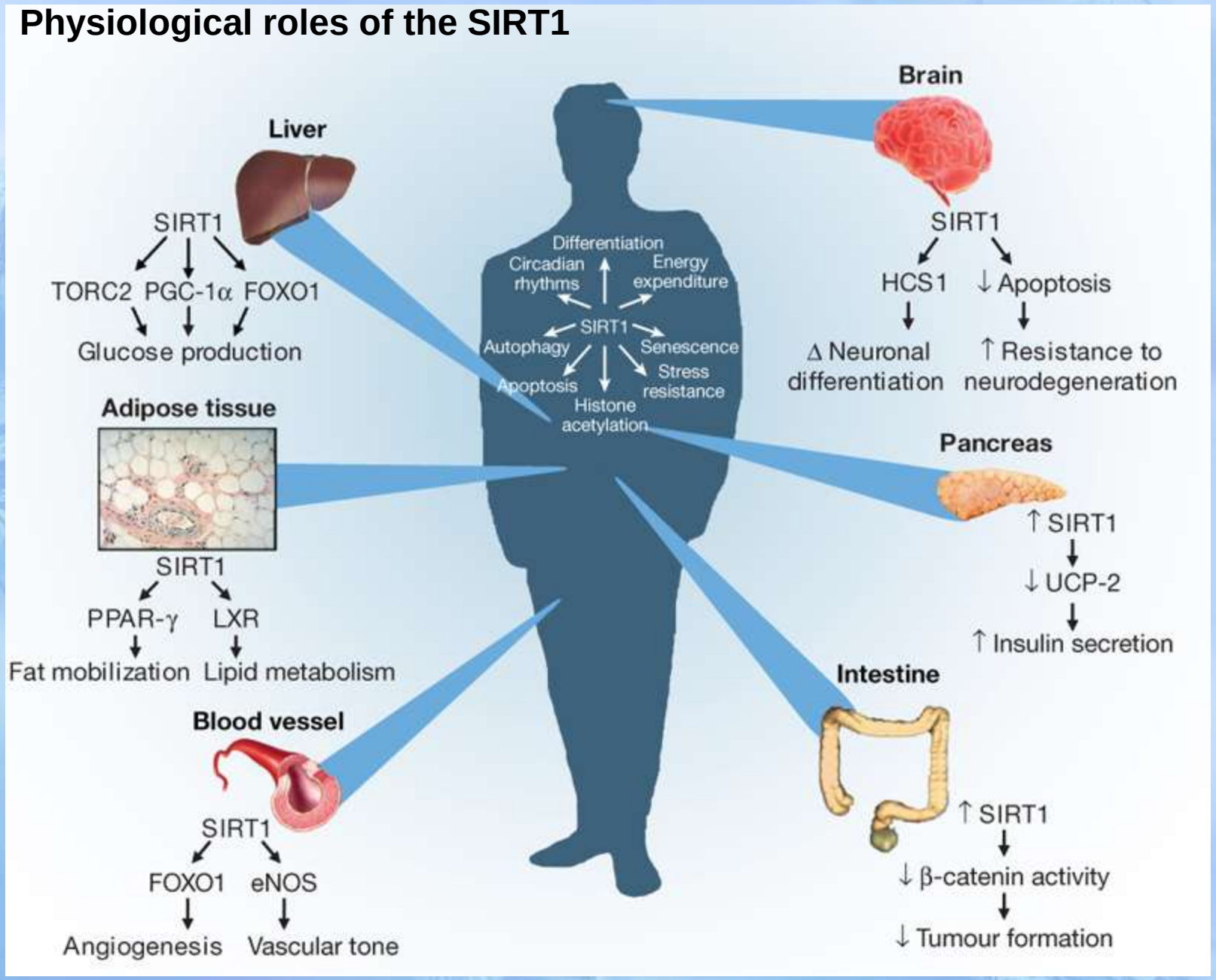
Function-Specific Homeostasis (FSH)

- FSH is a negative feedback for a function to be fully performed
  - Proliferation-specific homeostasis (**PISH**)
  - Sleep-specific homeostasis (SlSH)
  - Longevity-specific homeostasis (LoSH)

Liu TCY, Liu R, Zhu L,Yuan JQ, Hu M, Liu SH. 2009. Homeostatic **photobiomodulation**. Front Optoelectron China. 2009, 2(1): 1-8.

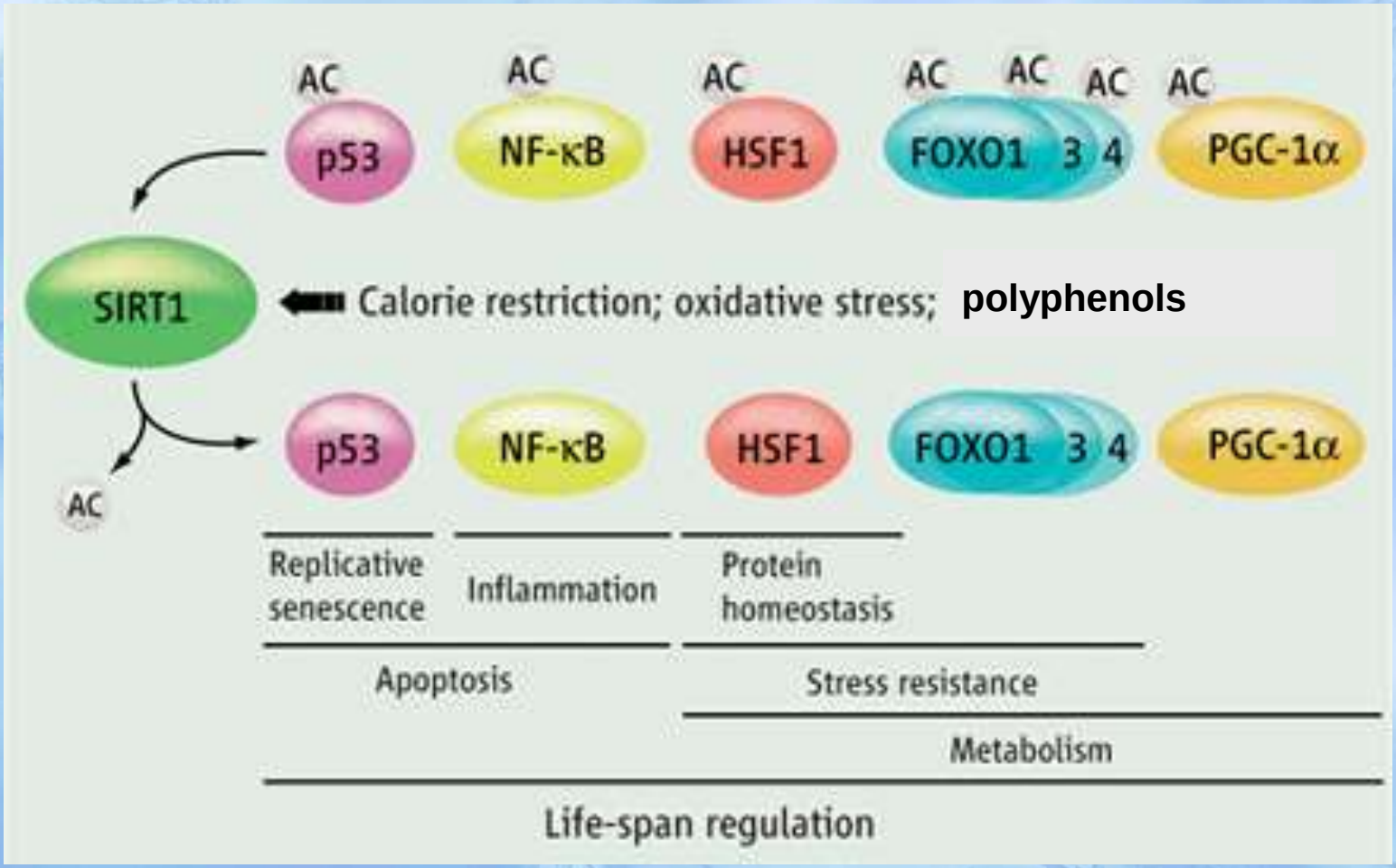
Liu CY, Zhu P (Eds). 2009. Intranasal **Low Intensity Laser** Therapy. Beijing: People's Military Medical Press.

Physiological roles of the SIRT1



Finkel T, Deng CX, Mostoslavsky R. 2009. Recent progress in the biology and physiology of sirtuins. Nature. 2009 Jul 30;460(7255):587-91.
http://www.nature.com/nature/journal/v460/n7255/full/nature08197.html

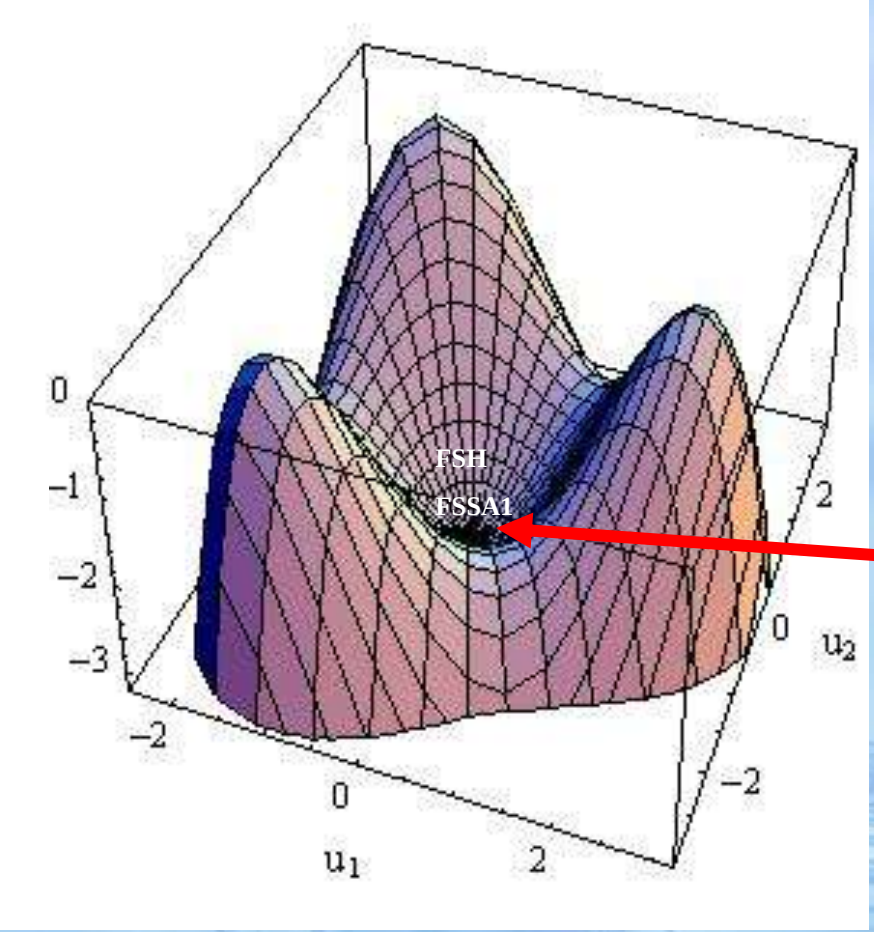
Handling stress



SIRT1 is a deacetylase that is activated by a variety of stressors and targets transcriptional regulators including p53, NF-kB, HSF1, FOXO1, 3, and 4, and PGC-1. These factors then control adaptive responses that modulate life span. AC: acetyl group;

Saunders LR, Verdin E. 2009. Stress Response and Aging. Science. 323(5917): 1021 – 1022.

SIRT1 activity



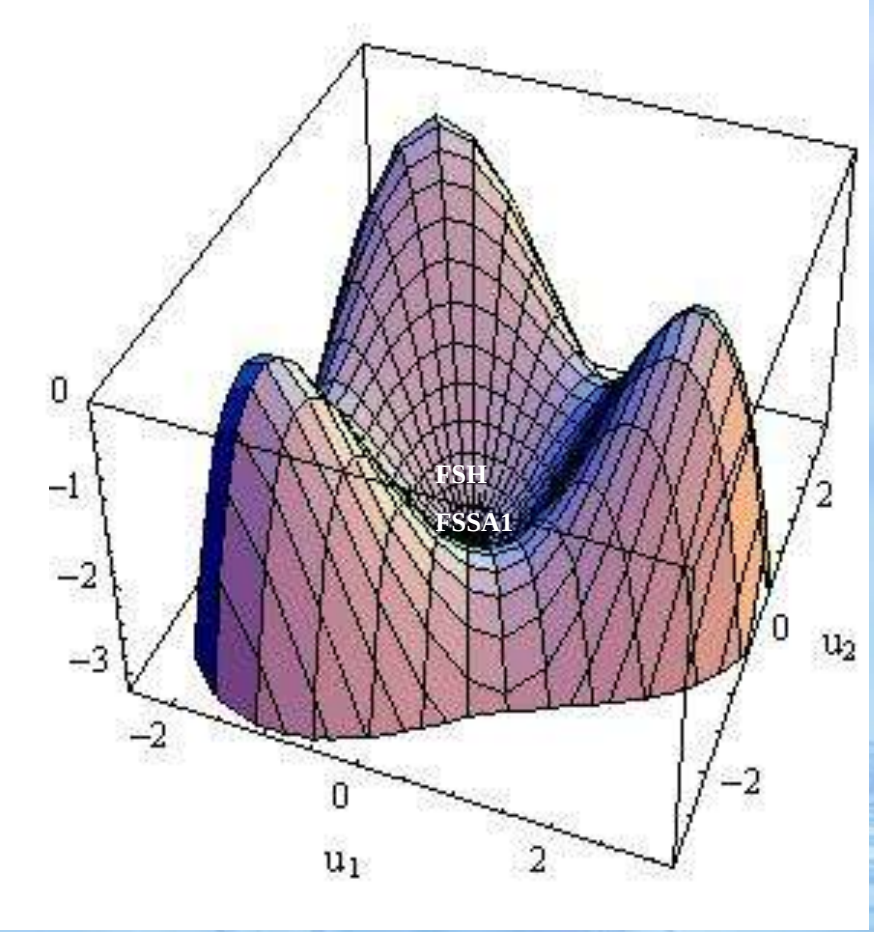
Function-specific homeostasis (FSH)

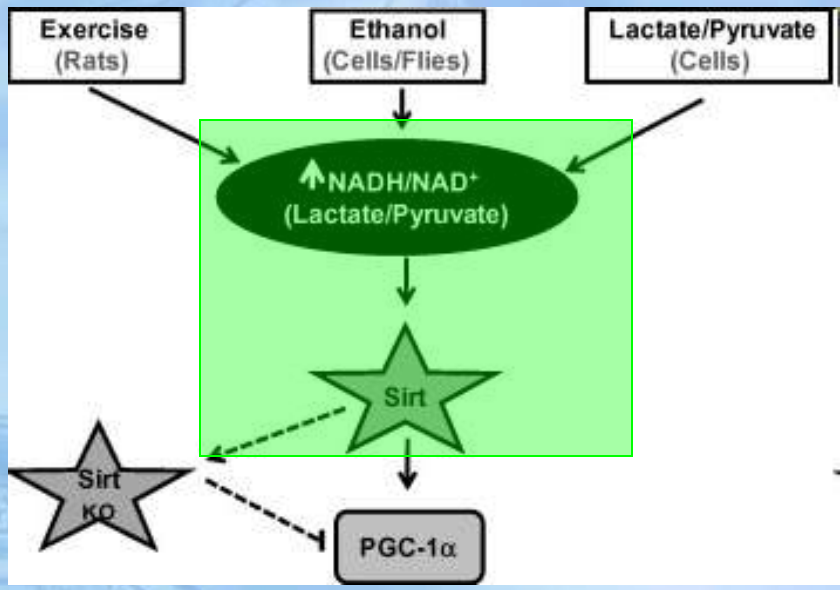
FSH-specific SIRT1 activity (FSSA1)

Sirtuin 1 (SIRT1) activity potential well.

FSSA1 denotes function-specific homeostasis specific SIRT1 activity

Economic FSH



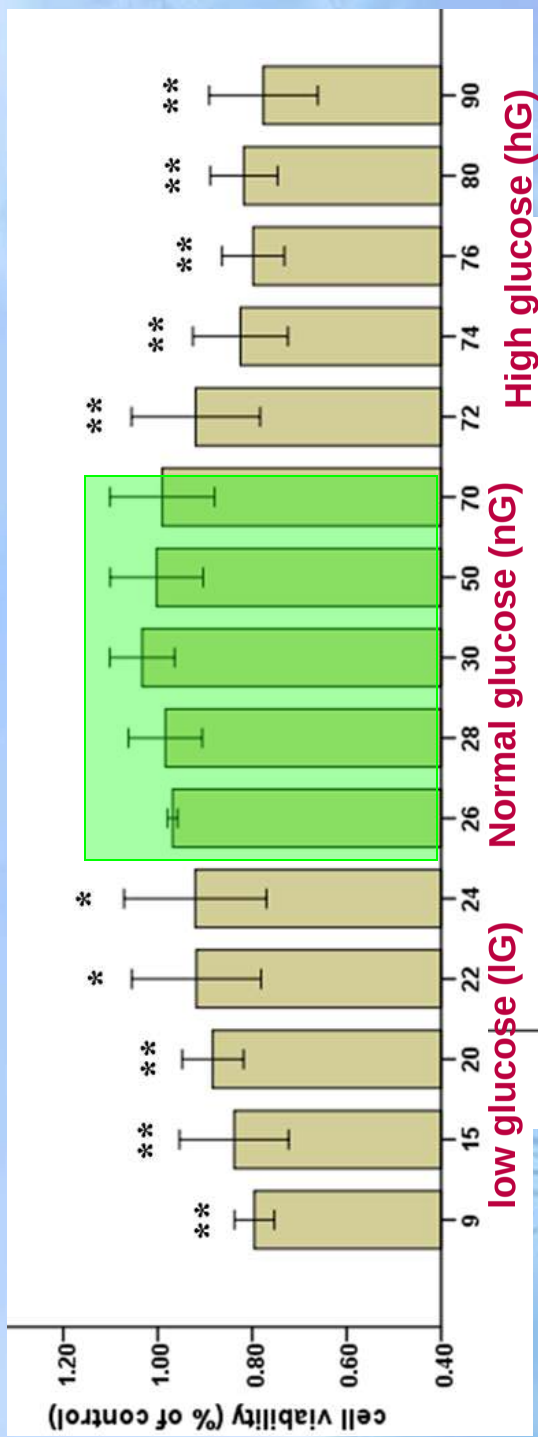


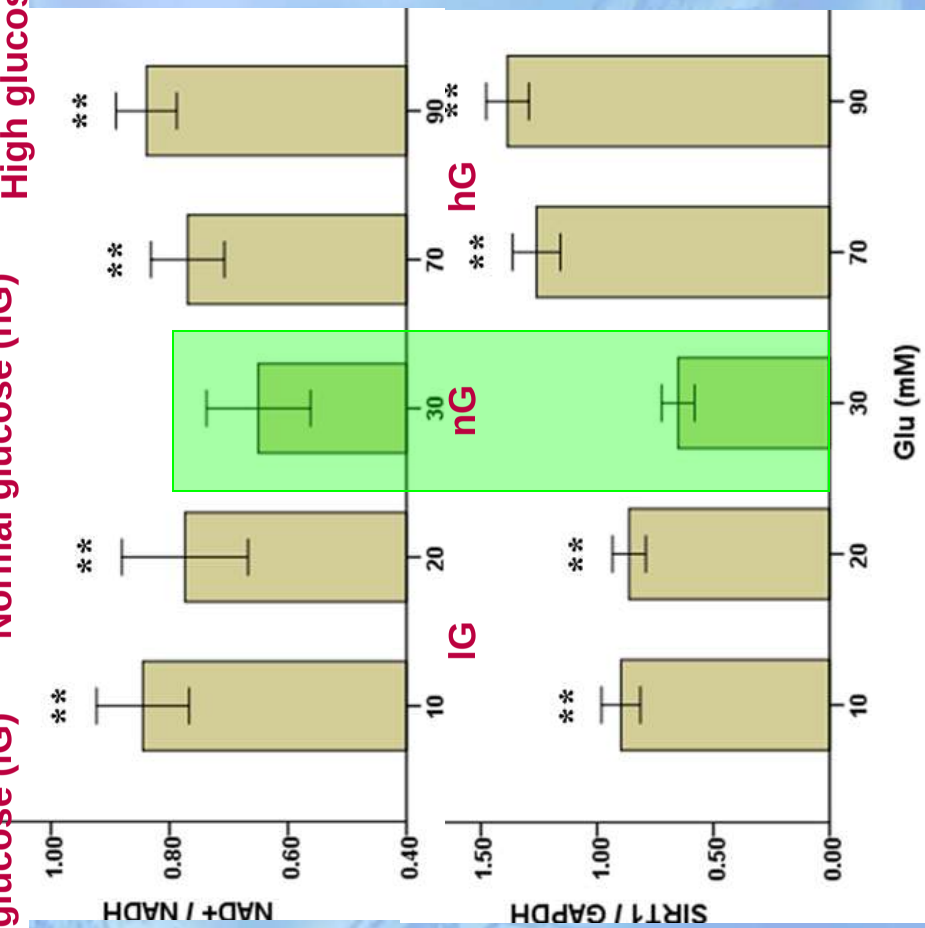
Sirtuin 1 (SIRT1) activity potential well.

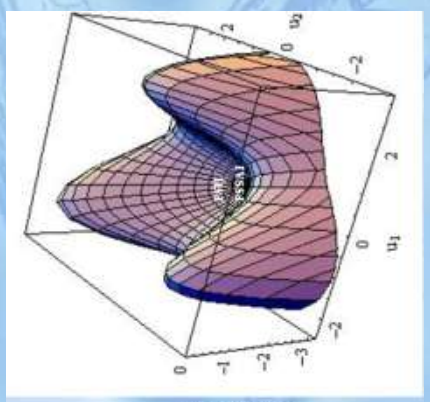
FSSA1 denotes function-specific homeostasis specific SIRT1 activity

Gambini J, Gomez-Cabrera MC, Borras C, Valles SL, Lopez-Grueso R, Martinez-Bello VE, Herranz D, Pallardo FV, Tresguerres JA, Serrano M, Viña J.Free [NADH]/[NAD(+)] regulates sirtuin expression. Arch Biochem Biophys. 2011 Aug 1;512(1):24-9. http://www.ncbi.nlm.nih.gov/pubmed/21575591

PlSH of PC12 cells in glucose





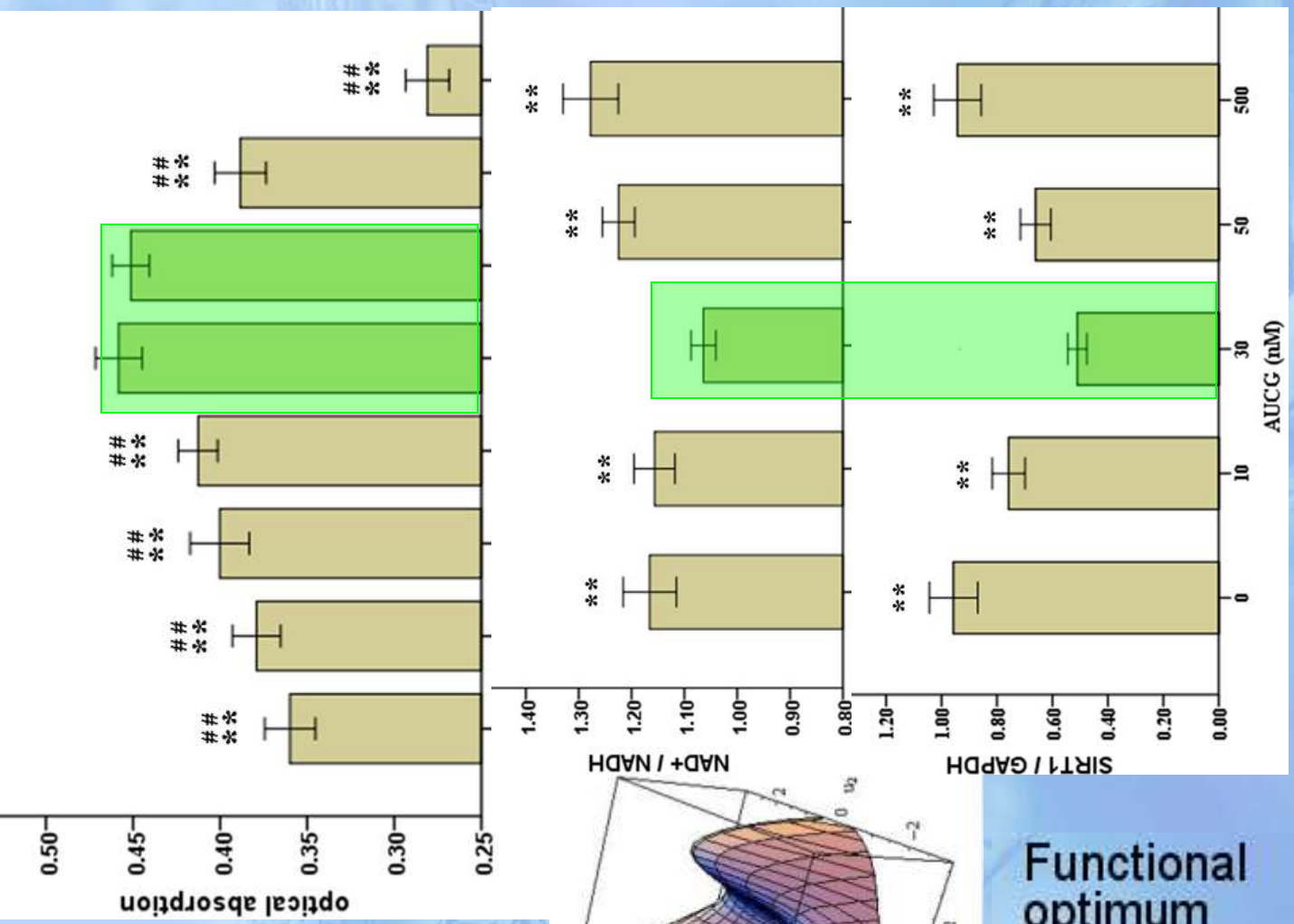


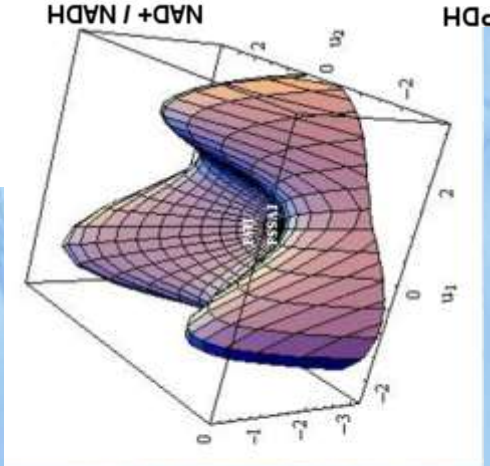
Functional optimum

Resistance

Lowest NAD/NADH and SIRT1 activity

PlSH of PC12 cells in nucleotide



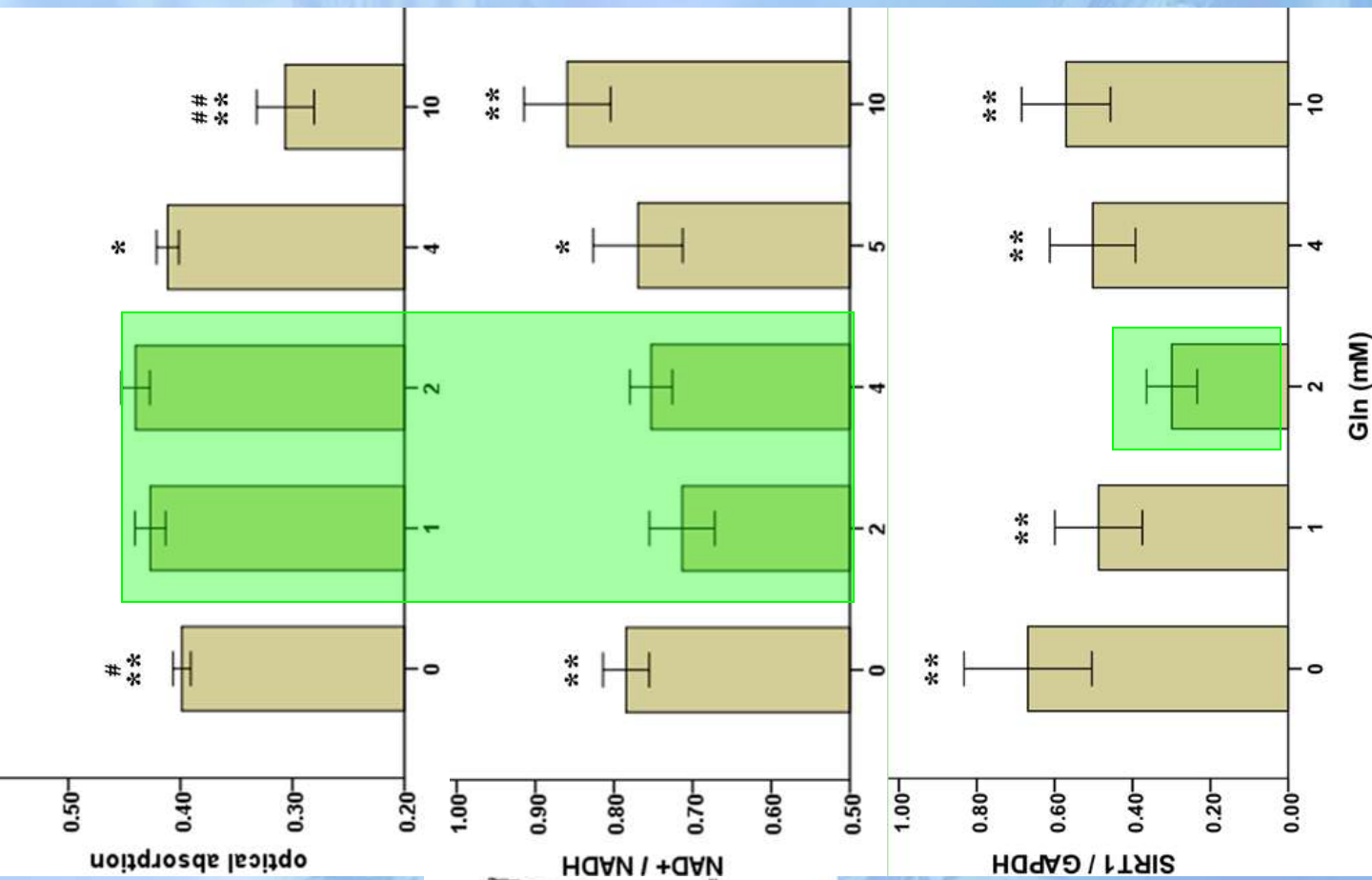


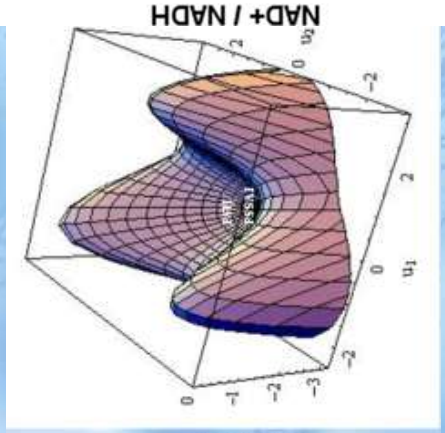
Functional optimum

Resistance

Lowest NAD/NADH and SIRT1 activity

PlSH of PC12 cells in glutamine



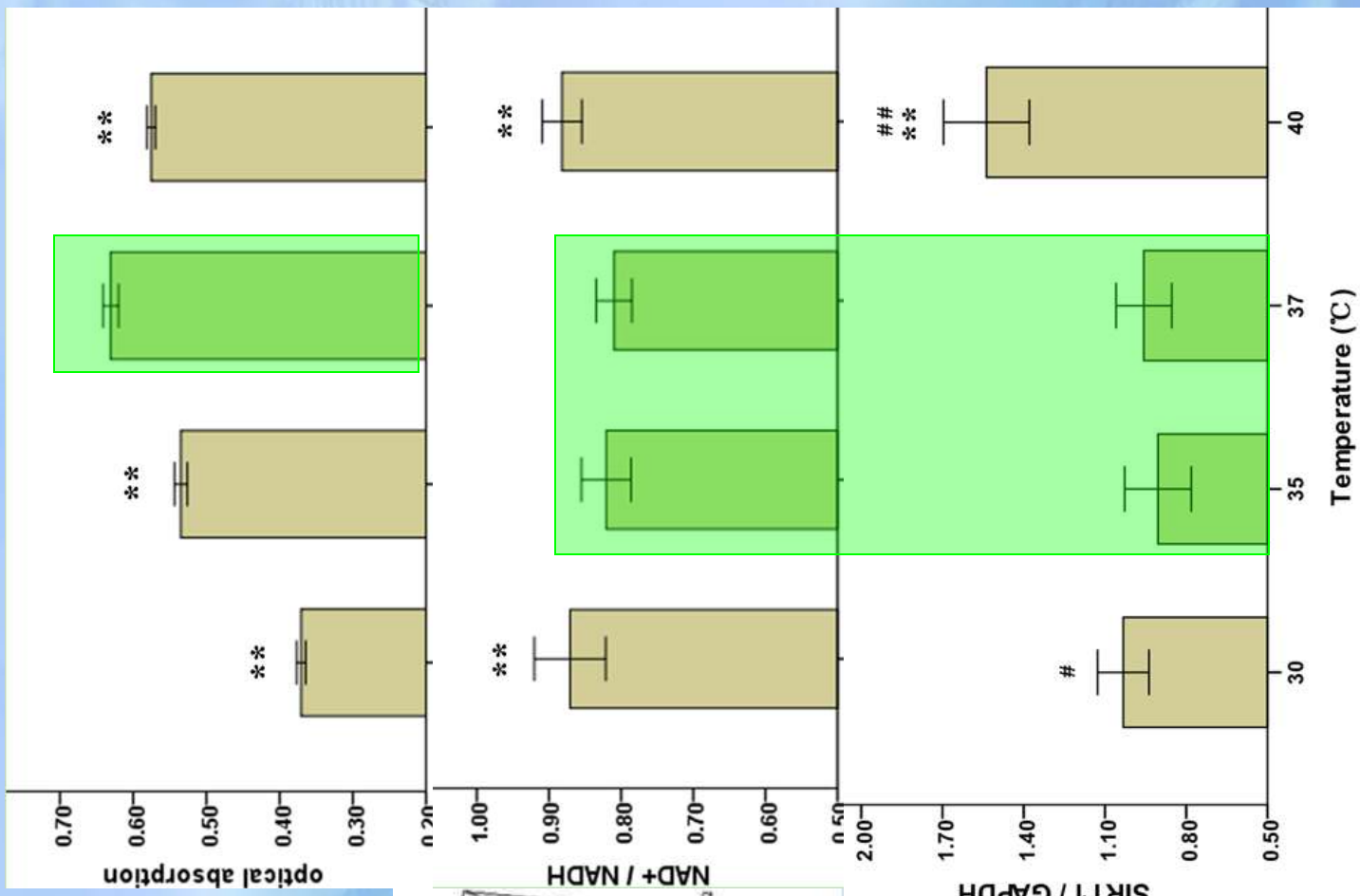


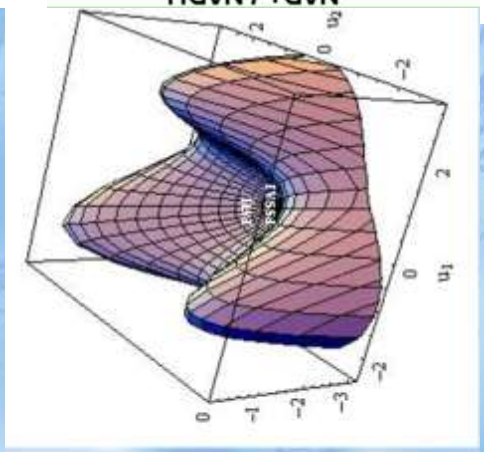
Functional optimum

Resistance

Lowest NAD/NADH and SIRT1 activity

PlSH of PC12 cells in temperature





Functional optimum

Resistance

Lowest NAD/NADH and SIRT1 activity

Shankar A, Charumathi S, Kalidindi S. 2011. Sleep duration and self-rated health: the national health interview survey 2008. Sleep. 2011 Sep 1;34(9):1173-7. http://www.ncbi.nlm.nih.gov/pubmed/21886354 free

Sleep-specific homeostasis

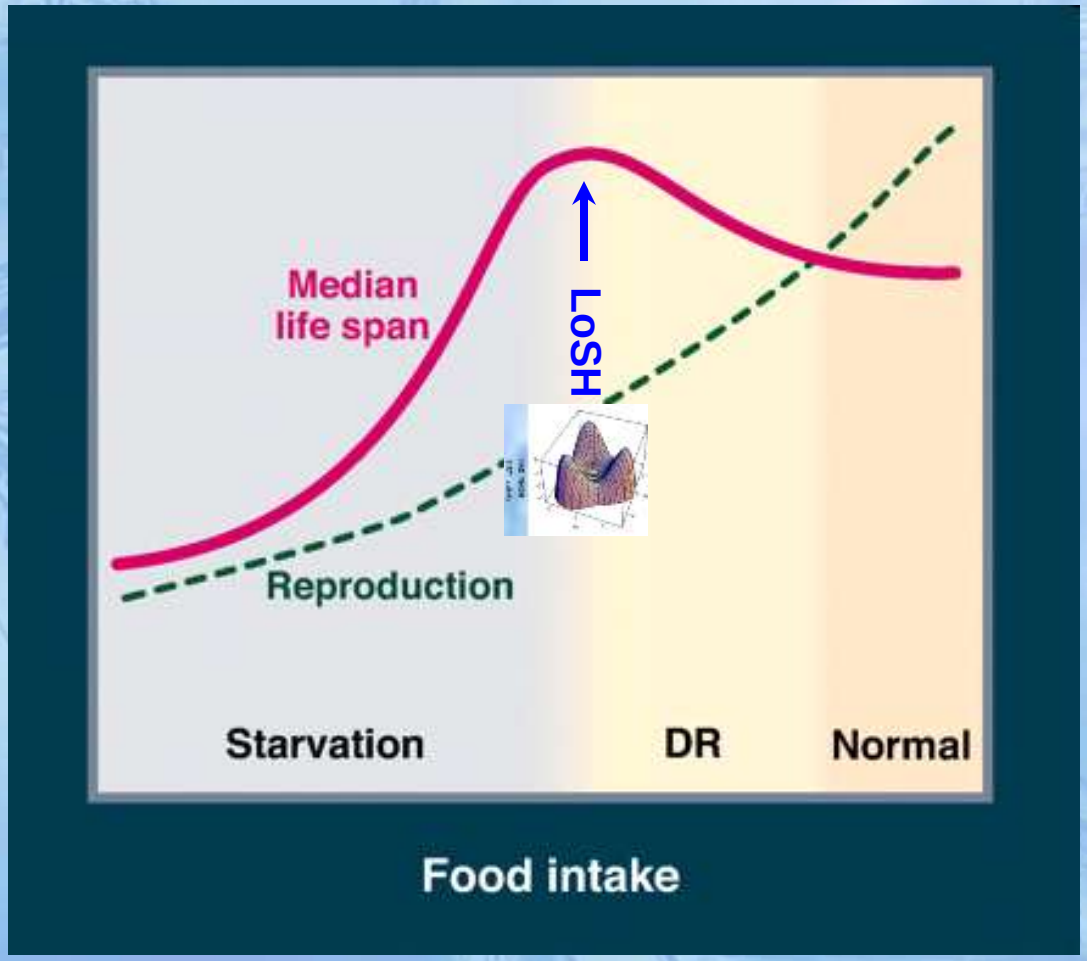
Sleep duration	Weighted prevalence of fair/poor SRH, %	Age, sex-adjusted OR (95% CI)†	Multivariable OR (95% CI)*†
Whole population (n = 20,663)			
≤ 5 h	23.4	3.84 (3.18-4.62)	2.29 (1.86-2.83)
6 h	13.8	2.01 (1.71-2.35)	1.68 (1.42-2.00)
7 h	7.5	1 (Referent)	1 (Referent)
8 h	12.1	1.59 (1.37-1.84)	1.38 (1.18-1.61)
≥ 9 h	23.8	3.10 (2.63-3.66)	1.98 (1.63-2.40)

Sleep duration	Weighted prevalence, %	Age-adjusted OR (95% CI)†	Multivariable OR (95% CI)*†
Men (n = 9058)			
≤ 5 h	18.8	3.45 (2.60-4.58)	2.04 (1.49-2.81)
6 h	12.3	1.92 (1.53-2.40)	1.63 (1.28-2.09)
7 h	7.1	1 (Referent)	1 (Referent)
8 h	11.3	1.53 (1.24-1.89)	1.25 (1.00-1.56)
≥ 9 h	23.2	3.03 (2.35-3.91)	1.85 (1.38-2.49)
Women (n = 11605)			
≤ 5 h	27.3	4.21 (3.35-5.31)	2.52 (1.97-3.24)
6 h	15.2	2.10 (1.71-2.58)	1.74 (1.38-2.18)
7 h	7.9	1 (Referent)	1 (Referent)
8 h	12.8	1.64 (1.34-2.00)	1.49 (1.19-1.86)
≥ 9 h	24.2	3.16 (2.54-3.92)	2.11 (1.64-2.70)

Sleep duration	Weighted prevalence, %	Age, sex-adjusted OR (95% CI)†	Multivariable OR (95% CI)*†
Non-obese (n = 14499)			
≤ 5 h	19.8	4.15 (3.26-5.28)	2.55 (1.94-3.36)
6 h	9.5	1.78 (1.45-2.20)	1.55 (1.25-1.92)
7 h	5.7	1 (Referent)	1 (Referent)
8 h	9.7	1.65 (1.37-1.99)	1.38 (1.13-1.68)
≥ 9 h	21.0	3.33 (2.66-4.16)	2.05 (1.59-2.63)
Obese (n = 6164)			
≤ 5 h	29.0	3.05 (2.33-3.97)	1.98 (1.47-2.67)
6 h	22.9	2.19 (1.73-2.76)	1.85 (1.42-2.41)
7 h	12.3	1 (Referent)	1 (Referent)
8 h	18.5	1.57 (1.26-1.96)	1.36 (1.06-1.73)
≥ 9 h	30.5	2.82 (2.17-3.65)	1.78 (1.34-2.36)

SRH, self-rated health; OR, odds ratio; CI, confidence interval.

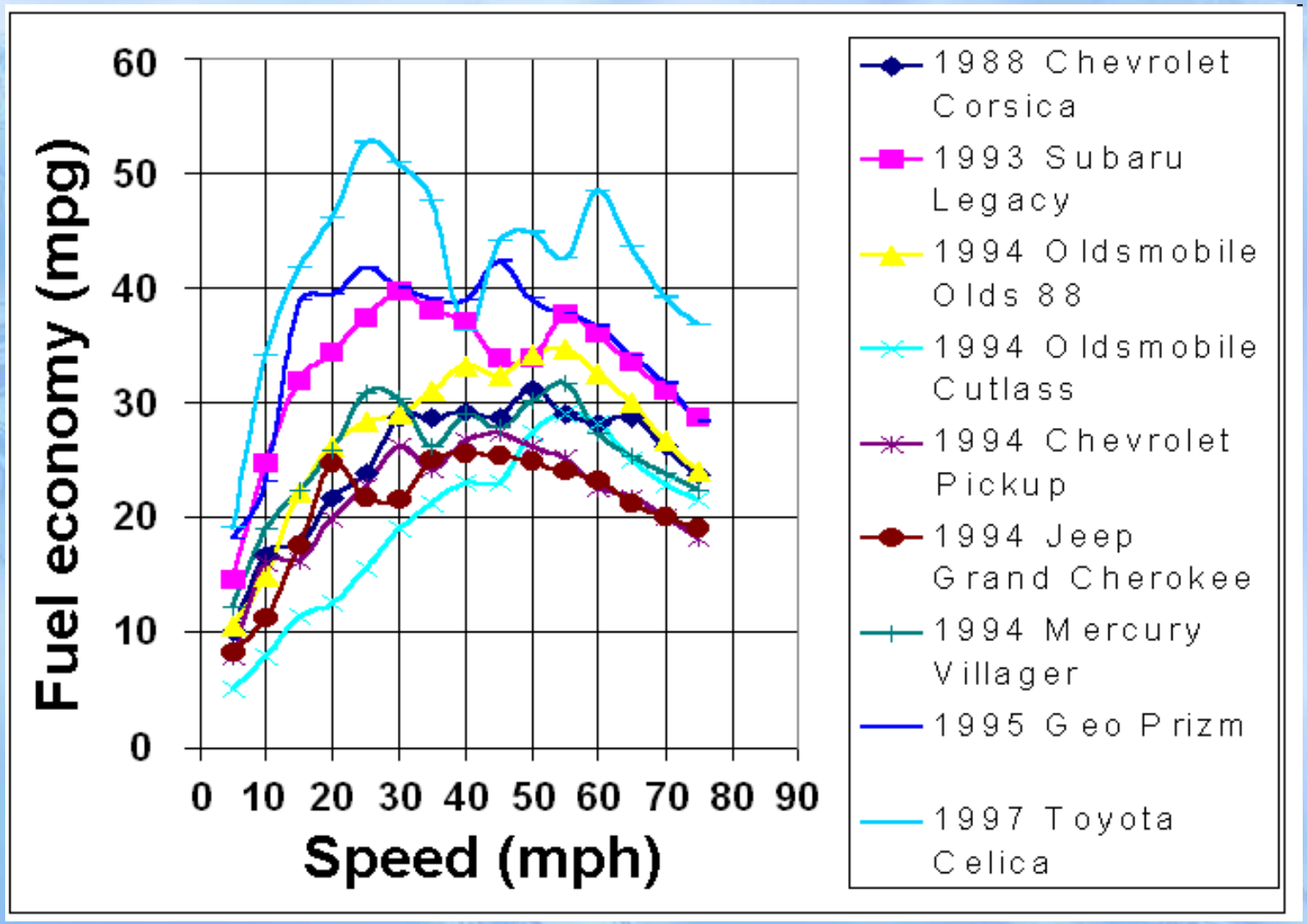
Longevity-specific homeostasis(LoSH)



Fontana L, Partridge L, Longo VD. 2010. Extending healthy life span--from yeast to humans. Science. 2010 Apr 16;328(5976):321-6. http://www.sciencemag.org/cgi/content/full/328/5976/321

http://forums.nasioc.com/downtime.html?p=35428522

Car-specific Optimum Speed



Each **car** has its **optimum speed**

FSH illustration

http://house.ifeng.com/home/roll/detail_2010_10/18/2813214_0.shtml

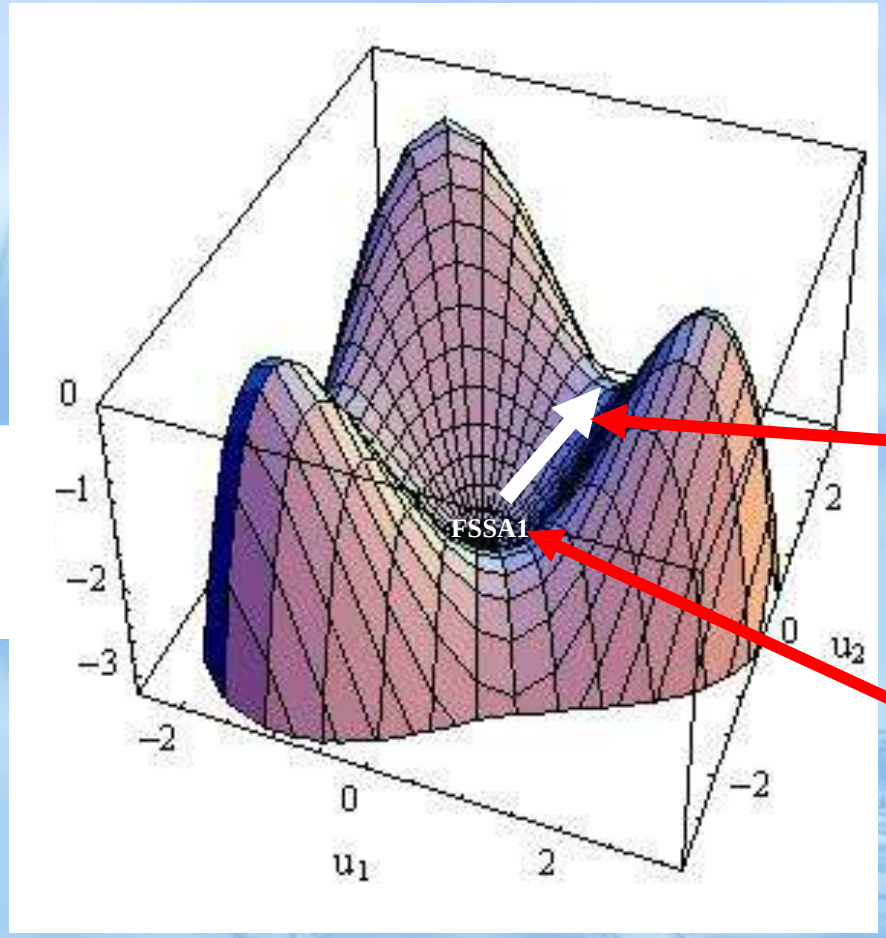
Negative feedback on stresses

PBM Biomechanism: FSS & FSSH

FSH-specific stress (**FSS**)

FSS-specific homeostasis (**FSSH**)

Successful stress: FSS in FSSH



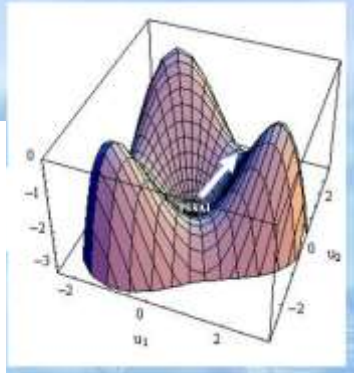
FSH-specific stress (FSS)

FSS-specific homeostasis(FSSH)

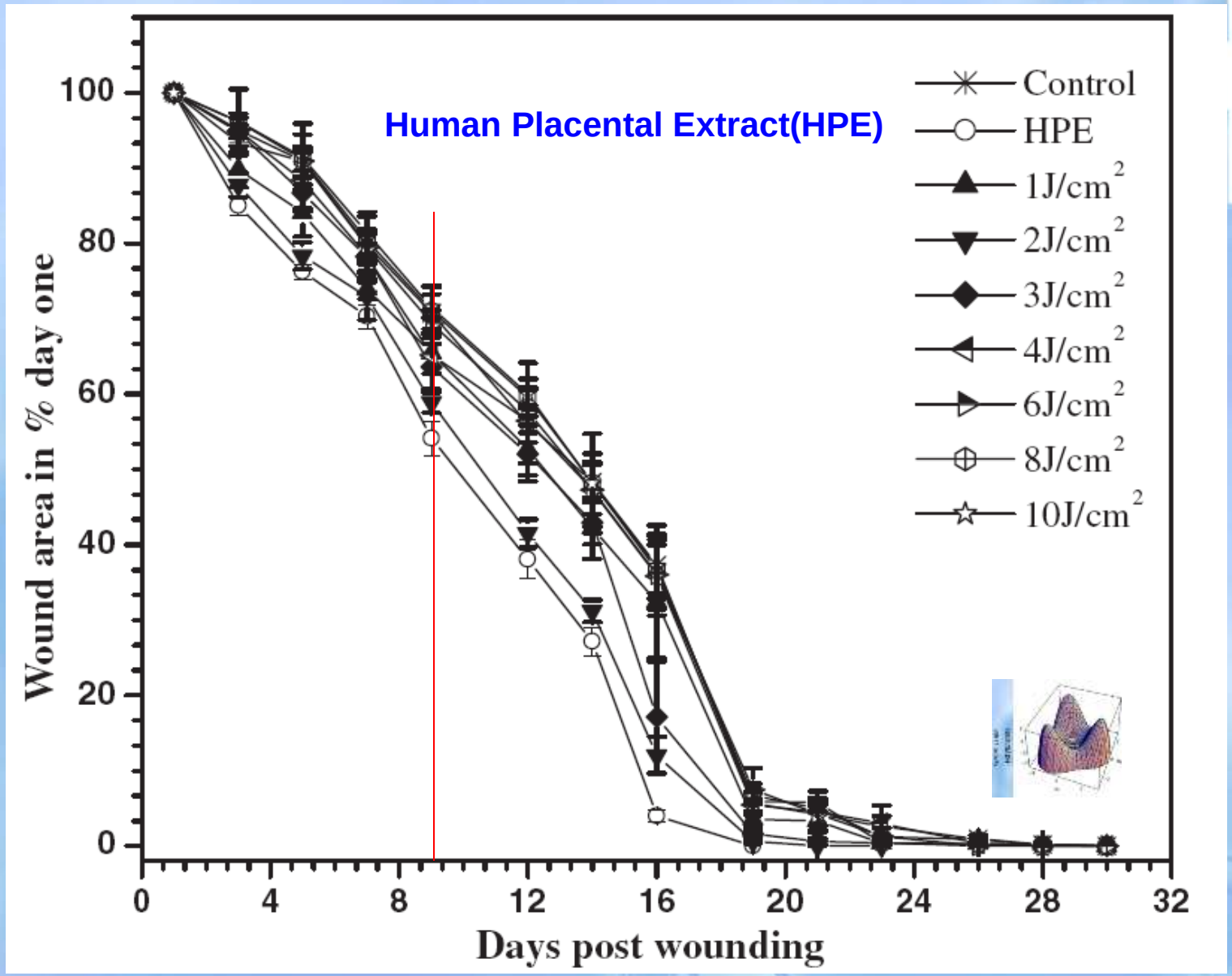
FSH

Sirtuin 1 (SIRT1) activity potential well.

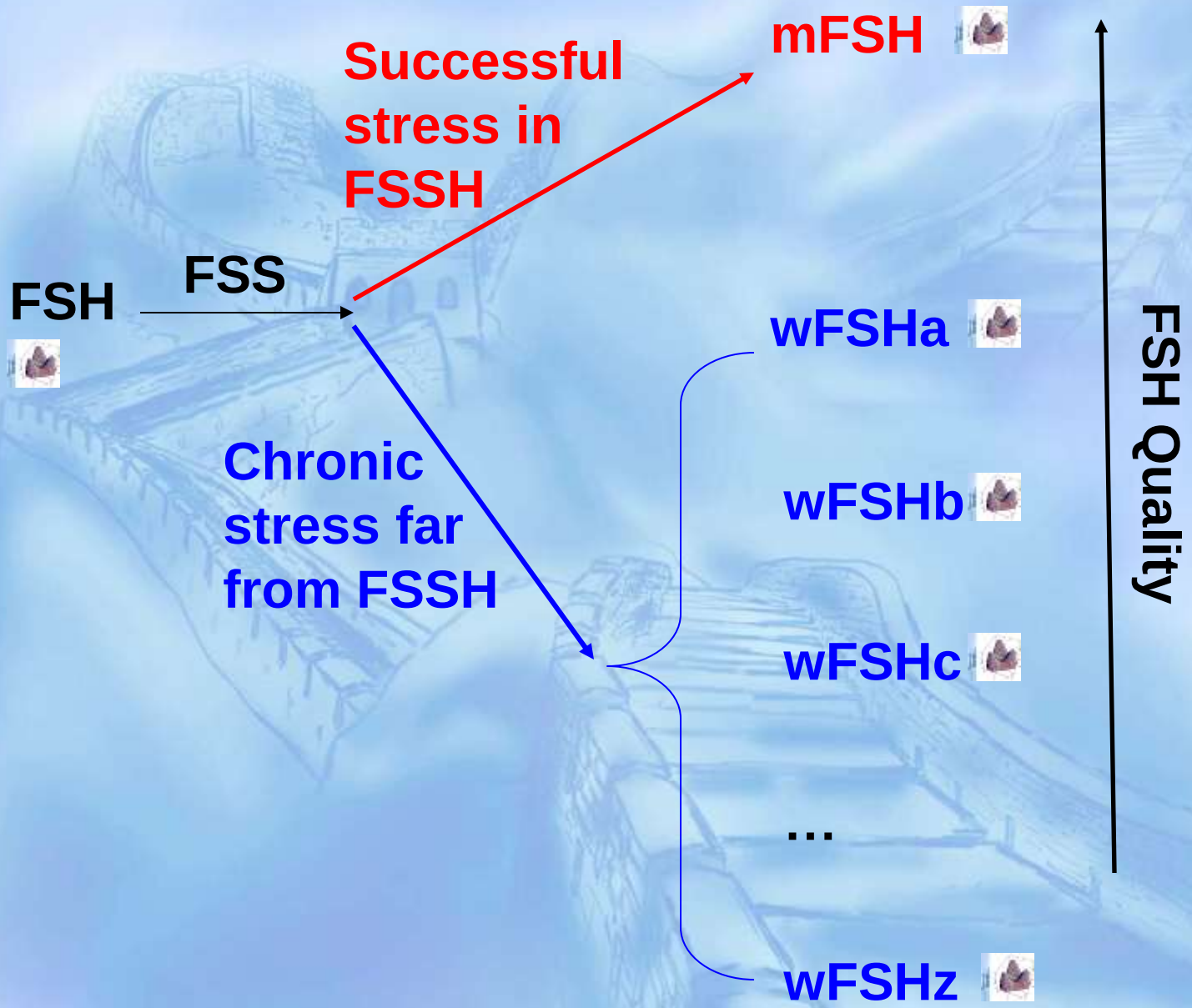
FSSA1 denotes function-specific homeostasis specific SIRT1 activity



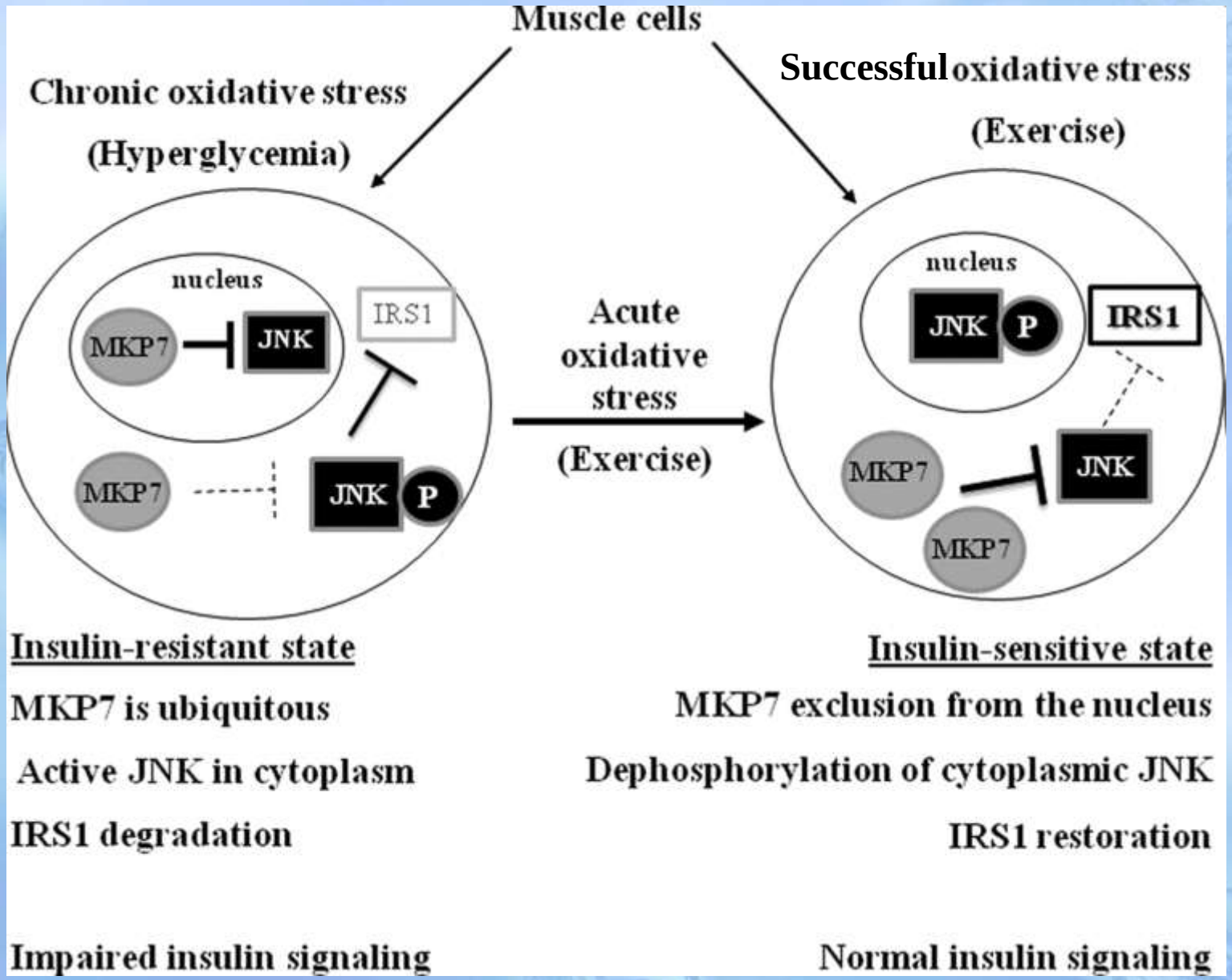
Wound healing



Prabhu V, Rao SB, Rao NB, Aithal KB, Kumar P, Mahato KK. 2010. Development and evaluation of fiber optic probe-based helium-neon **low**-level **laser** therapy system for tissue regeneration--an in vivo experimental study. Photochem Photobiol. **2010** Nov-Dec;86(6):1364-72. http://www.ncbi.nlm.nih.gov/pubmed/20735808


mFSH
Successful stress in FSSH
FSH
FSS
wFSHa
Chronic stress far from FSSH
wFSHb
wFSHc
...
wFSHz
FSH Quality

Oxidative stress on insulin sensitivity

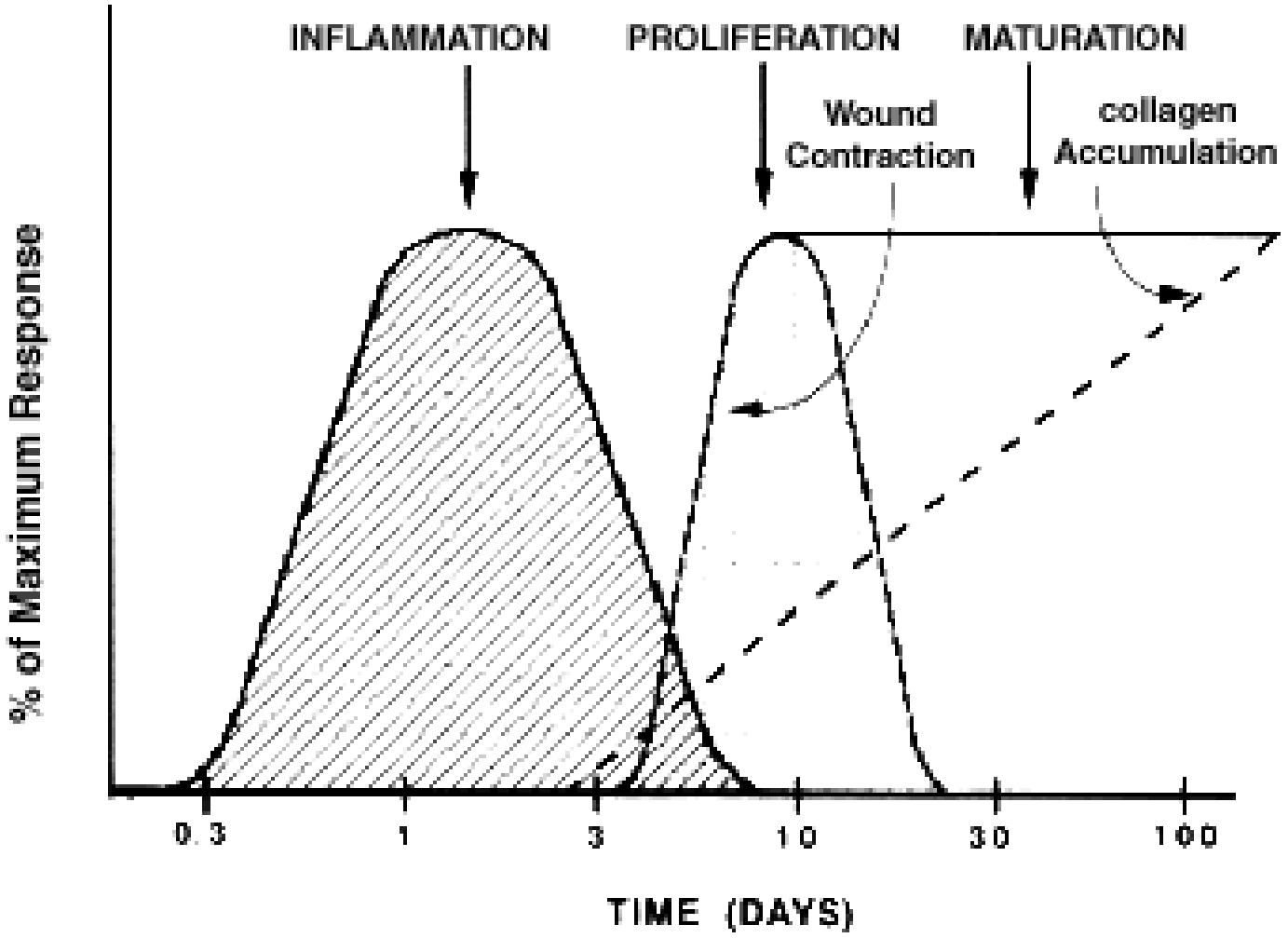


IRS1: insulin receptor substrate 1

Berdichevsky A, Guarente L, Bose A. 2010. Acute oxidative stress can reverse insulin resistance by inactivation of cytoplasmic JNK. J Biol Chem. 2010 Jul 9;285(28):21581-9. http://www.ncbi.nlm.nih.gov/pubmed/20430894 free

Menke MN, Menke NB, Boardman CH, Diegelmann RF. 2008. Biologic therapeutics and molecular profiling to optimize wound healing. Gynecol Oncol. 2008 Nov;111(2 Suppl):S87-91.
http://www.ncbi.nlm.nih.gov/pubmed/18829090

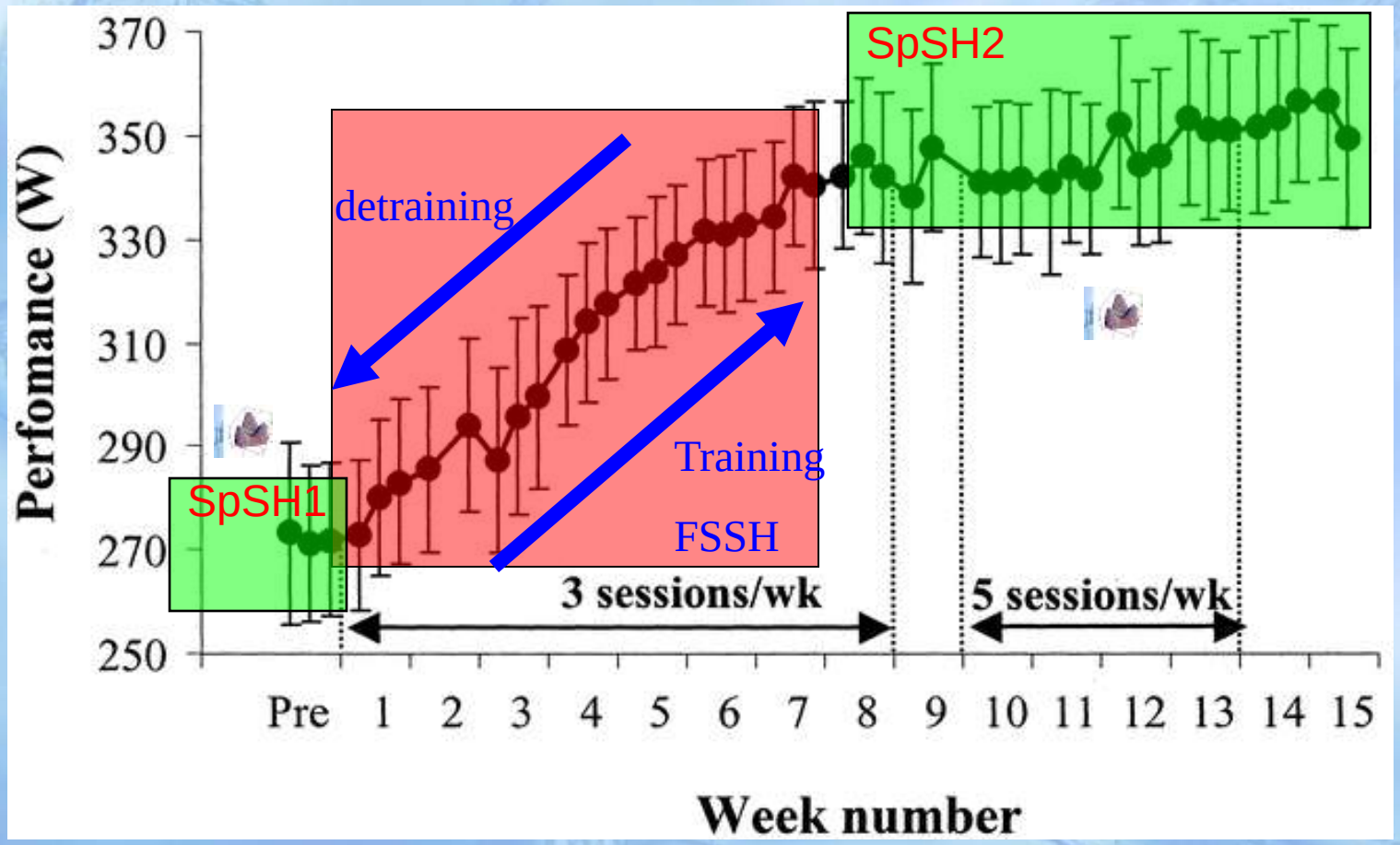
Factors that may impair normal wound healing
Age
Co-morbidities
Cardiac
Congestive heart failure
Connective tissue disease
Diabetes mellitus
Hepatic
Hypertension
Renal
Lifestyle
Illicit drug use
Nutrition
Obesity
Smoking
Therapeutic modalities
Chemotherapy
NSAIDs
Radiation
Steroids



Phases of wound repair. Wound healing has been arbitrarily divided into three phases: inflammation(0-5days), proliferation (3-14 days)and maturation(week-year)

Sport-specific homeostasis (SpSH)

Training program plateau



Pattern of performance measured with Plim5′ test over the experiment. *Dotted lines* delimit the two phases of training: phase 1 with three training sessions per week and phase 2 with five training sessions per week. Values are mean ± SE.

Busso T. Variable Dose-Response Relationship between Exercise Training and Performance. ***Med. Sci. Sports Exerc.***, Vol. 35, No. 7, pp. 1188-1195, 2003.

Negative feedback and PBM

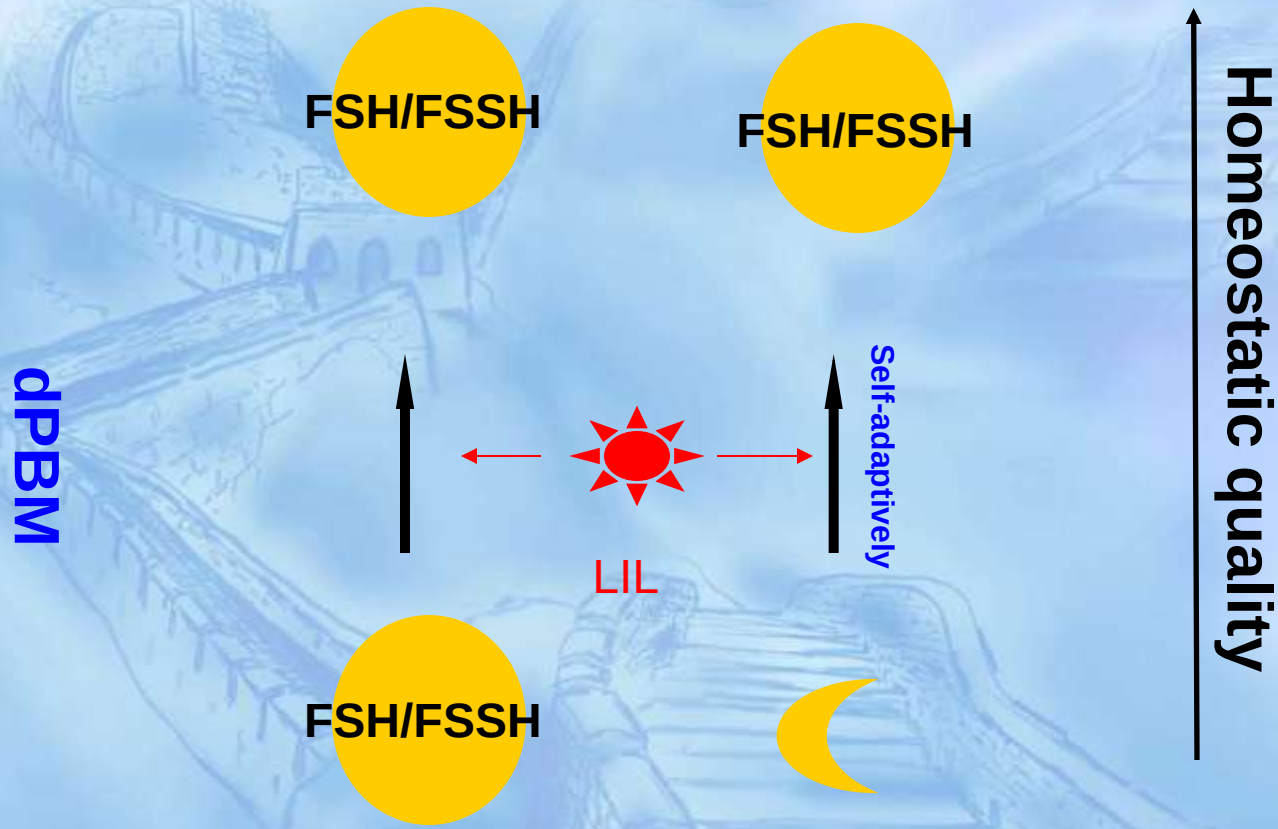
PBM Biomechanism: dPBM & iPBM

Direct photobiomodulation (dPBM)

Indirect photobiomodulation (iPBM)

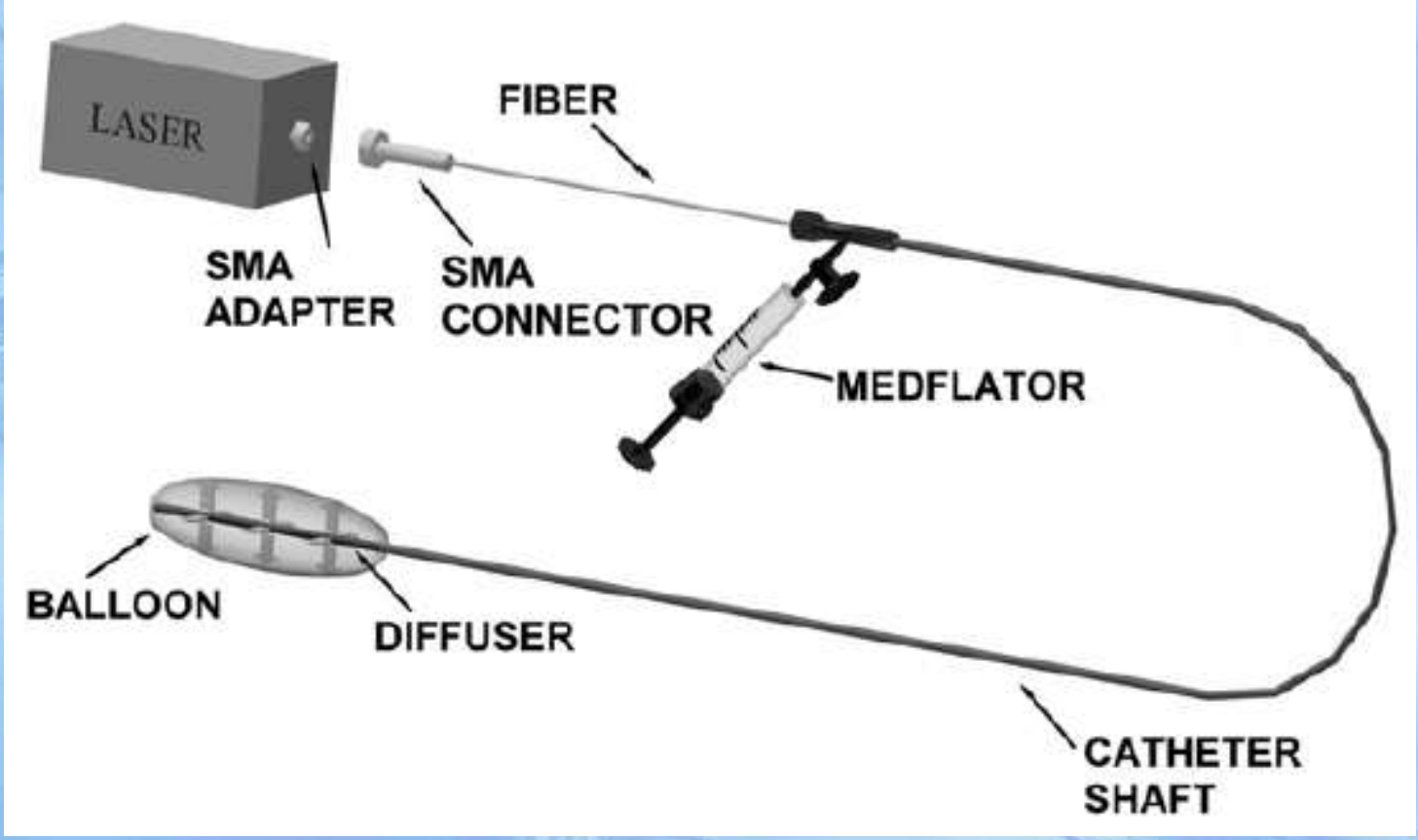
dPBM

- There is no dPBM on FSH/FSSH
- dPBM modulates a chronic stress self-adaptively until it becomes a successful stress so that the FSH/FSSH is established



Low intensity laser irradiation or monochromatic light（LIL）

Intravascular LIL



Derkacz A, Protasiewicz M, Poreba R, Szuba A, Andrzejak R. 2010. Usefulness of intravascular low-power laser illumination in preventing restenosis after percutaneous coronary intervention. Am J Cardiol. 106(8):1113-7. http://www.ncbi.nlm.nih.gov/pubmed/20920649

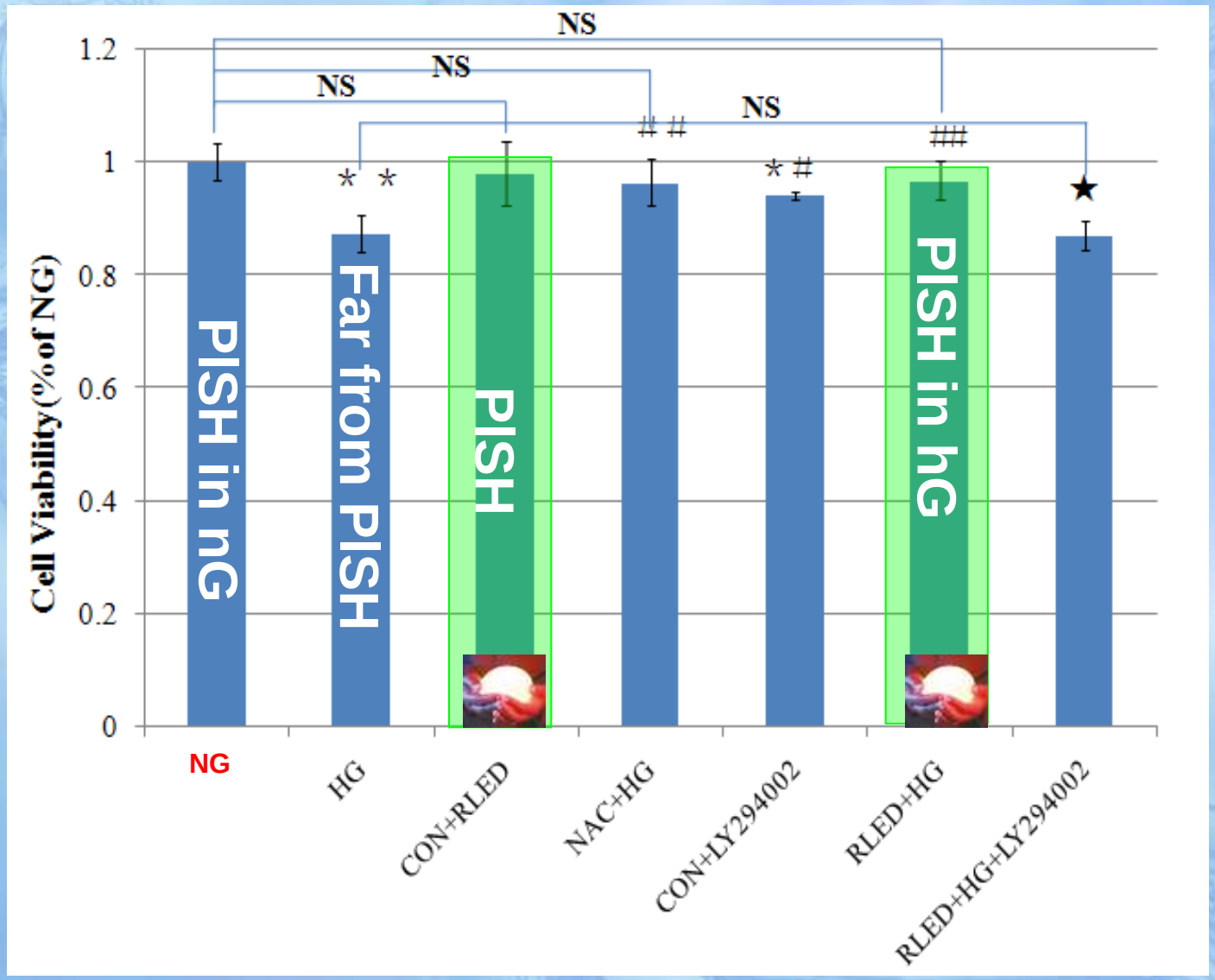
Percutaneous coronary intervention

Major adverse cardiac events (MACE) and mean extent of narrowing on follow-up coronary angiogram at 6 months, stratified by diagnosis of restenosis

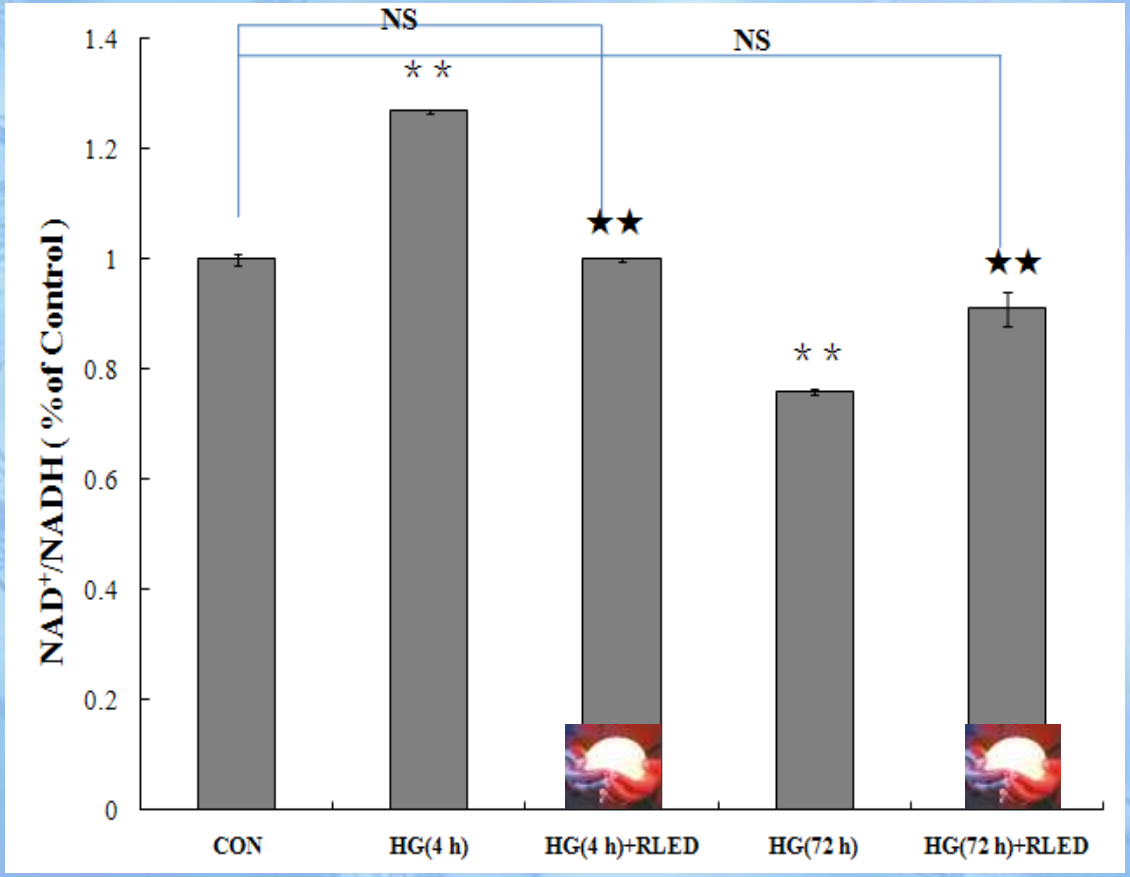
Variable	Laser (n = 52)	Control (n = 49)	p Value
Mean narrowing on angiogram (%)	32.0 ± 22.1	43.5 ± 23.6	<0.05
Patients with restenosis (%)	59.1 ± 22.0	71.8 ± 16.3	<0.01
Patients without restenosis (%)	27.5 ± 13.0	32.2 ± 17.8	0.128
Major adverse cardiac events			
At 6 months	4 (7.7%)	7 (14.3%)	0.525
At 12 months	4 (7.7%)	9 (18.4%)	0.266

Derkacz A, Protasiewicz M, Poreba R, Szuba A, Andrzejak R. 2010. Usefulness of intravascular low-power laser illumination in preventing restenosis after percutaneous coronary intervention. Am J Cardiol. 106(8):1113-7. http://www.ncbi.nlm.nih.gov/pubmed/20920649

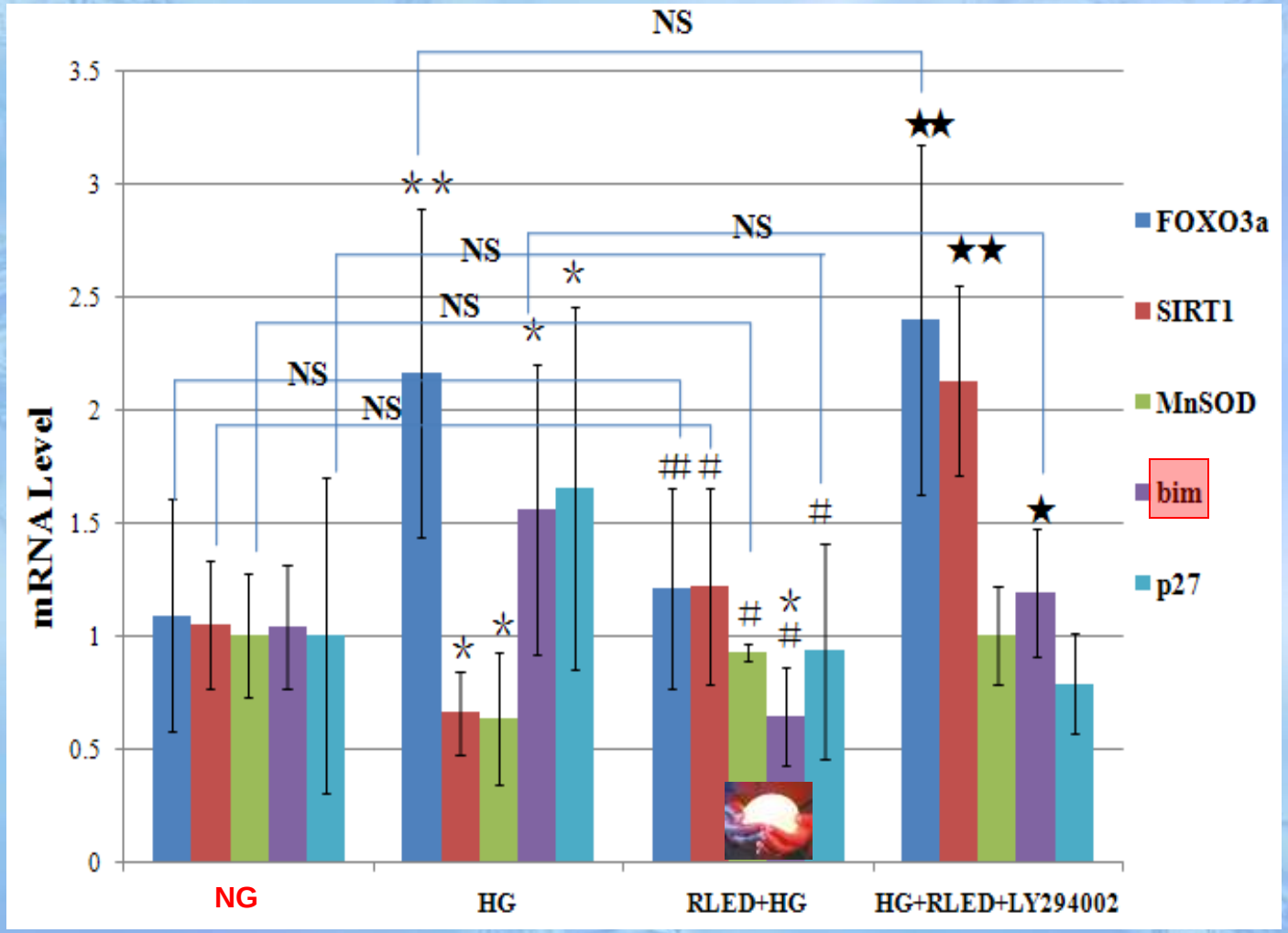
dPBM on hG induced dysfunction



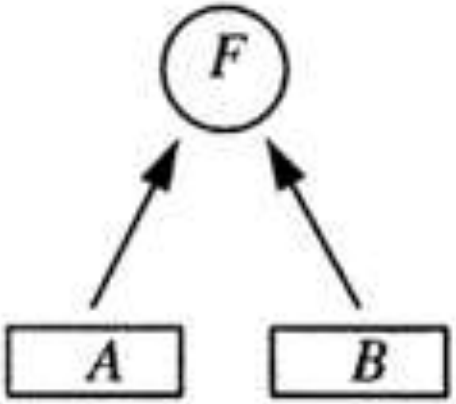
Self-adaptive dPBM



Self-adaptive dPBM



Redundant genes

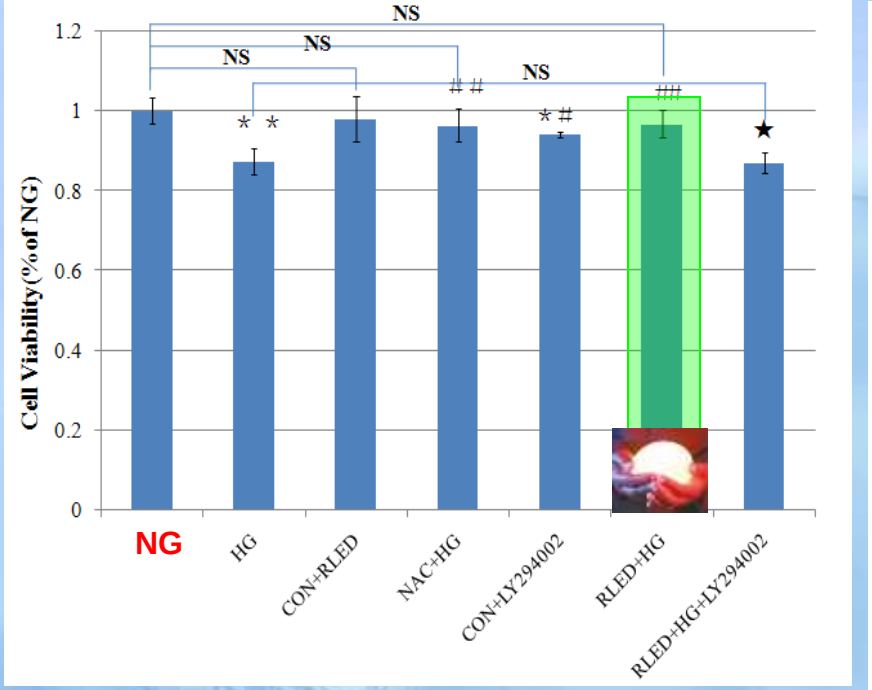


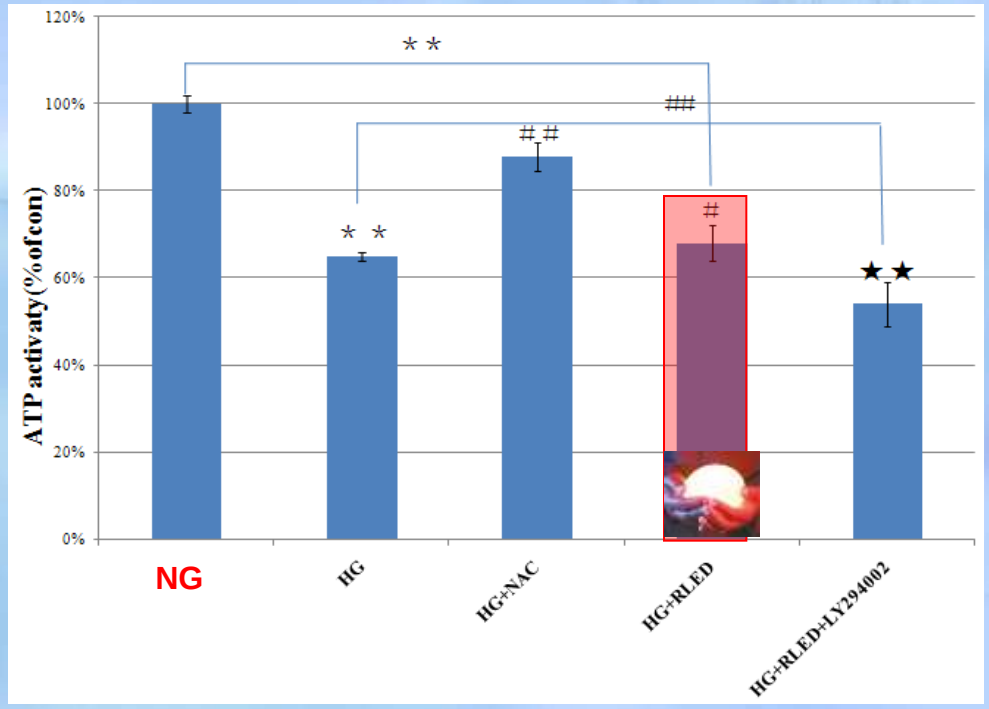
Gene	*F*
A	1
a	0
B	1
b	0

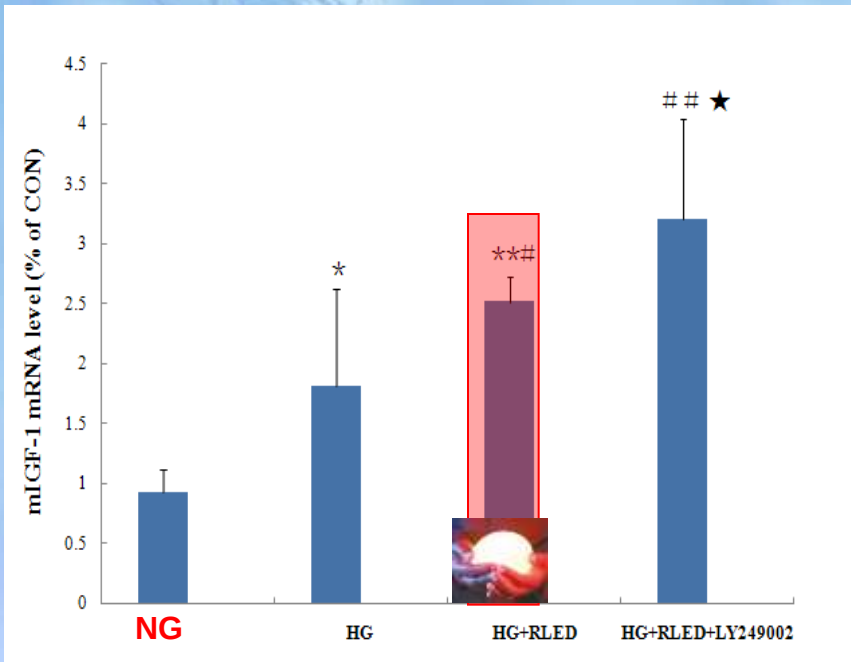
Genotype	Fitness
AB	1
Ab	1
aB	1
ab	0

If genes *A* and *B* perform function *F* with equal efficacy, then redundancy does not persist. For unequal mutation rates, the gene with higher mutation rate will become extinct.

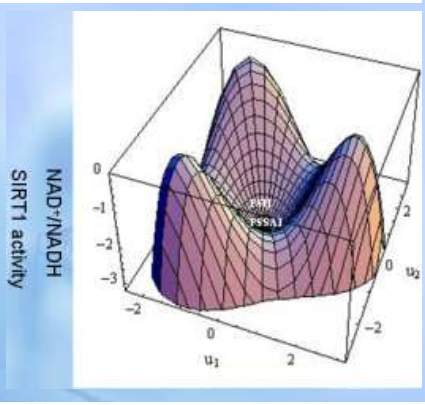
Nowak MA, Boerlijst MC, Cooke J, Smith JM. 1997. Evolution of genetic redundancy.**Nature**. 1997 Jul 10;388(6638):167-71. http://www.ncbi.nlm.nih.gov/pubmed/9217155

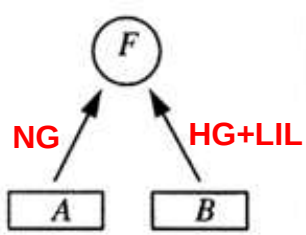






Redundant pathway





Gene	F
A	1
a	0
B	1
b	0

Genotype	Fitness
AB	1
Ab	1
aB	1
ab	0

iPBM

- A function in its FSH has three kinds of subfunctions in terms of their respective homeostasis (sFSH)
  - The FSH inhibits the establishment of sFSH (iFSH)
  - The FSH does not modulate the establishment of sFSH (nFSH)
  - The FSH promotes the establishment of sFSH (pFSH)
- iPBM self-adaptively modulates a subfunction far from its pFSH until the pFSH is established and then the FSH is upgrated into enhanced FSH (eFSH).

eFSH

FSH

non-modulation

inter-inhibition

nFSH

iPBM

promotion

inter-promotion

dPBM

Light

iFSH

pFSH

dPBM

dPBM

Homeostasis Quality

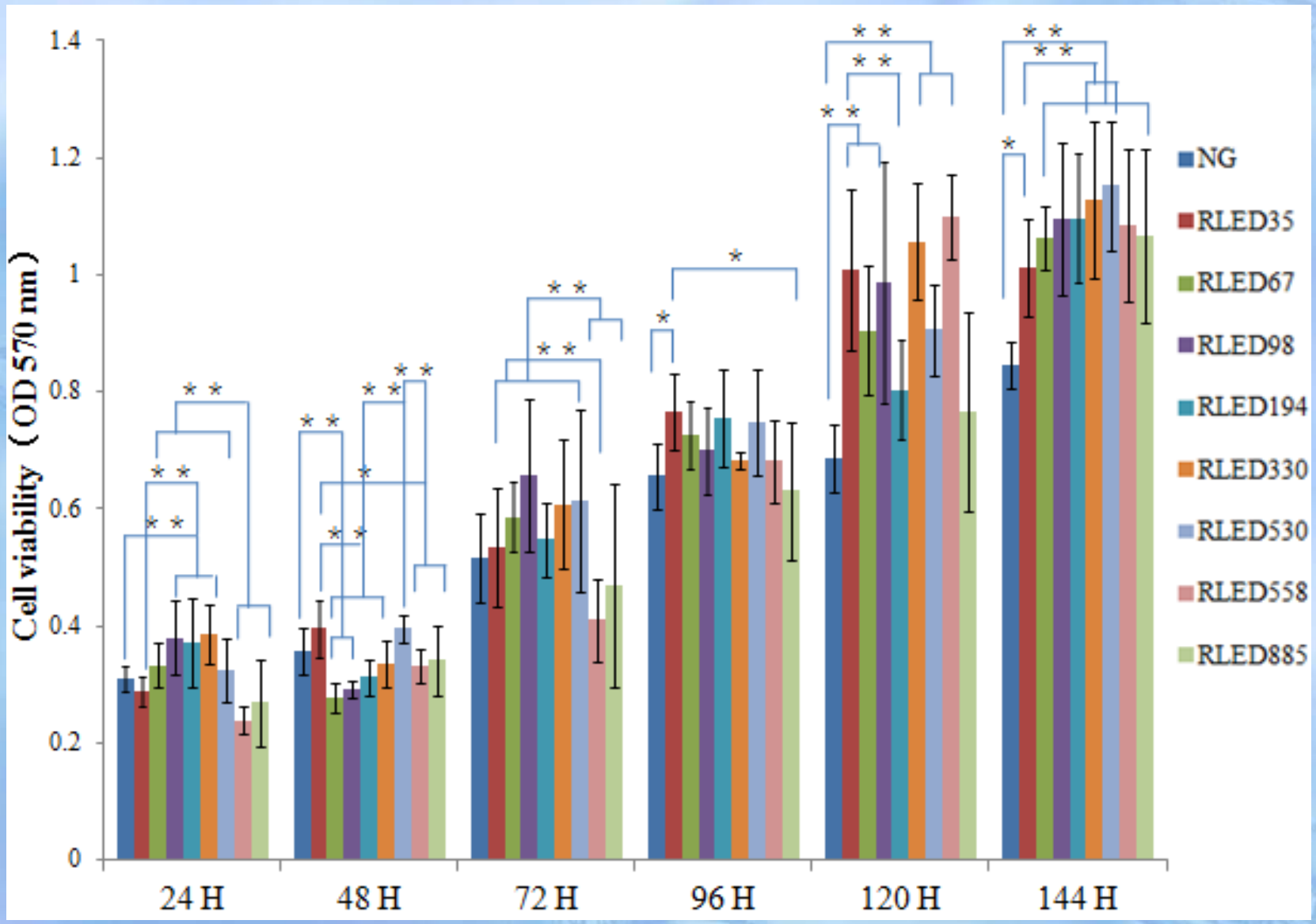
eFSH: ehanced FSH

nFSH: non-modulated FSH

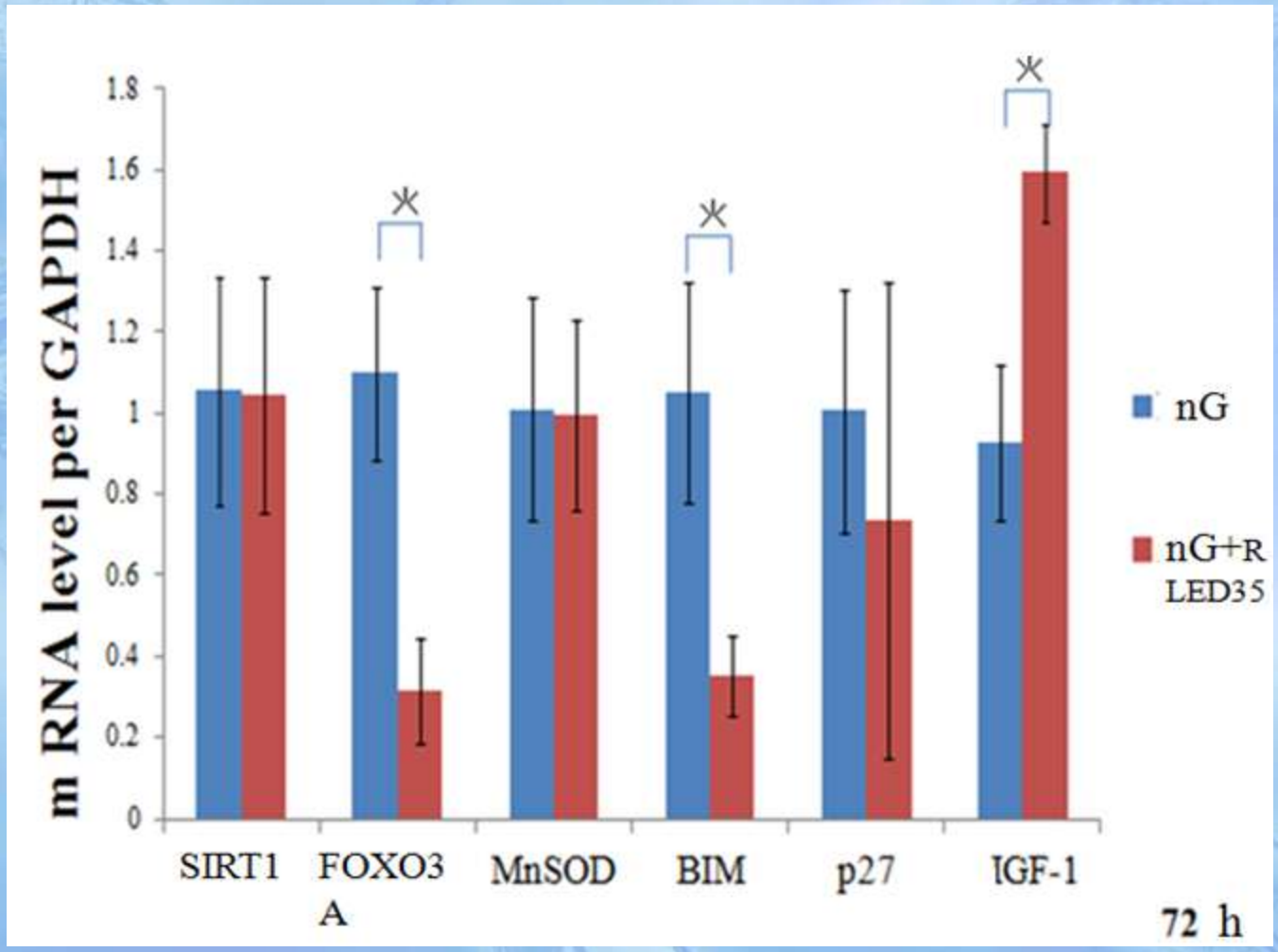
iFSH: inhibited FSH

pFSH: promoted FSH

iPBM on PlSH in nG

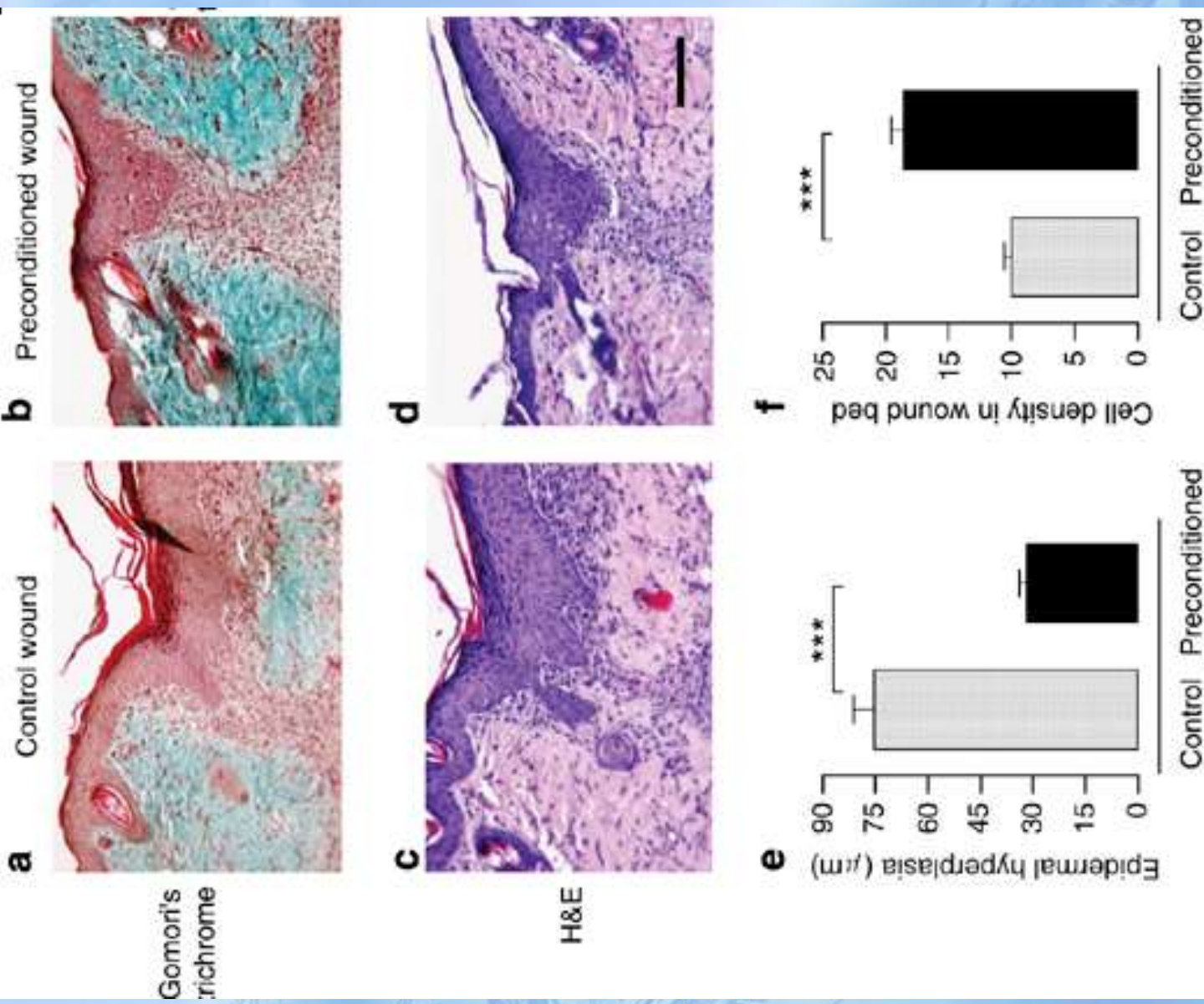


Redundancy mediated iPBM



The FNSH is differentiation-specific homeostasis

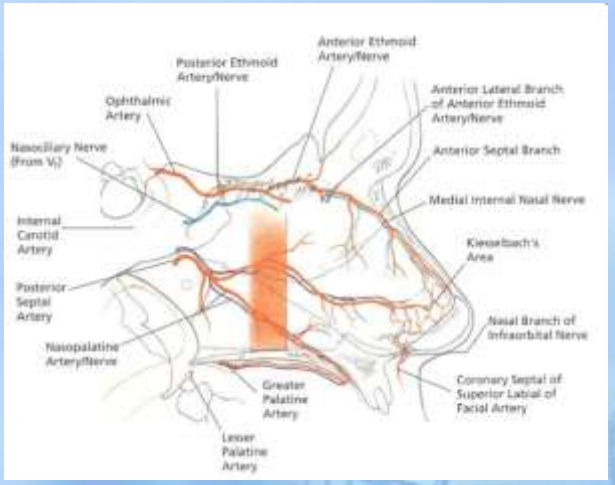
Collagen deposition and cellularity in preconditioned surgical wounds



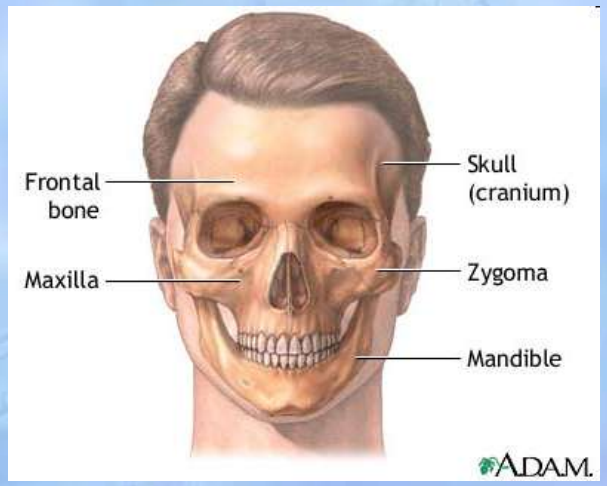
Wilmink GJ, Opalenik SR, Beckham JT, Abraham AA, Nanney LB, Mahadevan-Jansen A, Davidson JM, Jansen ED. 2009. Molecular imaging-assisted optimization of hsp70 expression during laser-induced thermal preconditioning for wound repair enhancement. J Invest Dermatol. 2009 Jan;129(1):205-16. http://www.ncbi.nlm.nih.gov/pubmed/18580963 free

ILIT Biomechanisms

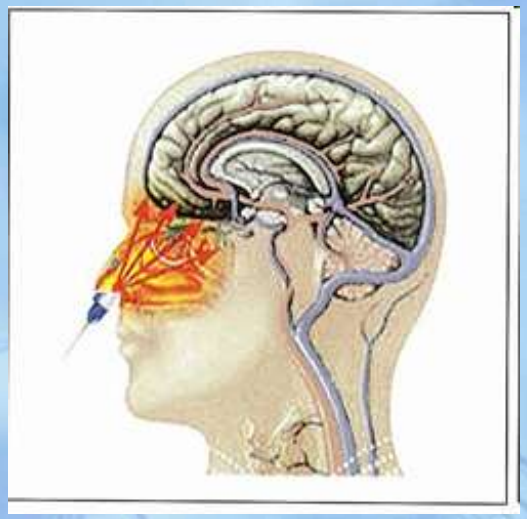
Pathways mediating ILIT

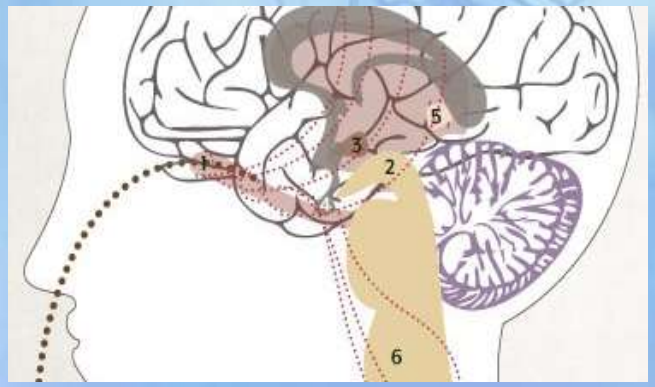


Blood

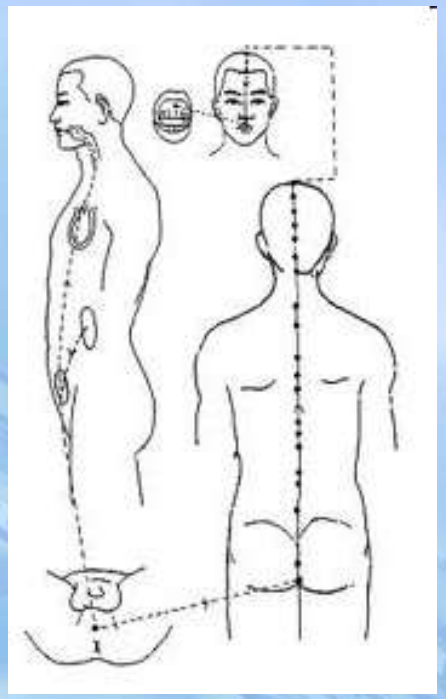


Bone

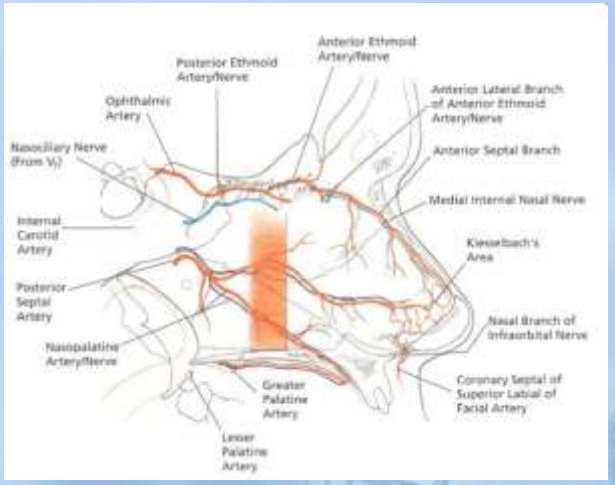




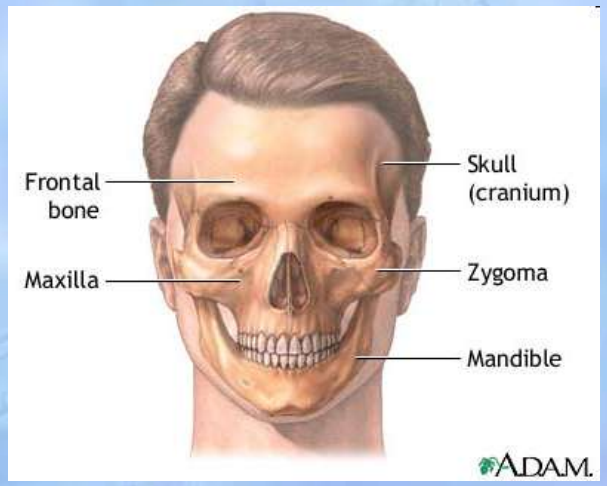
Olfactory, autonomic and central nervous system



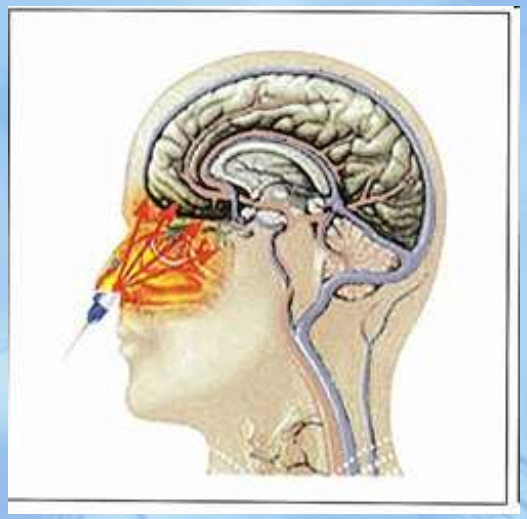
Acupoints and meridians

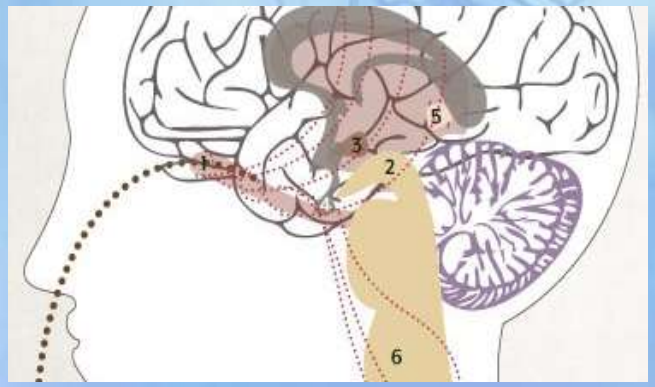


Blood

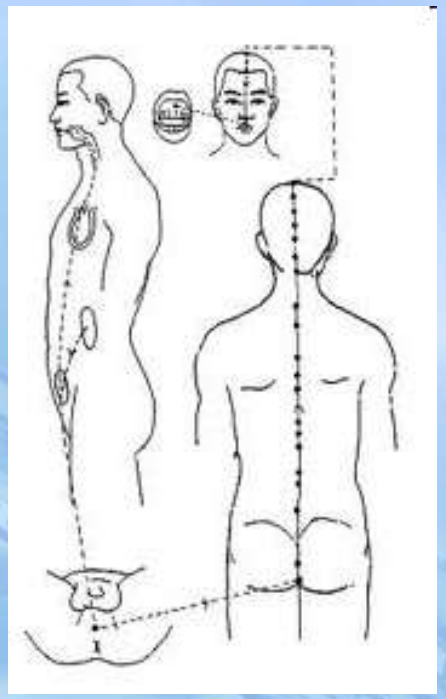


Bone



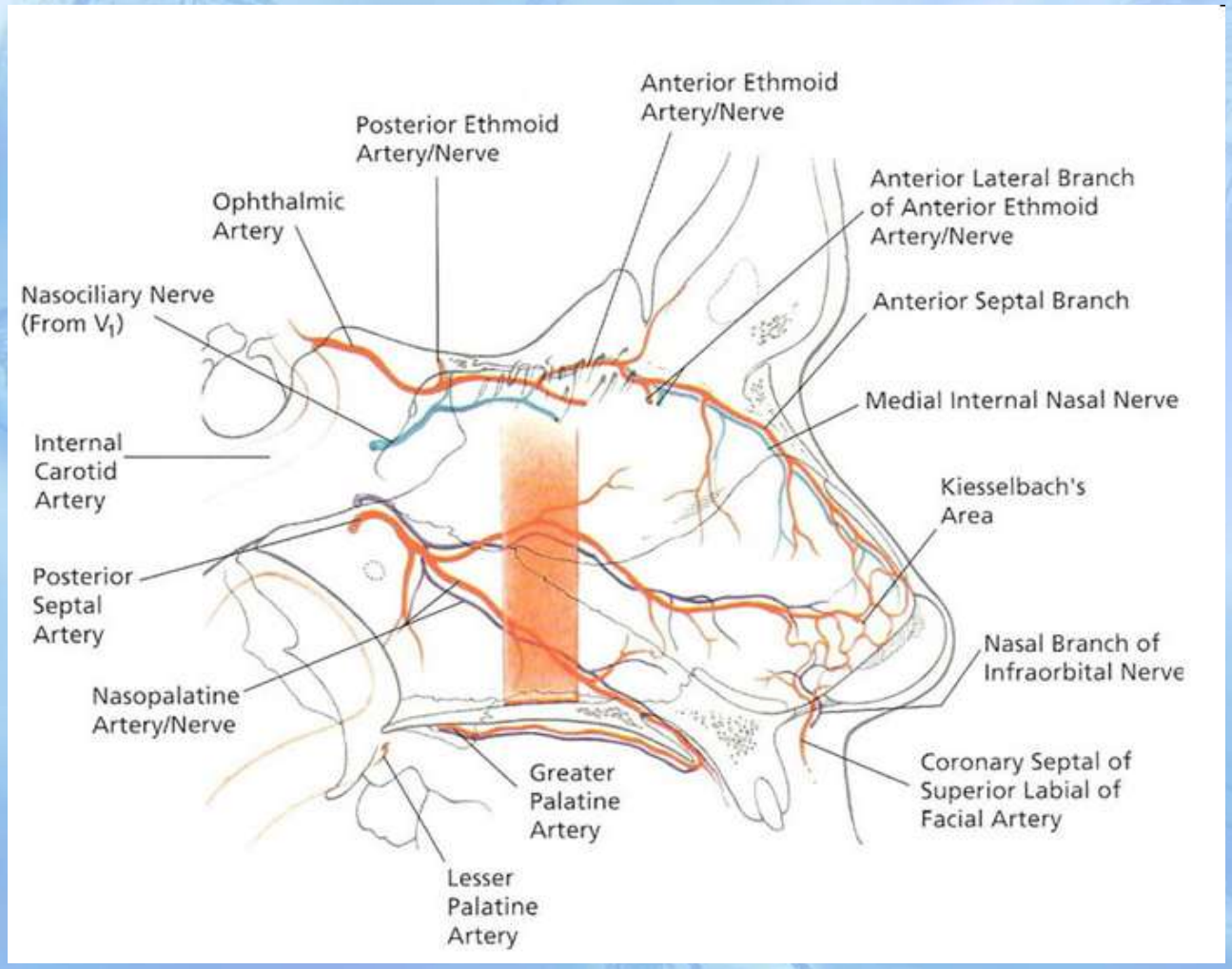


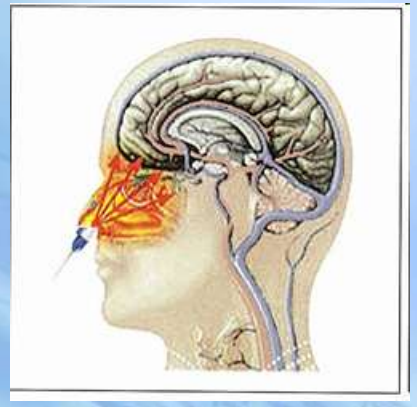
Olfactory, autonomic and central nervous system



Acupoints and meridians

ILIT Biomechanism: blood mediation





Thermal Texture Map before and after ILILT treatment

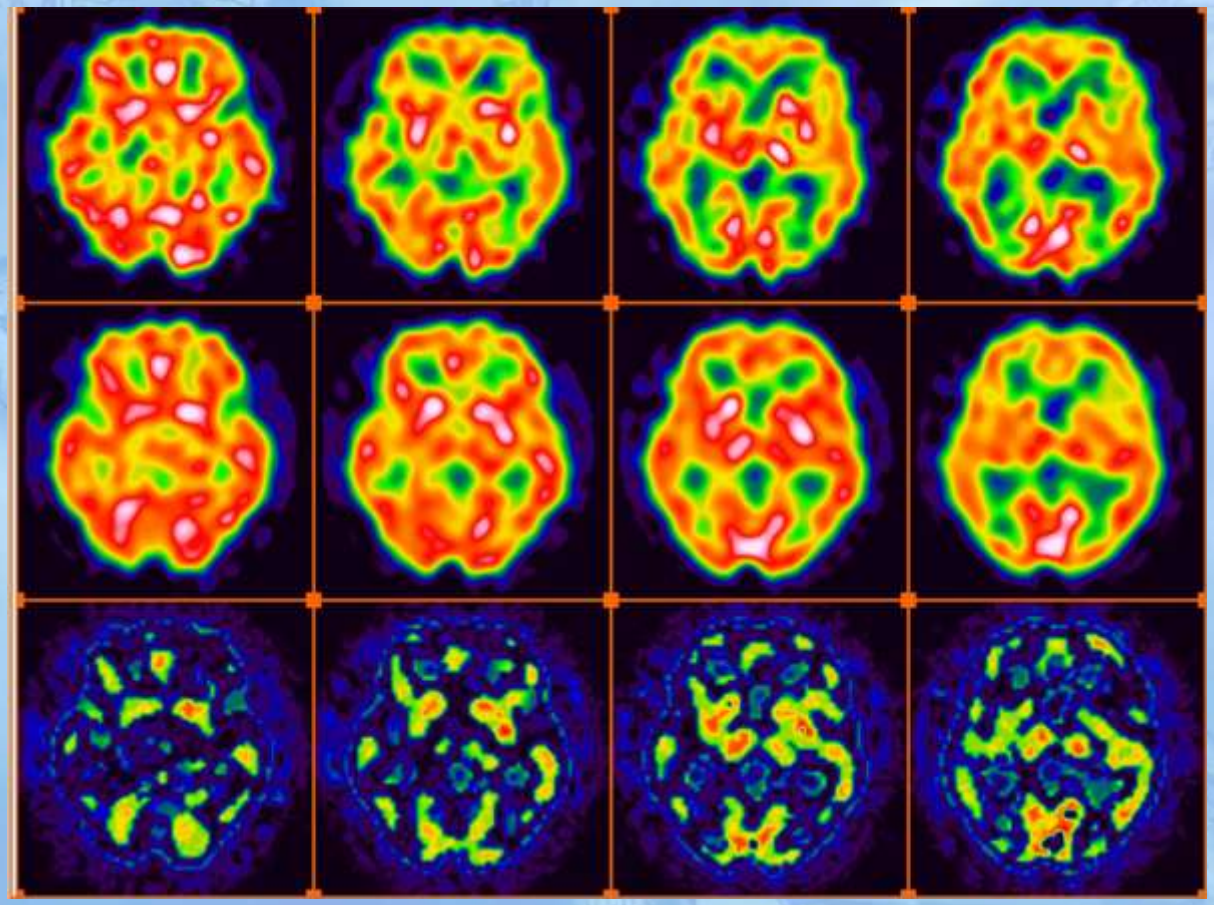
Before

After

From Prof. Liu SH

single photon emission computed tomography (SPECT)

Improved regional cerebral blood flow

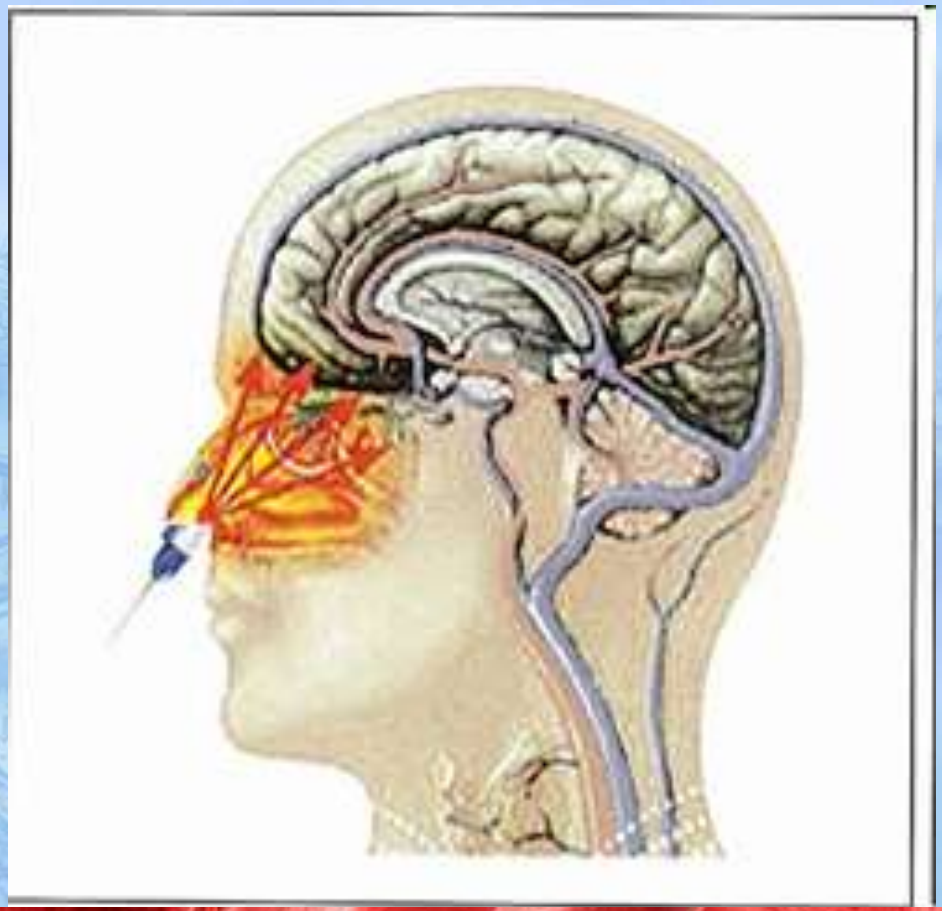


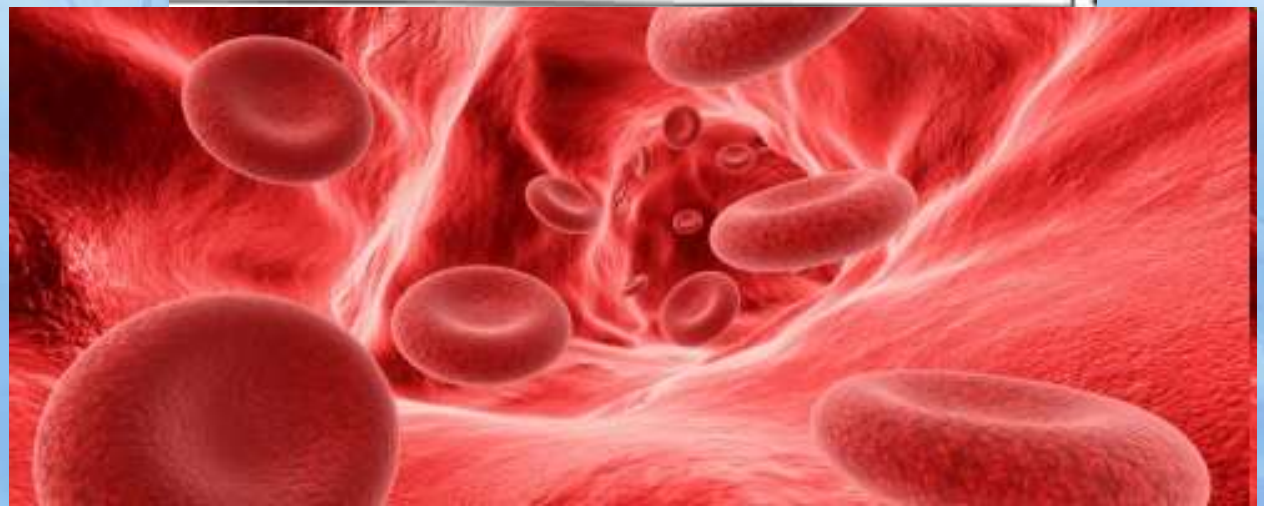
before

after

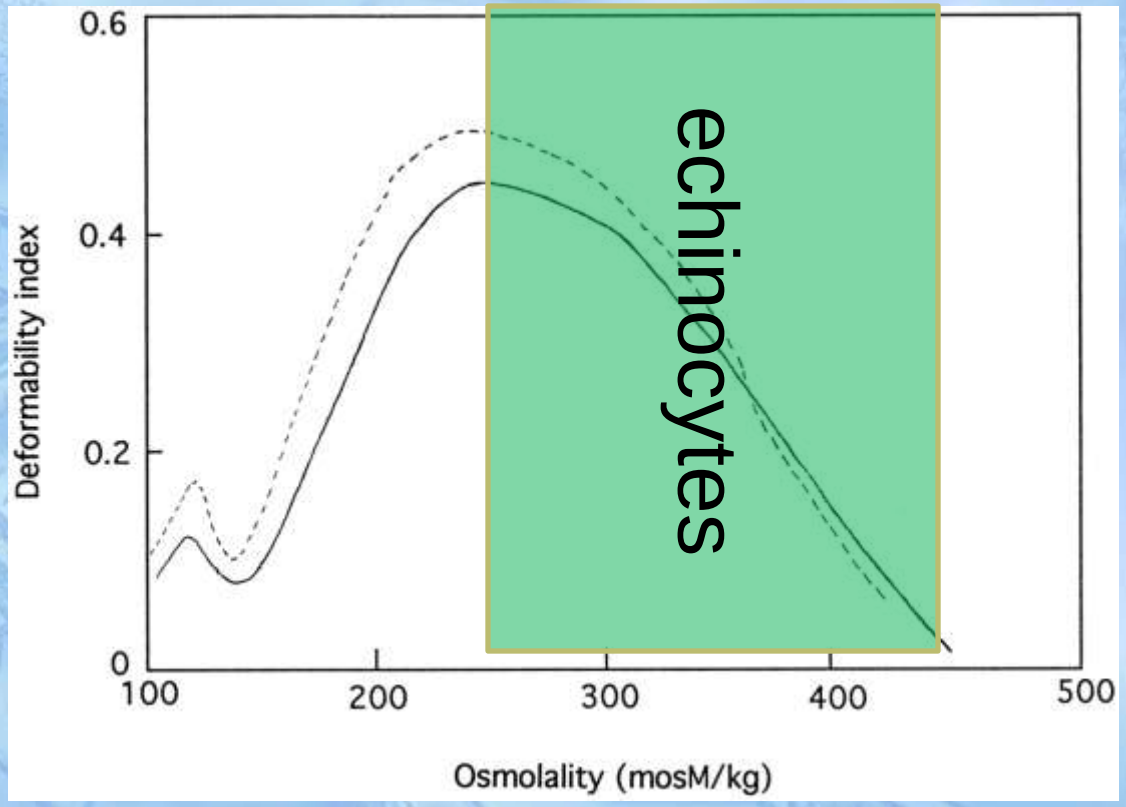
net increase

SPECT for old men before and after ILIT from Prof. Xiao XC





Osmotic deformability profiles of RBC



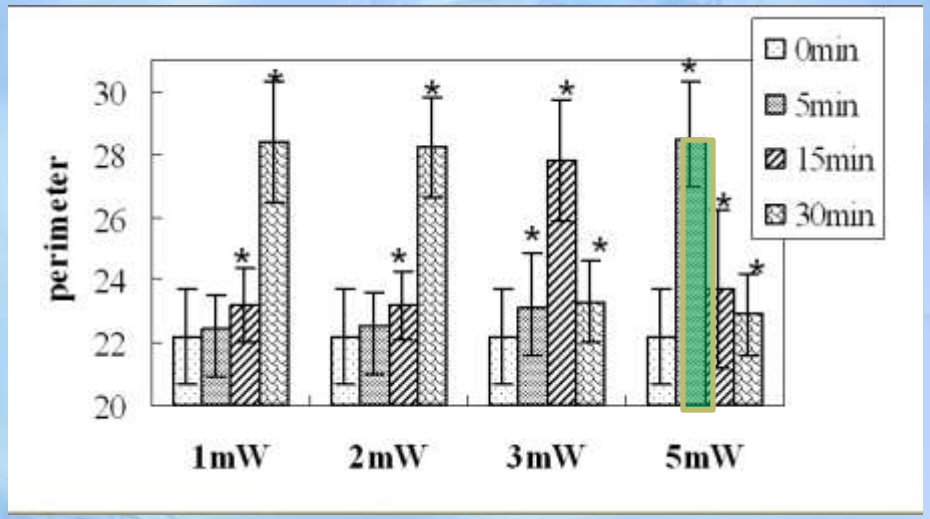
Peripheral red cells from an unrelated control individual (+/+, *dashed line*) and an individual homozygous for AQP1 deficiency (subject IIa, -/-, *solid line*) were analyzed by osmotic gradient ektacytometry, a technique that determines whole cell deformability while the osmolality of the suspending medium is continuously being changed. Consistent with a small reduction in membrane surface area and a small decrease in surface-to-volume ratio, the Colton-null red cells exhibit a minor reduction in maximum deformability (at 290 mosM/kg) and a small shift in the osmolality value at which red cells exhibit minimum deformability in hypotonic medium (140 mosM/kg).

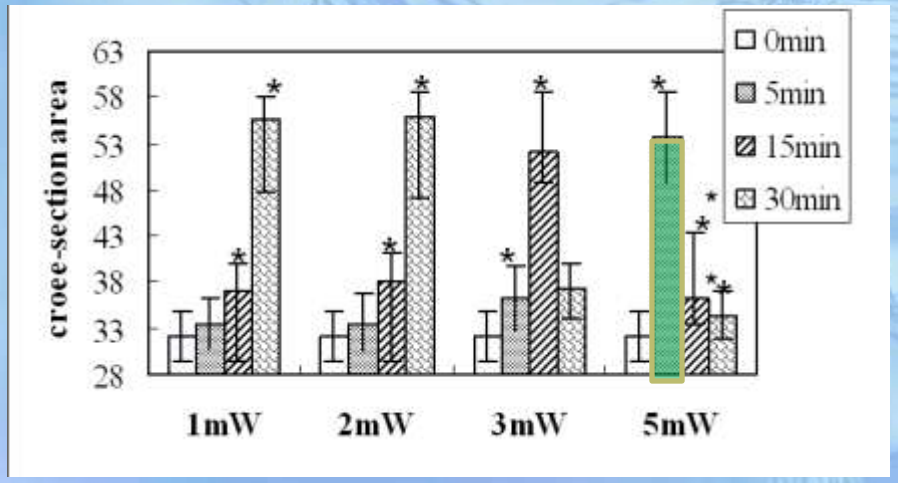
http://www.jbc.org/cgi/content/full/271/3/1309

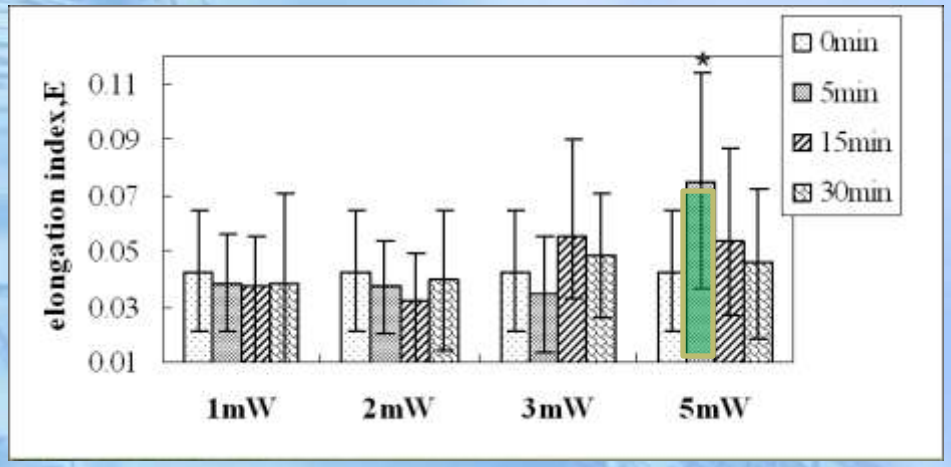
Mathai JC, Mori S, Smith BL, Preston GM, Mohandas N, Collins M, van Zijl PC, Zeidel ML, Agre P. 1996. Functional analysis of aquaporin-1 deficient red cells. The Colton-null phenotype. J Biol Chem. 1996 Jan 19;271(3):1309-13.

Dose relationship

- Low-intensity He-Ne laser irradiation (LHNL) was irradiated at 5 mW (4.4 mW/cm2) for 5 minutes.

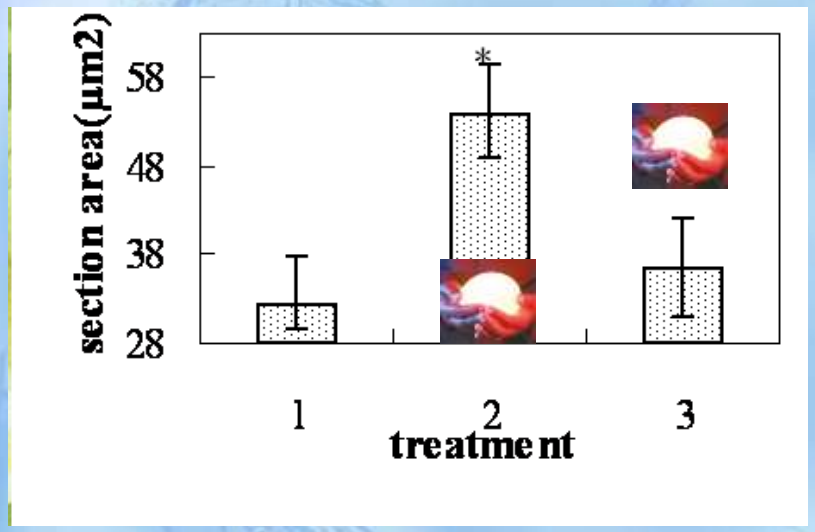


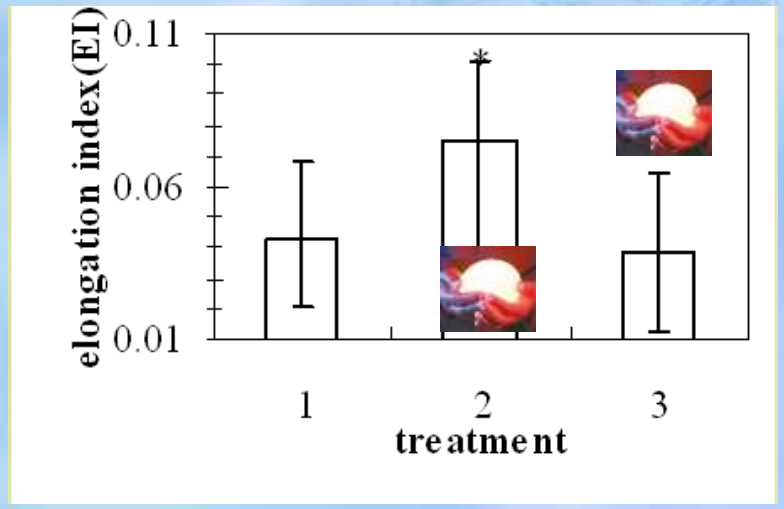




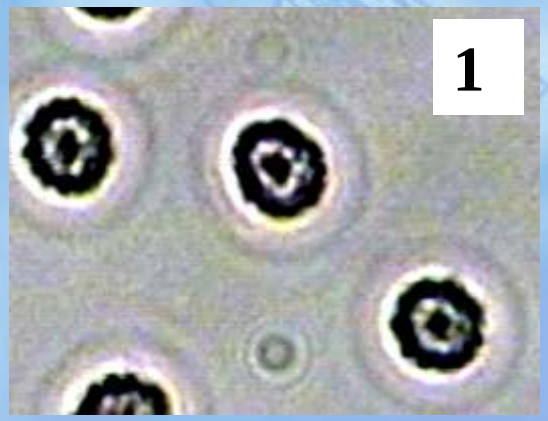
Luo GY, **Liu TCY**, Zhao YP, Liu SH. 2009. Studies on the deformability for human erythrocyte by modulation of low-intensity laser on aquaporin-1. Lasers Surg Med. 41(S21): 63.

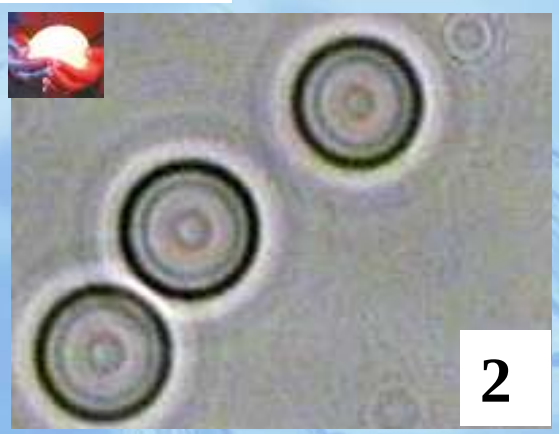
Aquaporin 1 mediated LPBM

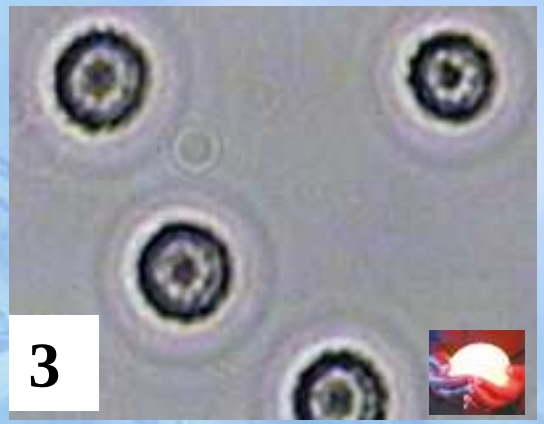




$HgCl_2$ is an inhibitor of **aquaporin 1**







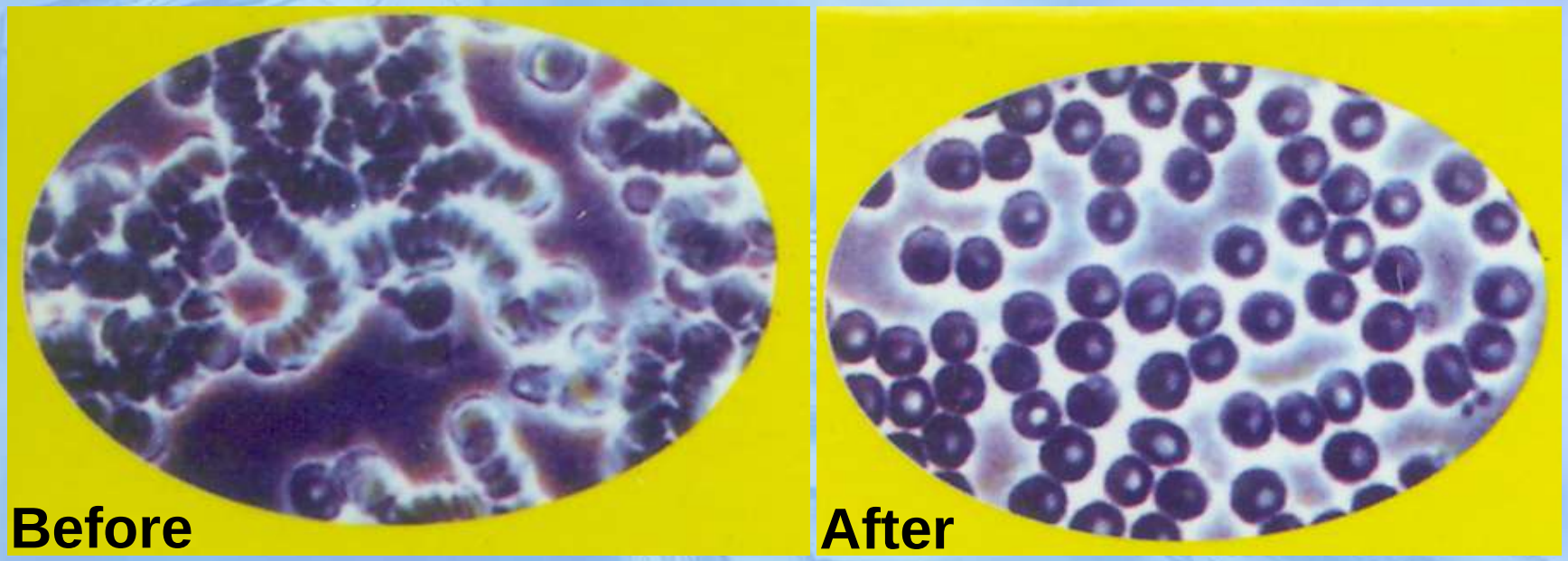
1 echinocytes， 2 LIL， 3 $HgCl_2$+LIL

Volunteer Subjects

- Coronary Heart Disease (CHD) was diagnosed on electrocardiogram and coronary angiography,
- Cerebral Infarction (CI) was diagnosed on coronal CT appearance.

Group	Patients (n)	Gender		Age (years)	CHD (n)	CI (n)	CHD&CI(n)
		Male	Female				
Treatment Group	60	34	26	76.6±7.81	21	20	19
Control Group	30	15	15	75.5±9.52	13	14	3
t Value		0.358		0.561		5.157	
P		>0.05		>0.05		>0.05	

Rehabilitation of dPBM

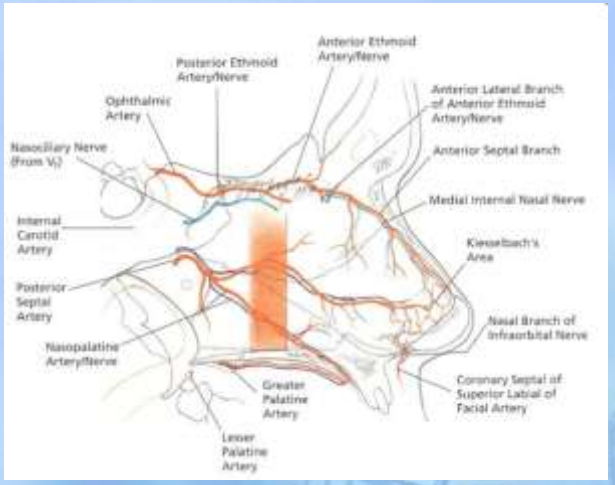


Blood Corpuscle Examination

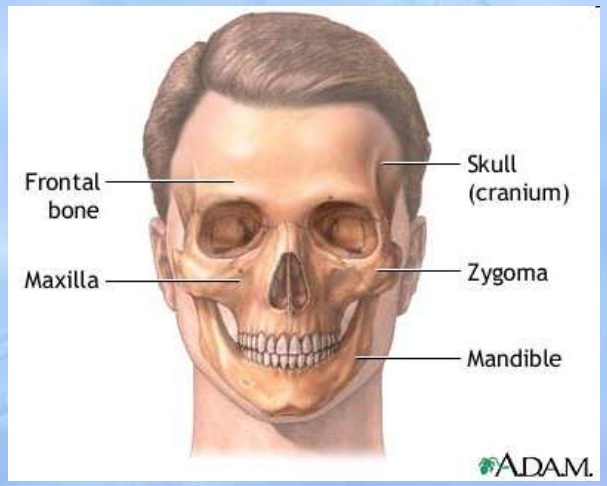
Blood Viscosity Index (mean ± SEM)

BV	Treatment Group(n)		Verified Statistics		Control Group(n)		Verified Statistics	
	Before	After	t	P	Before	After	t	P
BV(l)	8.34±1.91	8.15±1.91	0.545	>0.05	6.54±1.75	7.87±1.99	2.735	<0.05
BV(h)	4.23±0.82	3.94±0.74	2.020	<0.05	3.56±0.65	4.02±1.64	1.428	>0.05
PV	1.23±0.02	1.14±0.22	2.233	<0.05	1.23±0.18	1.23±0.01	--	--
RBCP	39.88±7.72	41.66±4.79	1.526	>0.05	37.92±6.04	38.55±6.52	0.388	>0.05
RV(l)	17.35±4.03	15.24±2.82	3.323	<0.01	14.09±3.26	16.88±4.04	2.944	<0.01
RV(h)	6.99±0.75	6.63±0.55	2.120	<0.05	6.27±1.17	7.21±1.54	2.662	<0.05
RBCA	2.15±0.41	1.95±0.24	3.263	<0.01	1.77±0.35	1.92±0.23	1.961	>0.05

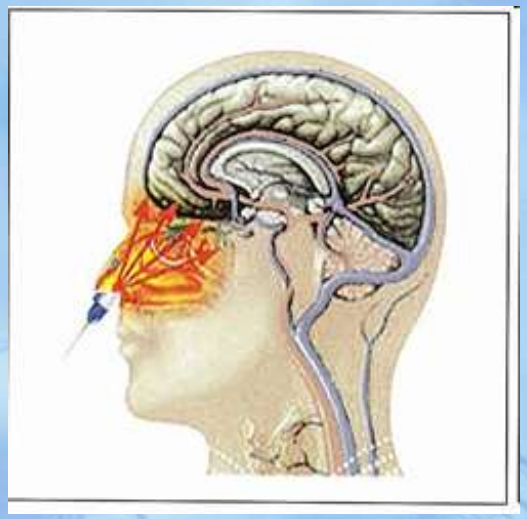
BV: Blood Viscosity, l: low shear h: high shear,
PV: Plasma Viscosity, RBCP: Red Blood Cell Pressure, RV: Redox Viscosity,
RBCA: Red Blood Cell Aggregation

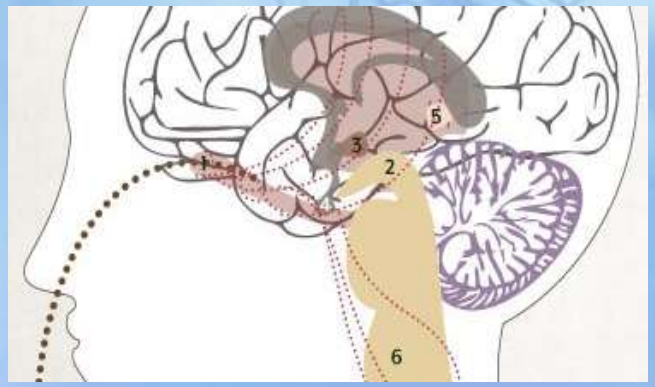


Blood

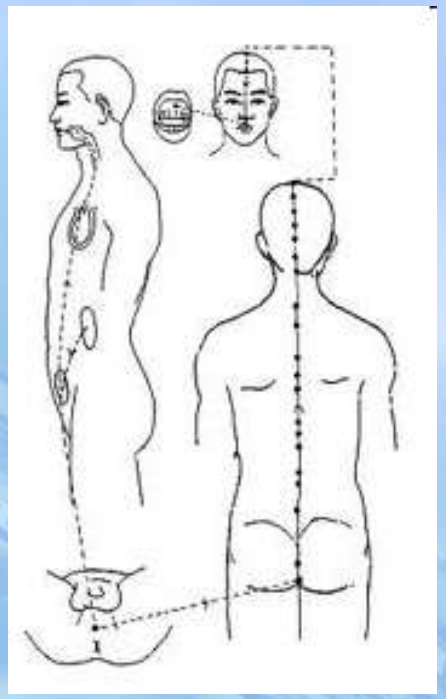


Bone



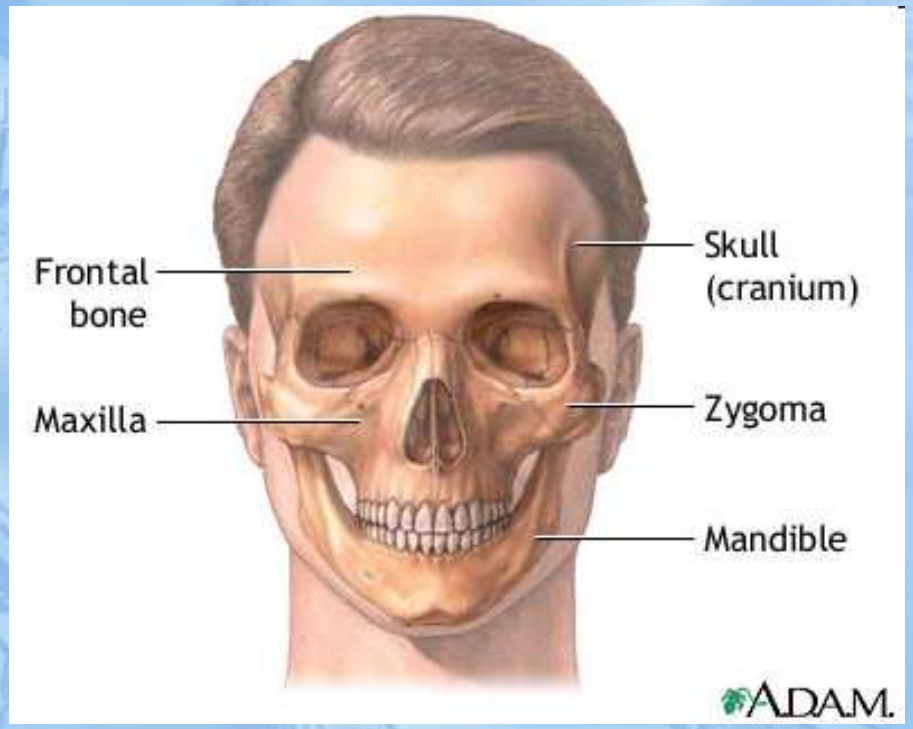


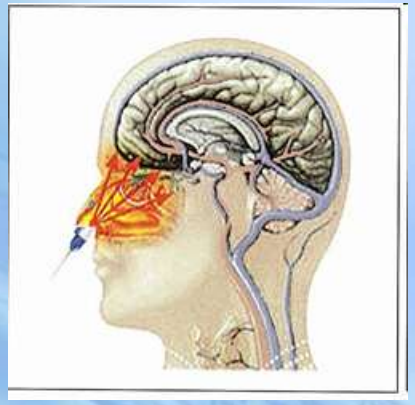
Olfactory, autonomic and central nervous system



Acupoints and meridians

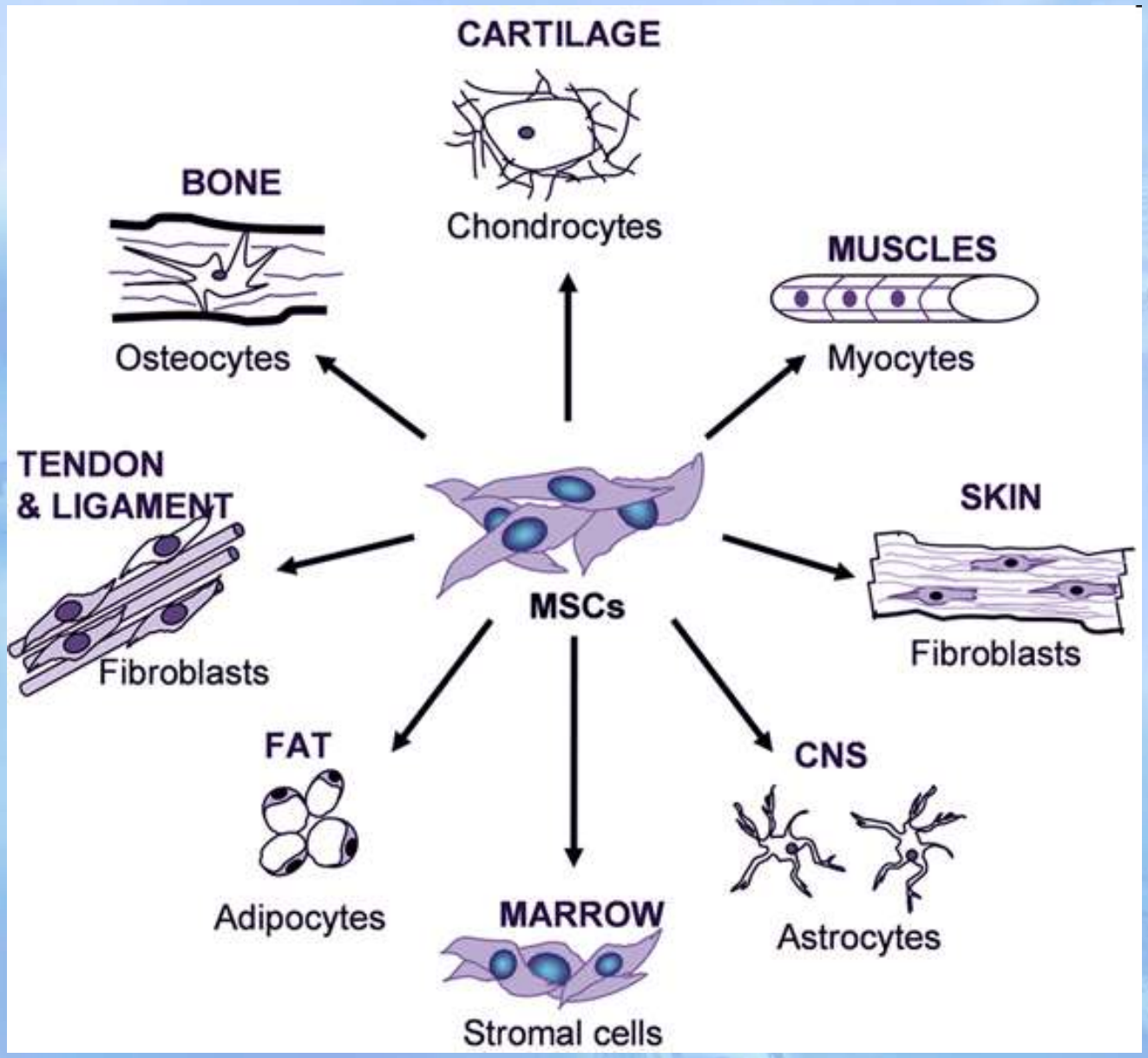
ILIT Biomechanism: bone mediation





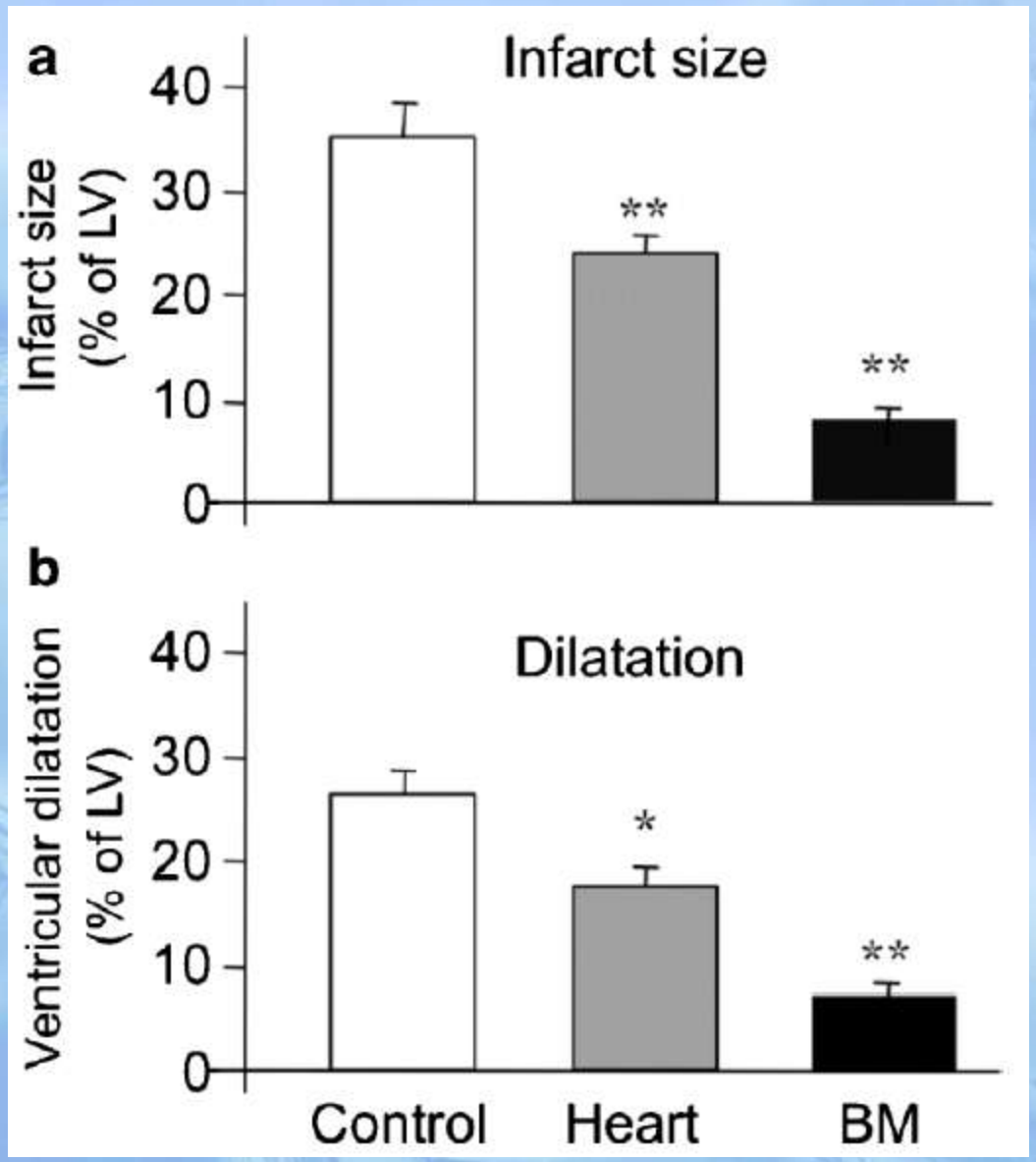
Mesenchymal stem cells/marrow stromal cells (MSCs) mediated ILIT

Mesenchymal stem cells (MSCs)



http://www.xpand-biotech.com/technology_bioreactor.htm

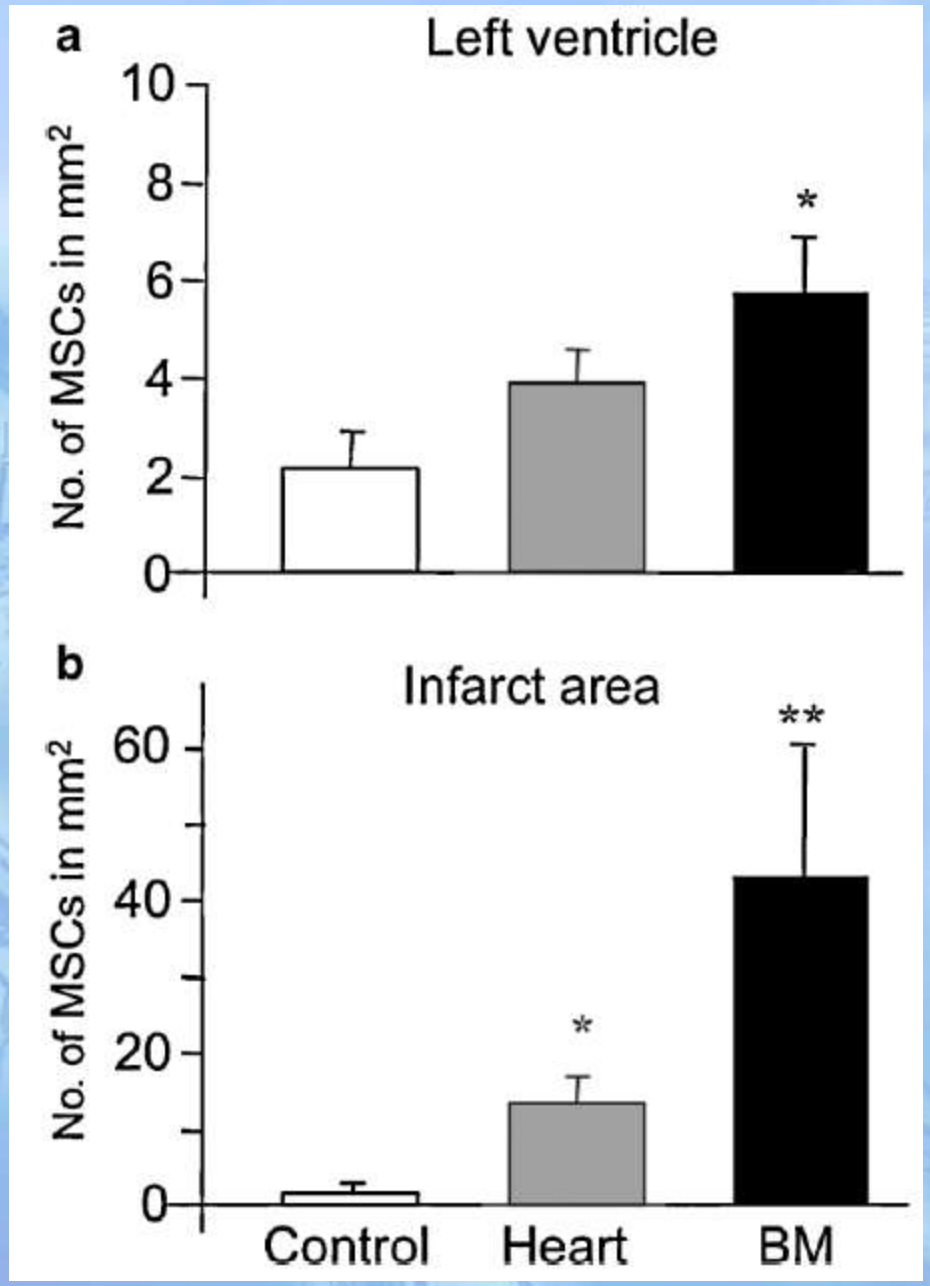
Heart or bone marrow



Effect of LIL on infarct size (a) and ventricular dilatation (b) in infarcted control non-laser-treated (open column), LIL applied to the heart (dashed column), and LIL applied to the BM (solid column) in rats. Rats were sacrificed 3 weeks post-MI and LIL was applied 20 minutes post-MI. *P < 0.05 and **P < 0.01.

Tuby H, Maltz L, Oron U. 2011. Induction of autologous mesenchymal stem cells in the bone marrow by low-level laser therapy has profound beneficial effects on the infarcted rat heart. Lasers Surg Med. 2011 Jul;43(5):401-9. http://www.ncbi.nlm.nih.gov/pubmed/21674545

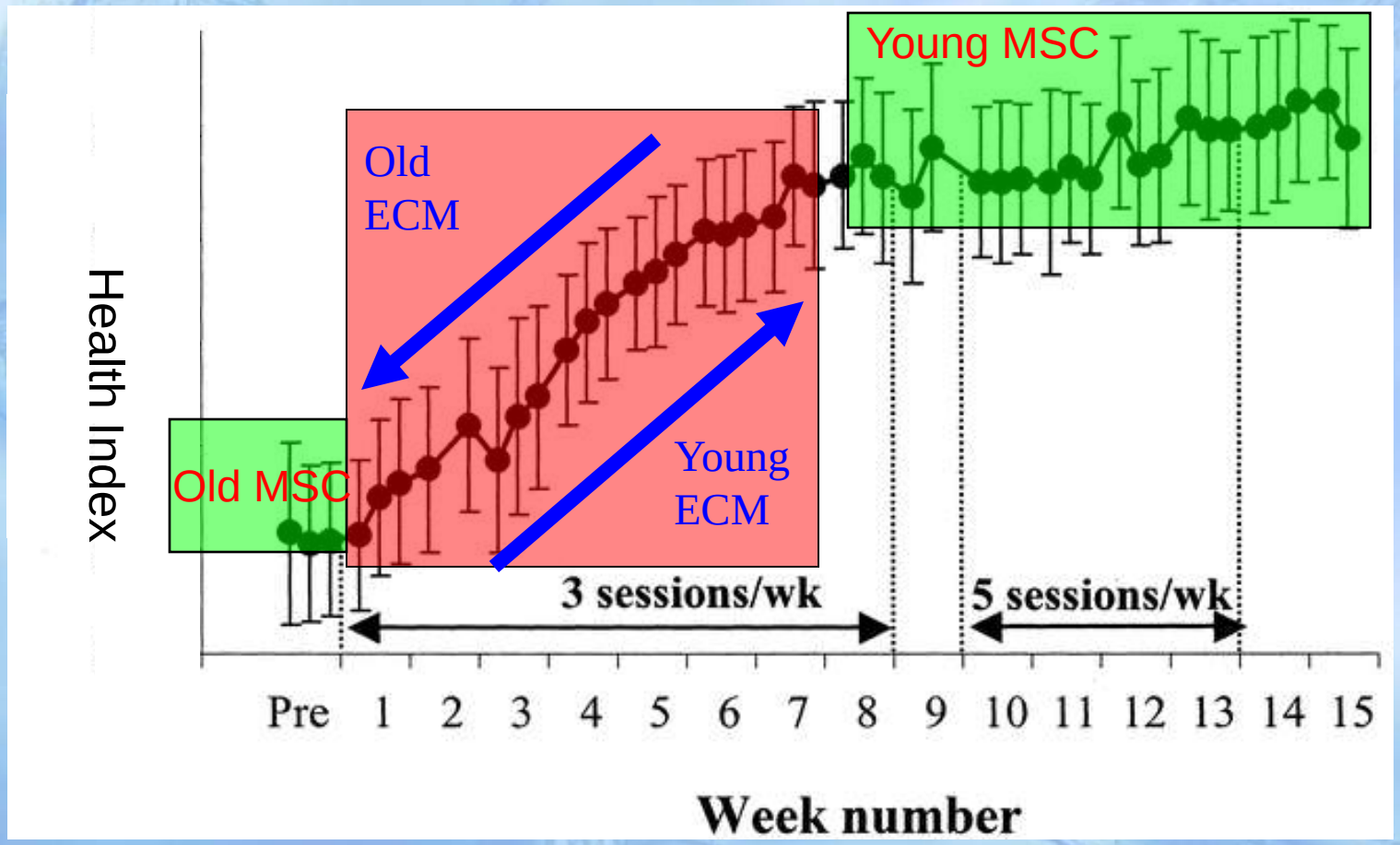
Heart or bone marrow



Effect of LIL application on the density of c-kitt in the entire left ventricle (a) or infarcted area (b) in control non-laser-treated (open column), LIL applied to the heart (dashed column), or LIL applied to the BM (solid column) in rats. *P < 0.05 and **P < 0.01.

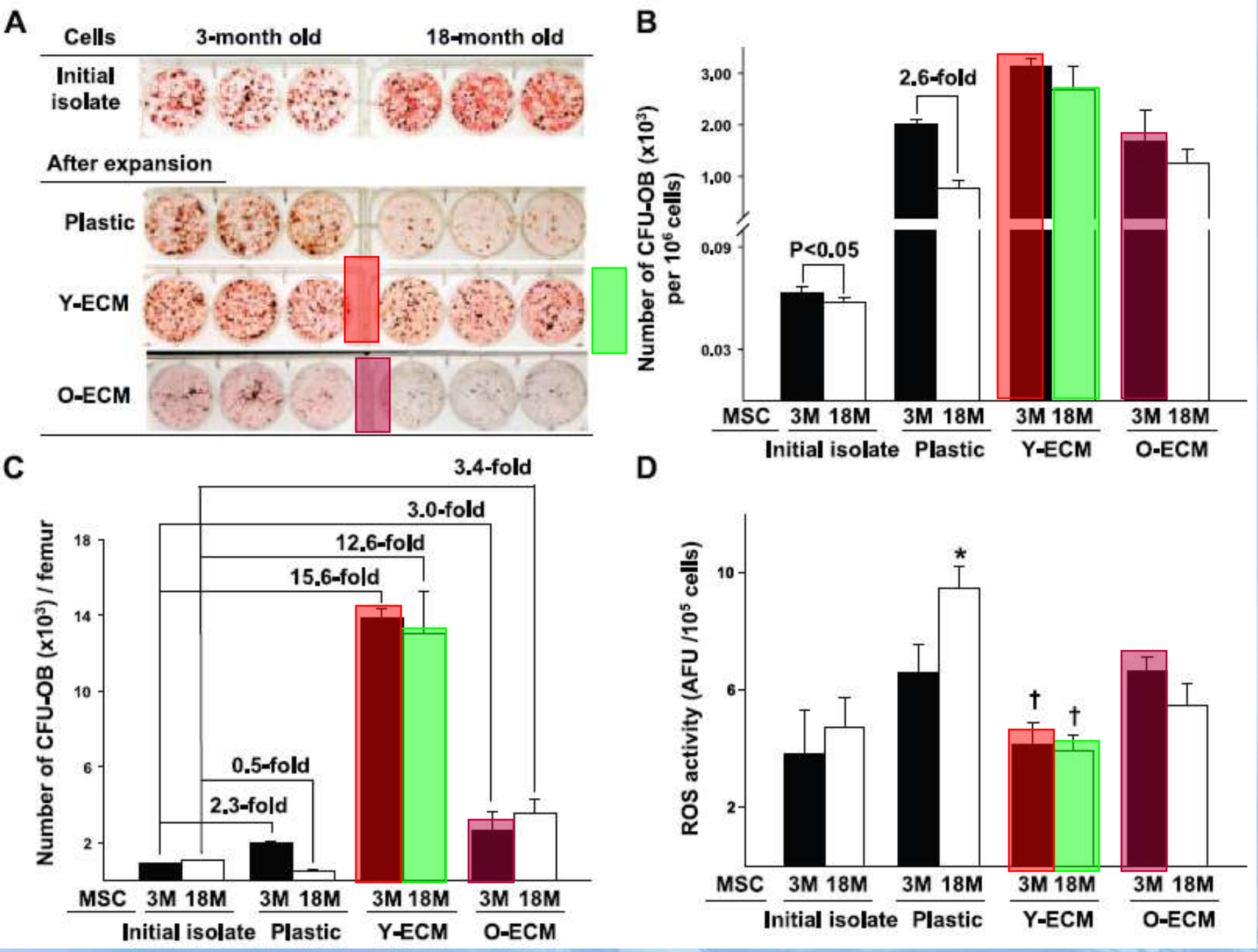
Tuby H, Maltz L, Oron U. 2011. Induction of autologous mesenchymal stem cells in the bone marrow by low-level laser therapy has profound beneficial effects on the infarcted rat heart. Lasers Surg Med. 2011 Jul;43(5):401-9. http://www.ncbi.nlm.nih.gov/pubmed/21674545

Extracellular matrix(ECM)

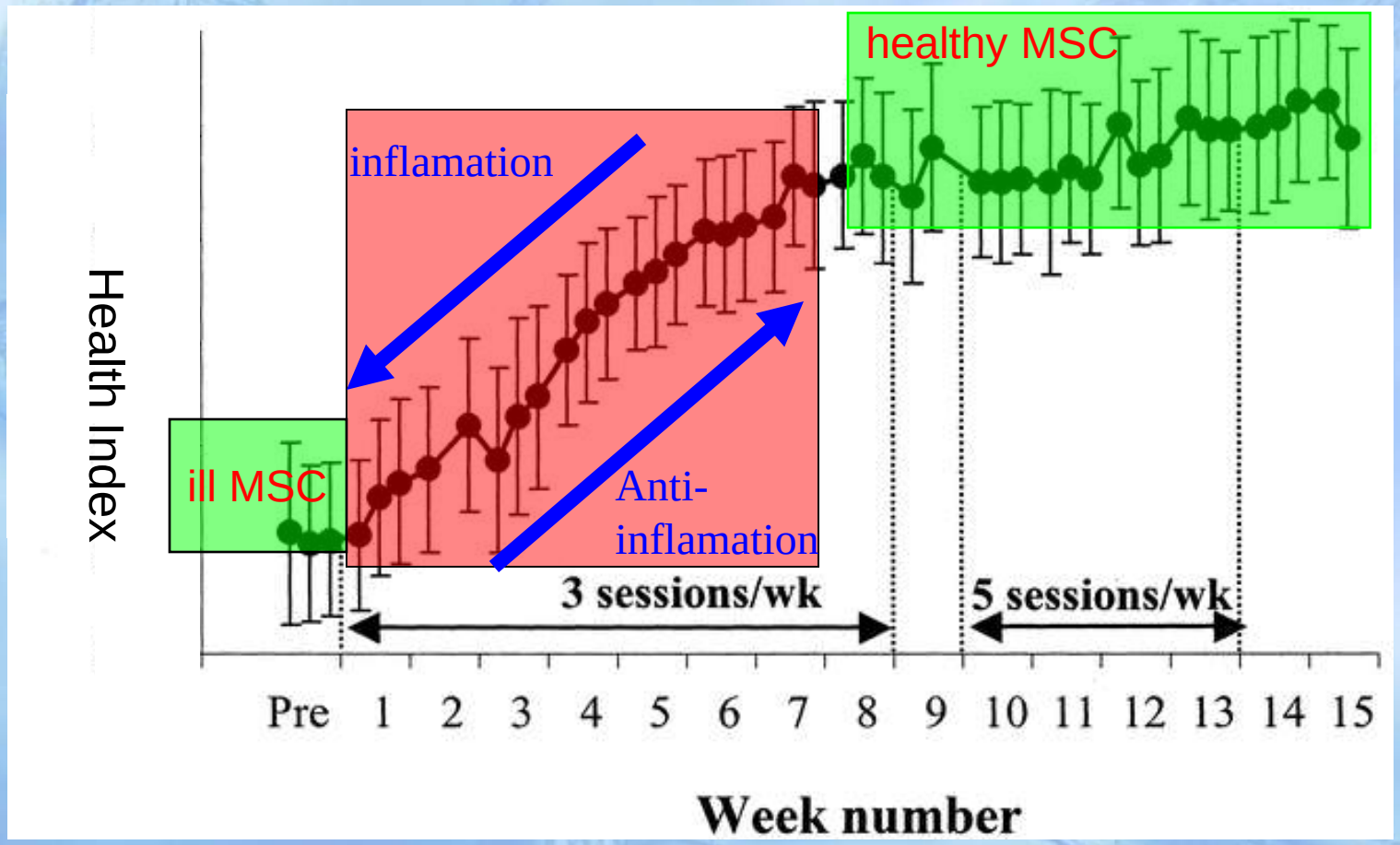


Sun Y, Li W, Lu Z, Chen R, Ling J, Ran Q, Jilka RL, Chen XD. 2011. Rescuing replication and osteogenesis of aged **mesenchymal stem** cells by exposure to a **young** extracellular matrix. FASEB J. 2011 May;25(5):1474-85. http://www.ncbi.nlm.nih.gov/pubmed/21248241

Busso T. Variable Dose-Response Relationship between Exercise Training and Performance. ***Med. Sci. Sports Exerc.***, Vol. 35, No. 7, pp. 1188-1195, 2003.


A
Cells
3-month old
18-month old
Initial isolate
After expansion
Plastic
Y-ECM
O-ECM
B
Number of CFU-OB (x10³) per 10⁶ cells)
3.00
2.00
1.00
0.09
0.03
P<0.05
2.6-fold
MSC
3M 18M
3M 18M
3M 18M
3M 18M
Initial isolate
Plastic
Y-ECM
O-ECM
C
Number of CFU-OB (x10³) / femur
18
14
10
6
2
3.4-fold
3.0-fold
12.6-fold
15.6-fold
0.5-fold
2.3-fold
MSC
3M 18M
3M 18M
3M 18M
3M 18M
Initial isolate
Plastic
Y-ECM
O-ECM
D
ROS activity (AFU /10⁵ cells)
10
6
2
*
†
†
MSC
3M 18M
3M 18M
3M 18M
3M 18M
Initial isolate
Plastic
Y-ECM
O-ECM

Extracellular matrix (ECM)



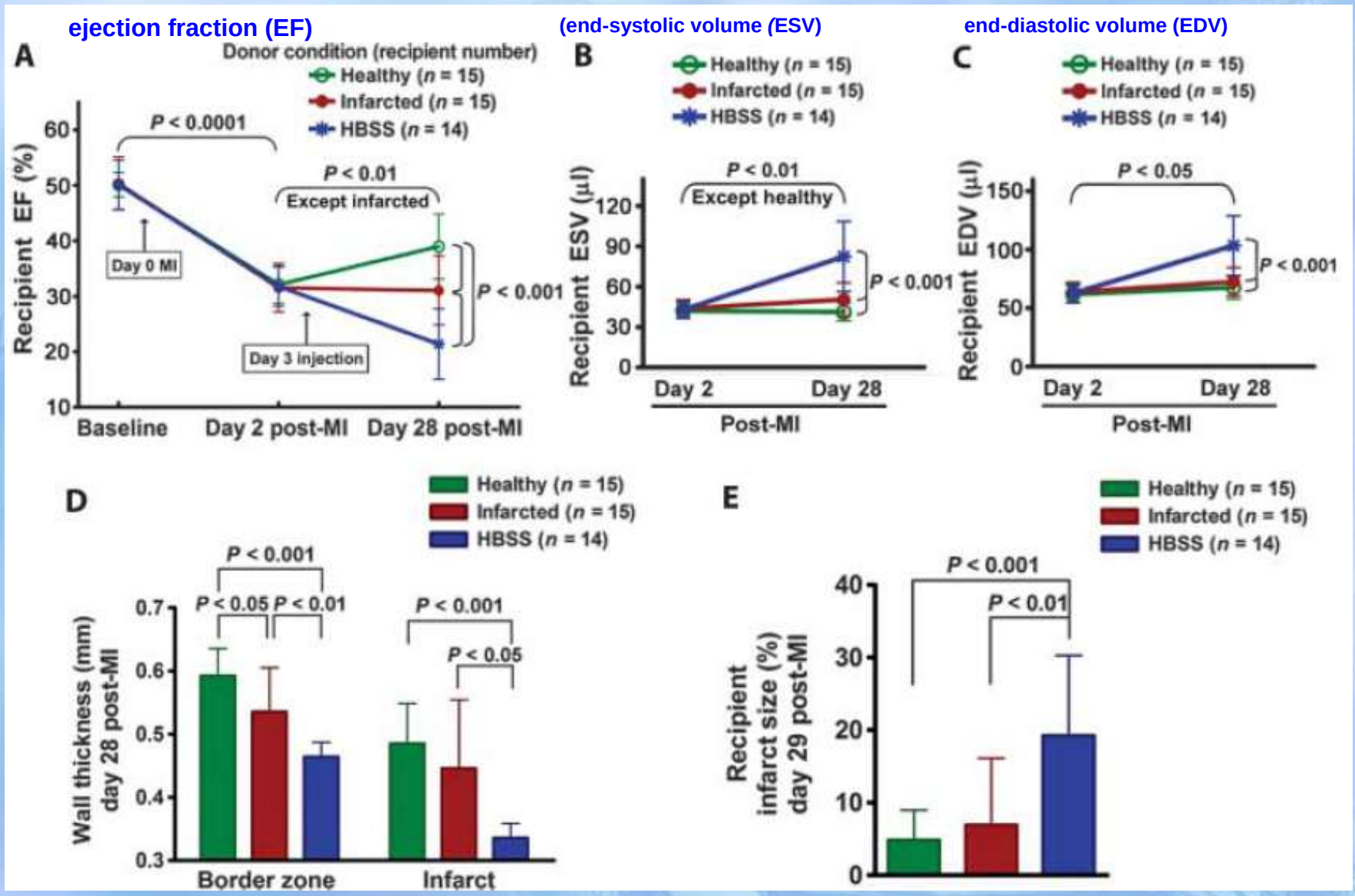
Wang X, Takagawa J, Lam VC, Haddad DJ, Tobler DL, Mok PY, Zhang Y, Clifford BT, Pinnamaneni K, Saini SA, Su R, Bartel MJ, Sievers RE, Carbone L, Kogan S, Yeghiazarians Y, Hermiston M, Springer ML. 2011. Donor myocardial infarction impairs the therapeutic potential of **bone marrow** cells by an interleukin-1-mediated inflammatory response. Sci Transl Med. 2011 Sep 14;3(100):100ra90. http://www.ncbi.nlm.nih.gov/pubmed/21918107

Busso T. Variable Dose-Response Relationship between Exercise Training and Performance. ***Med. Sci. Sports Exerc.***, Vol. 35, No. 7, pp. 1188-1195, 2003.

Wang X, Takagawa J, Lam VC, Haddad DJ, Tobler DL, Mok PY, Zhang Y, Clifford BT, Pinnamaneni K, Saini SA, Su R, Bartel MJ, Sievers RE, Carbone L, Kogan S, Yeghiazarians Y, Hermiston M, Springer ML. 2011. Donor myocardial infarction impairs the therapeutic potential of **bone marrow** cells by an interleukin-1-mediated inflammatory response. Sci Transl Med. 2011 Sep 14;3(100):100ra90. http://www.ncbi.nlm.nih.gov/pubmed/21918107

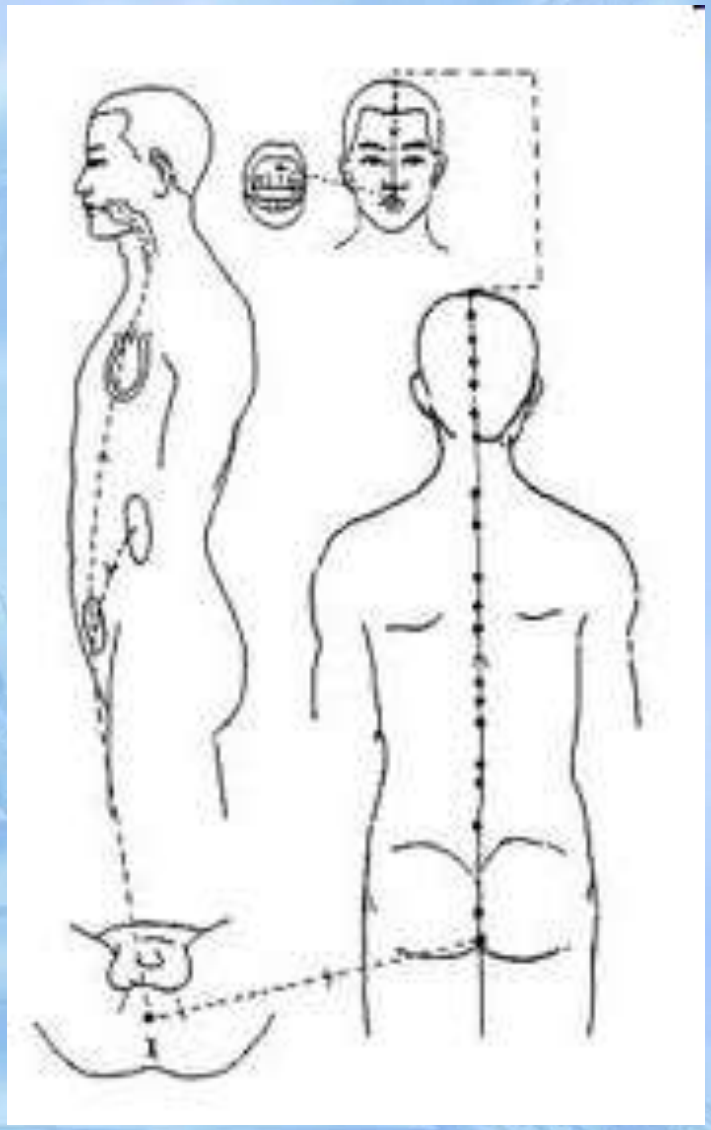
Donor Effects

ejection fraction (EF) **(end-systolic volume (ESV)** **end-diastolic volume (EDV)**



MSC-mediated ILIT mechanism

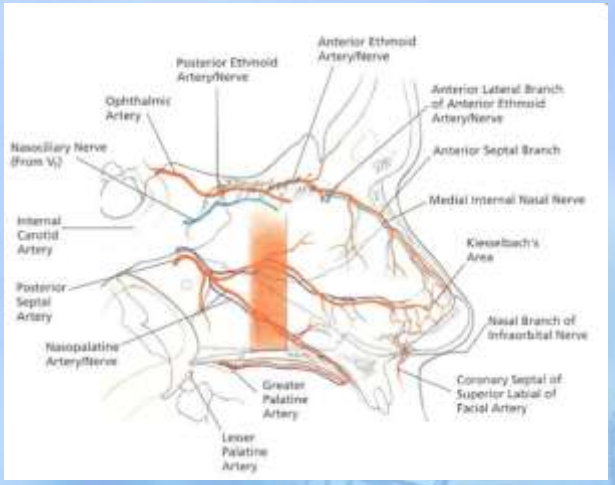
- Improved MSCs
  - Nasal bone
  - Du meridian
- Improved ECM
  - olfactory nerve (melatonin),
  - blood cells,
  - autonomic nervous system



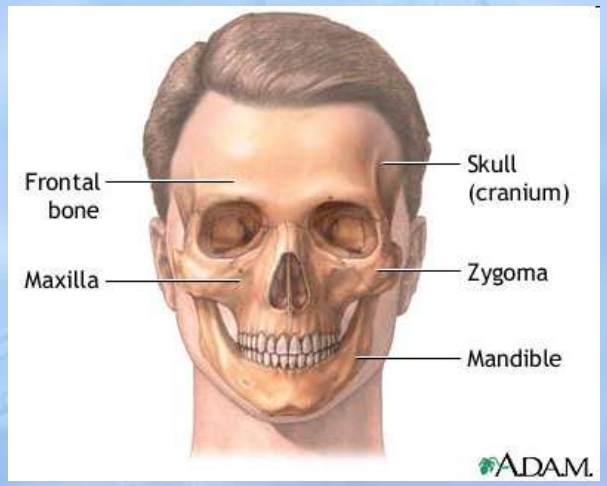
ILIT: intranasal light therapy

ILIT → MSCs →

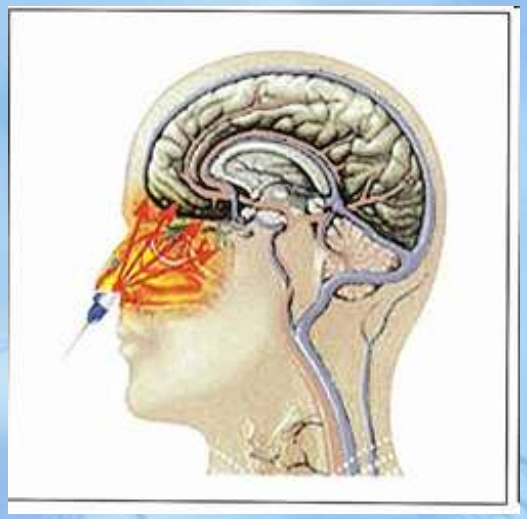
- myocardial infarction
- Carpal tunnel syndrome
- Epicondylitis
- Exercise-induced muscle damage
- Osteoarthritis
- Stroke (cerebral infarction, …)
- Wound

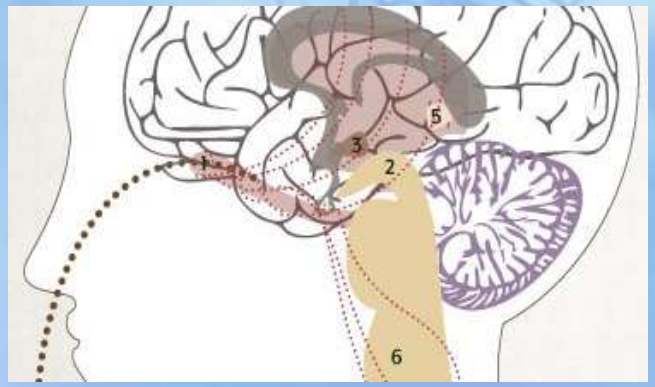


Blood

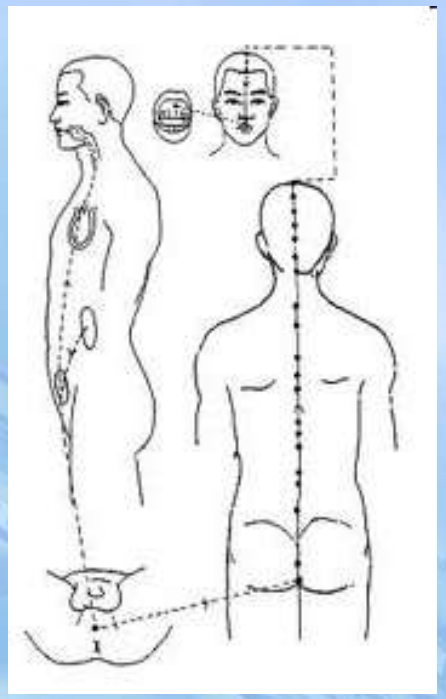


Bone

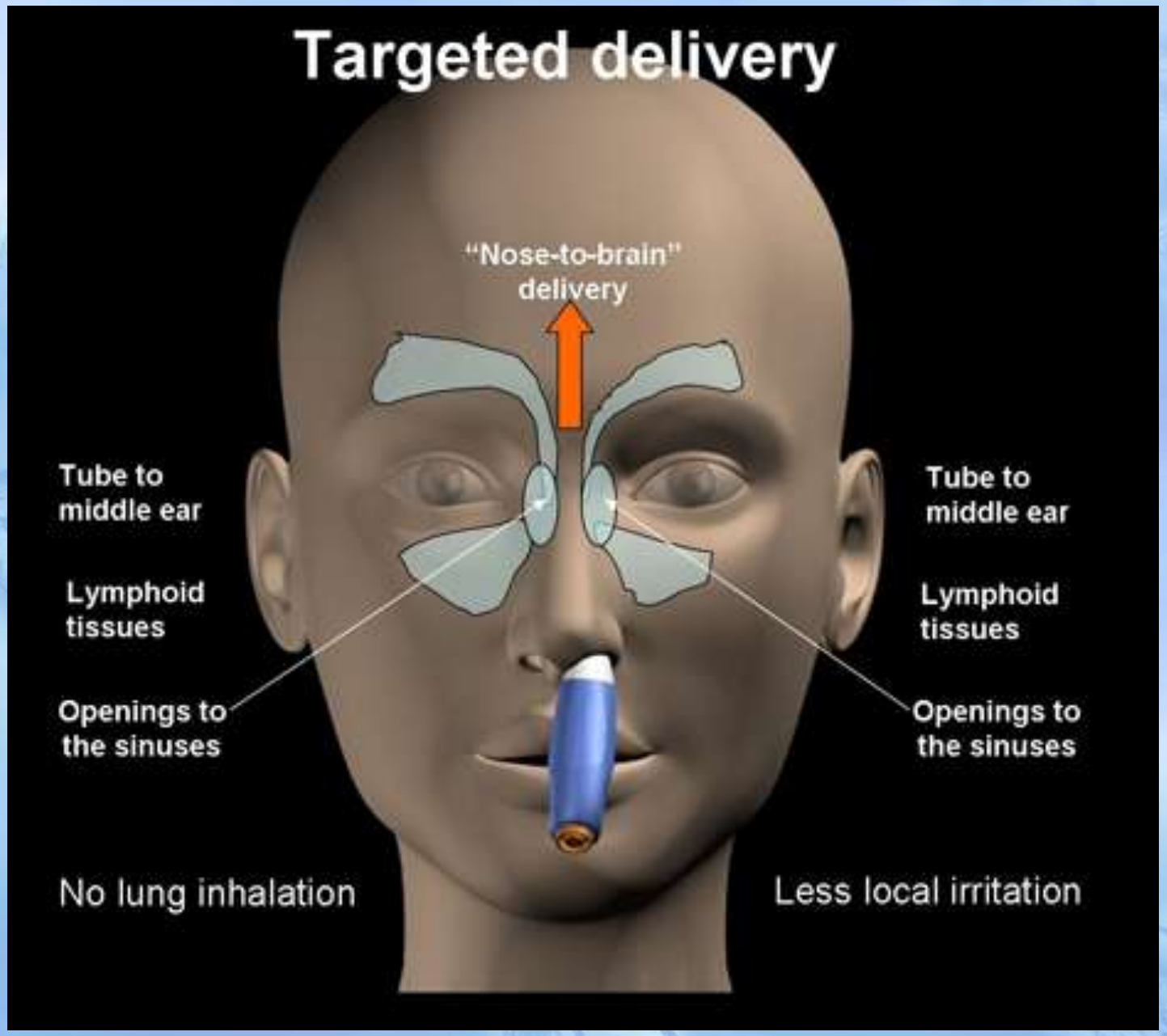




Olfactory, autonomic and central nervous system



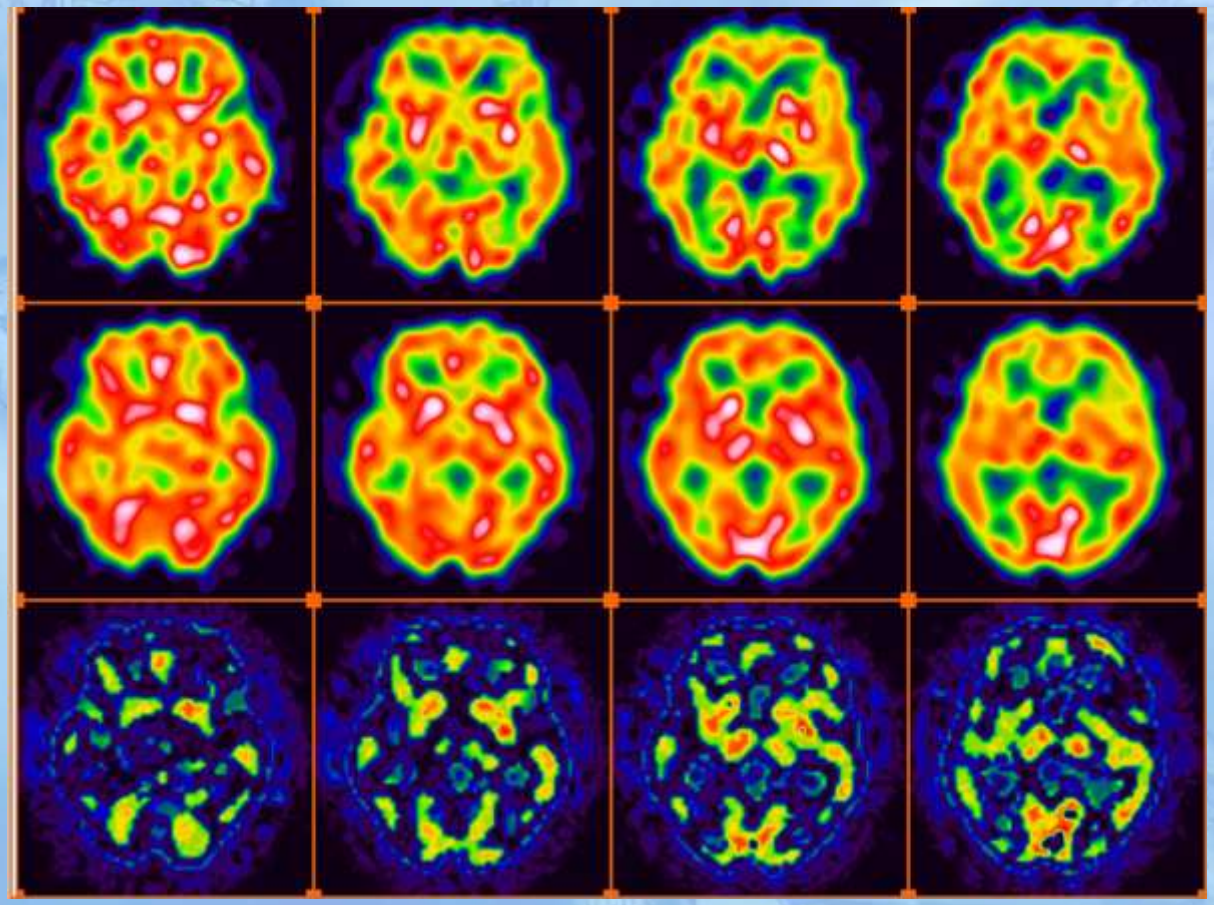
Acupoints and meridians



http://medgadget.com/2010/09/optinose_hopes_to_revolutionize_nasal_drug_delivery_with_its_novel_spray_devices.html

single photon emission computed tomography (SPECT)

Improved regional cerebral blood flow



before

after

net increase

SPECT for old men before and after ILILT from Prof. Xiao XC

ILIT: intranasal light therapy

DMN: default mode network

ILIT → **DMN** →

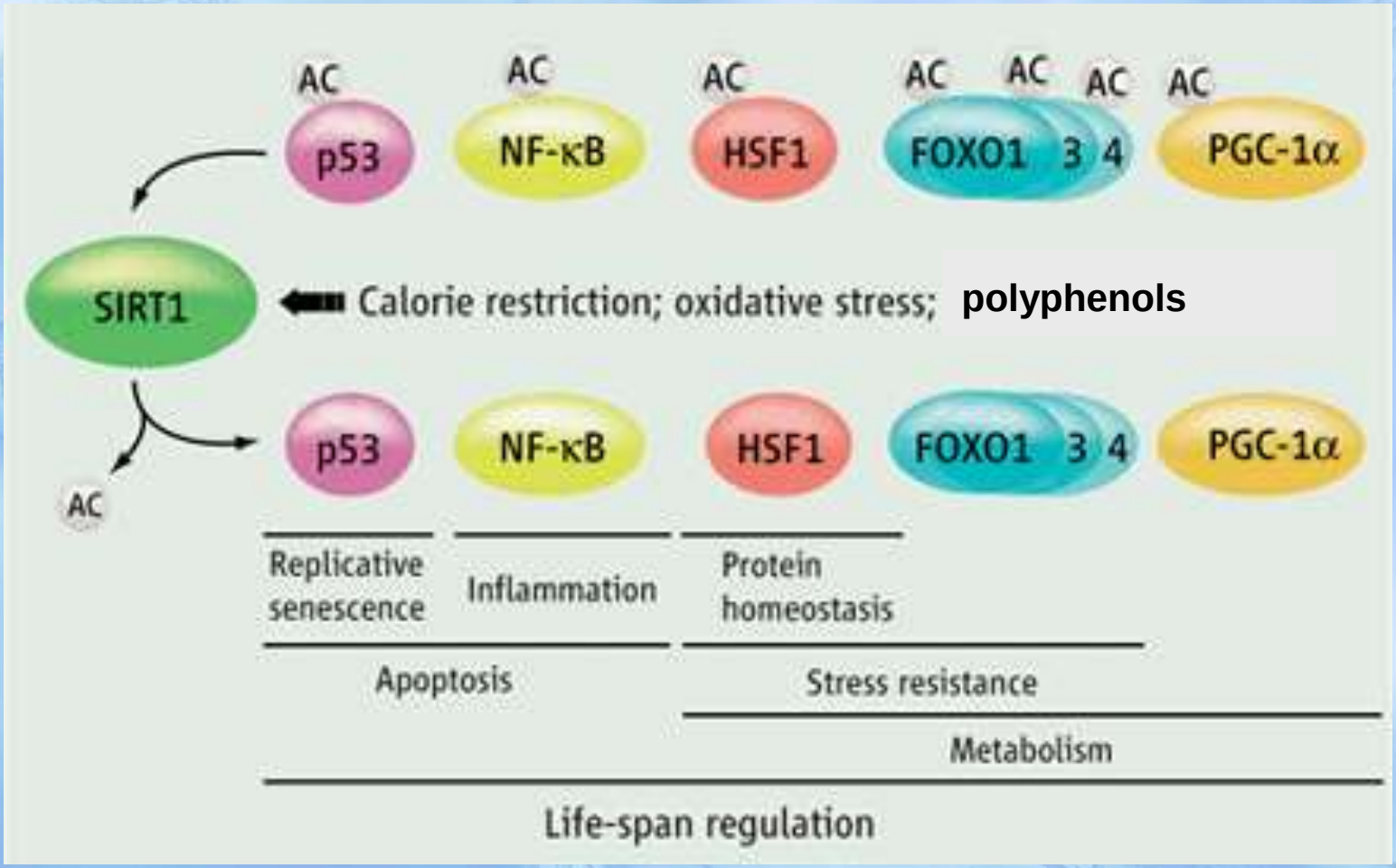
- Cerebral Palsy
- Depression
- Insomnia
- Mild cognitive impairment
- Alzheimer's disease
- Parkinson's disease
- **Schizophrenia**

Clinical applications

Liu CY, Zhu P (ED). 2009. Intranasal low intensity laser therapy. Beijing: People's Military Medical Press.

In Summary

Handling stress

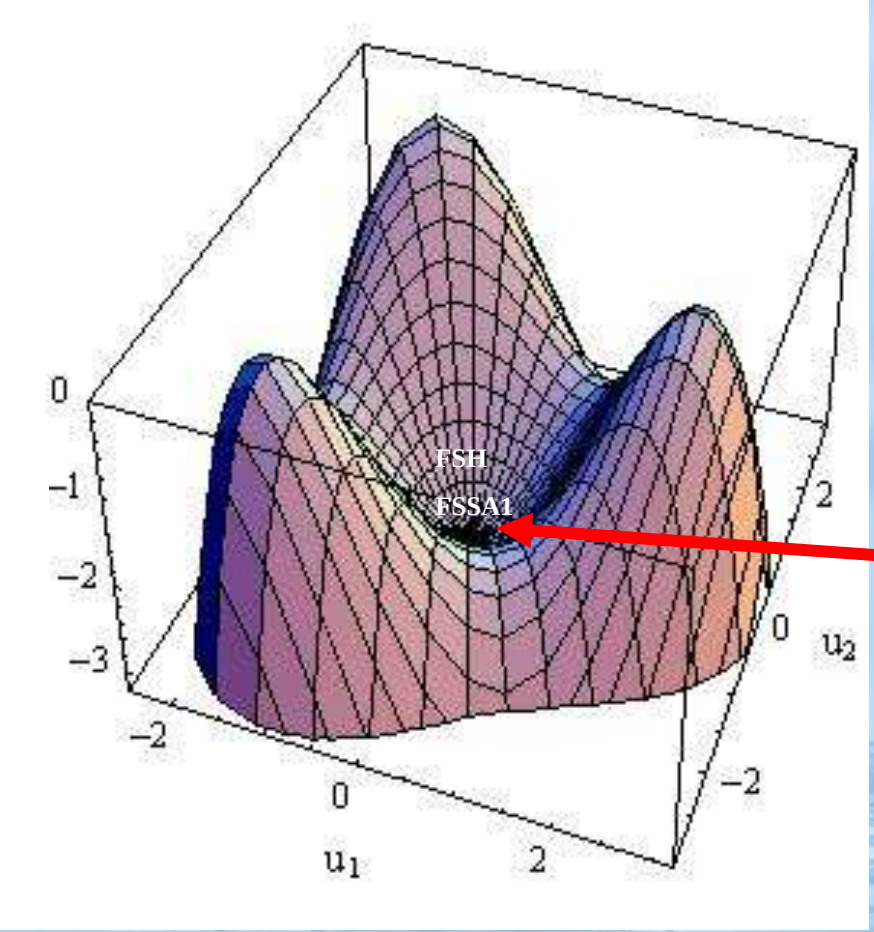


SIRT1 is a deacetylase that is activated by a variety of stressors and targets transcriptional regulators including p53, NF-kB, HSF1, FOXO1, 3, and 4, and PGC-1. These factors then control adaptive responses that modulate life span. AC: acetyl group; TH:Tyrosine hydroxylase

Saunders LR, Verdin E. 2009. Stress Response and Aging. Science. 323(5917): 1021 – 1022.

http://www.sciencemag.org/cgi/content/full/sci;323/5917/1021?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&andorexactfulltext=and&searchid=1&FIRSTINDEX=0&volume=323&firstpage=1021&resourcetype=HWCIT

SIRT1 activity



Function-specific homeostasis (FSH)

FSH-specific SIRT1 activity (FSSA1)

Sirtuin 1 (SIRT1) activity potential well.

FSSA1 denotes function-specific homeostasis specific SIRT1 activity

ILIT: intranasal light therapy

SIRT1: Sirtuin 1, one of longevity factors

ILILT → SIRT1 →

- Pain Relief
- Cerebral Palsy
- Stroke (cerebral infarction, …)
- Coronary Heart Disease
- myocardial infarction
- Inflammation
- Depression

Clinical applications

Liu CY, Zhu P (ED). 2009. Intranasal low intensity laser therapy. Beijing: People's Military Medical Press.

ILIT: intranasal light therapy

SIRT1: Sirtuin 1, one of longevity factors

ILILT → SIRT1 →

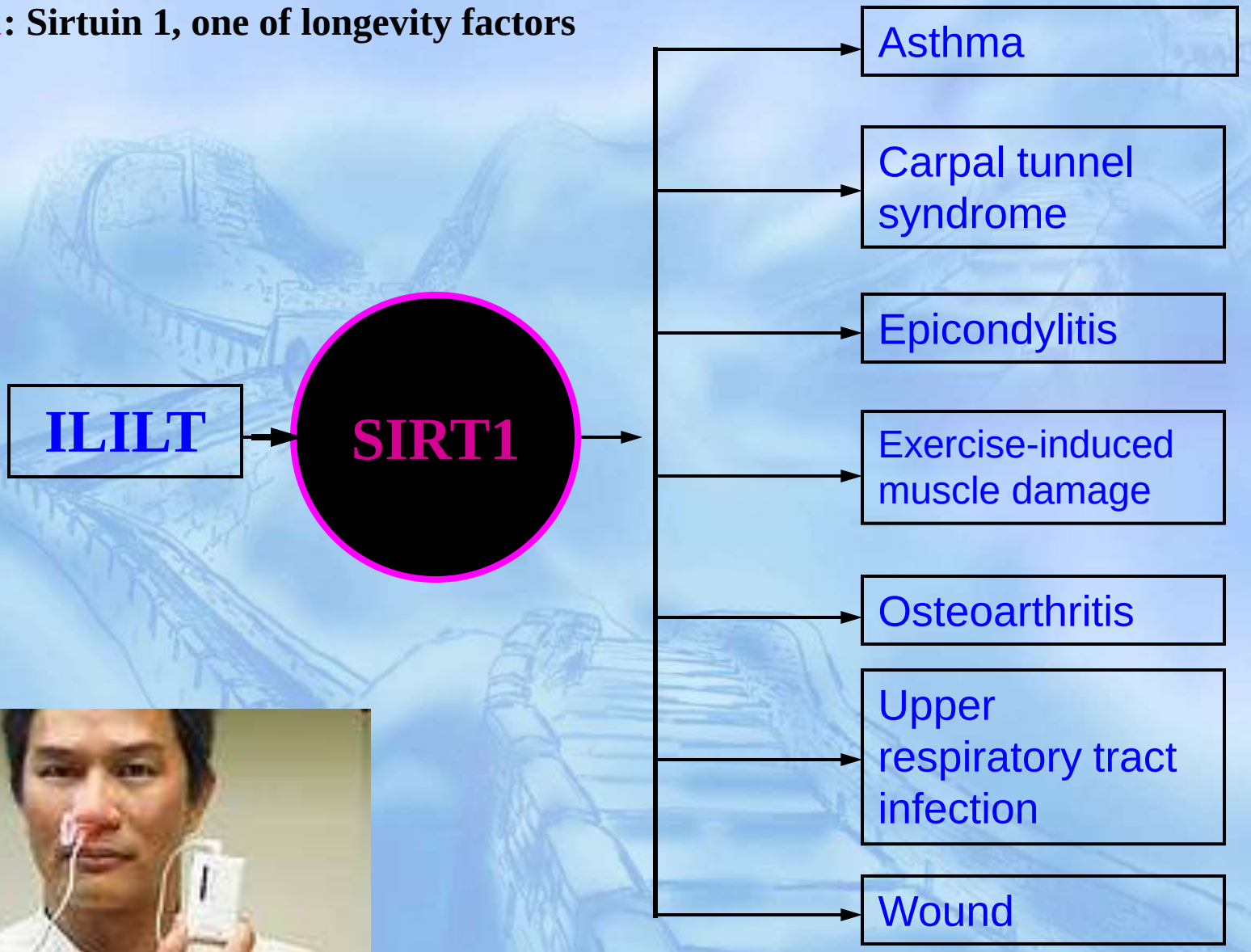
- **Hyperlipidemia**
- Blood hyperviscosity
- Insomnia
- Mild cognitive impairment
- Alzheimer's disease
- Parkinson's disease
- **Schizophrenia**

Clinical applications

Liu CY, Zhu P (ED). 2009. Intranasal low intensity laser therapy. Beijing: People's Military Medical Press.

ILIT: intranasal light therapy

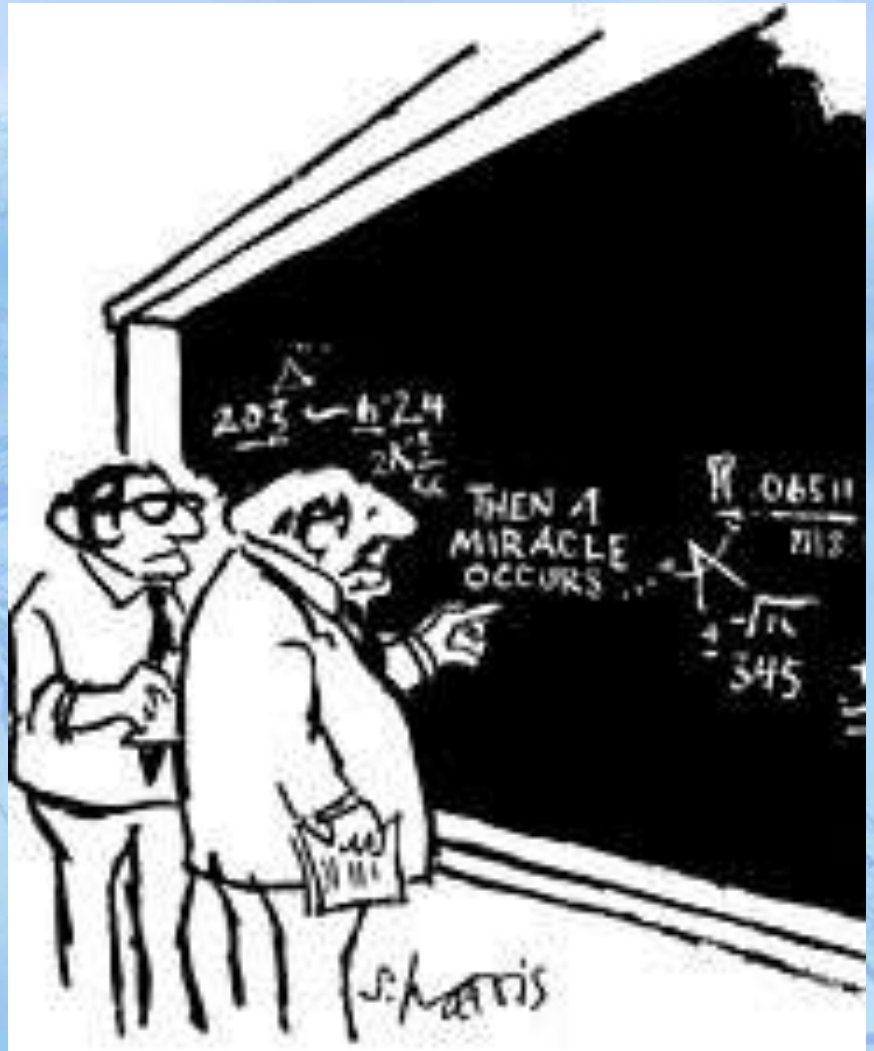
SIRT1: Sirtuin 1, one of longevity factors



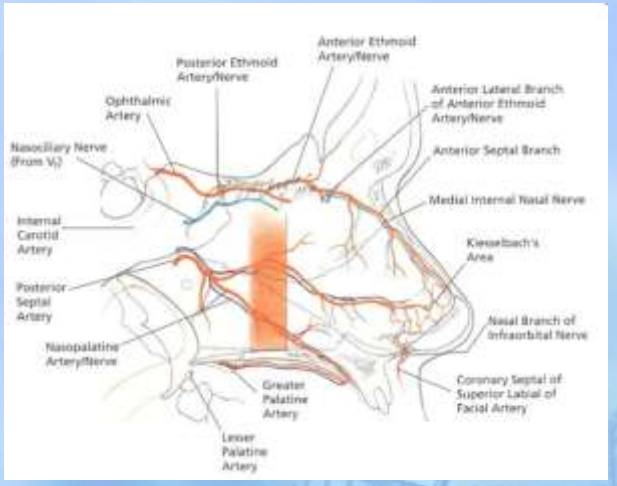
Possible applications in sports medicine

Liu TCY, Wu DF, Gu ZQ, Wu M. 2010. Applications of intranasal low intensity laser therapy in sports medicine. Journal of Innovation in Optical Health Science. 3(1): 1-16.

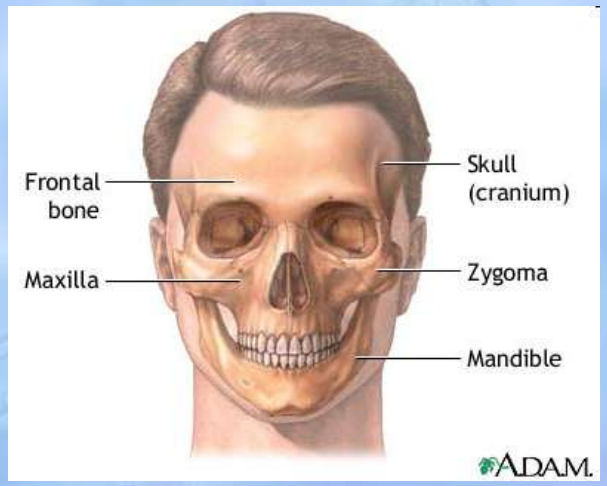
Discussion



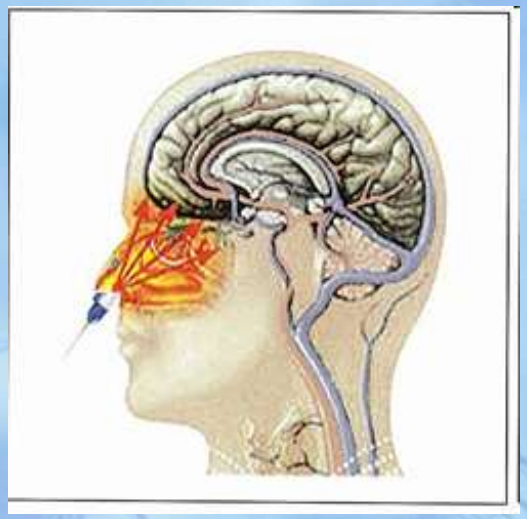
"I think you should be more explicit here in step two."

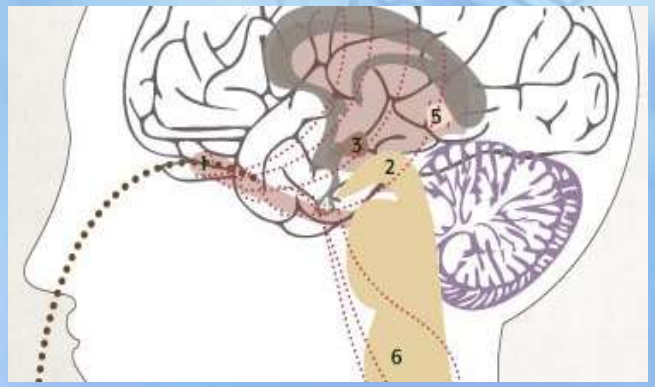


Blood

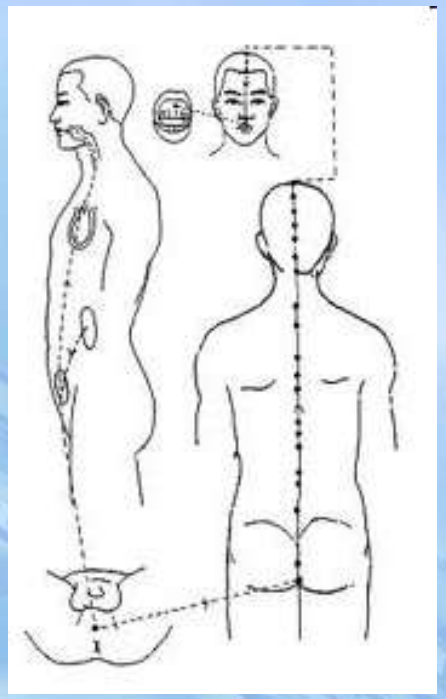


Bone



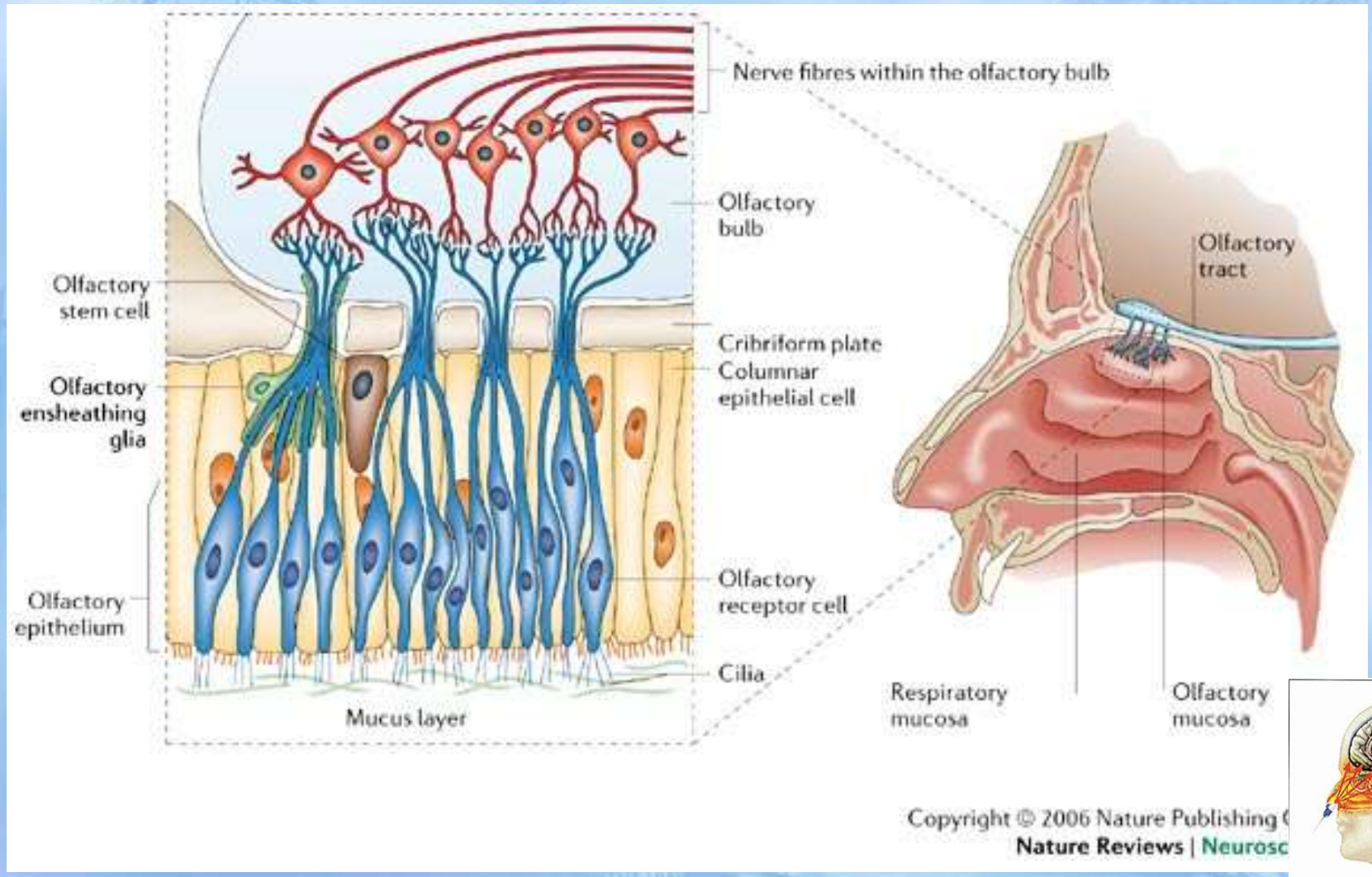


Olfactory, autonomic and central nervous system



Acupoints and meridians

ILIT Biomechanism: Olfaction



Hierarchical regression analyses

- Proficiency in executive functioning and semantic memory contributed significantly to odor discrimination and identification performance (Hedner *et al*. 2010)
- Age, sex, education, cognitive speed and vocabulary were reliable correlates of performance in the odor identification task (Larsson *et al*. 2004).

Hedner M, Larsson M, Arnold N, Zucco GM, Hummel T. 2010. **Cognitive** factors in odor detection, odor discrimination, and **odor identification** tasks. J Clin Exp Neuropsychol. 2010 Dec;32(10):1062-7. http://www.ncbi.nlm.nih.gov/pubmed/20437286
Larsson M, Nilsson LG, Olofsson JK, Nordin S. 2004. Demographic and cognitive predictors of cued **odor identification**: evidence from a population-based study. Chem Senses. 2004 Jul;29(6):547-54. http://www.ncbi.nlm.nih.gov/pubmed/15269128 free

Odor identification and decline in different cognitive domains in old age

- A person with a low odor identification score (6, 10th percentile) declined more than twice as rapidly in perceptual speed and episodic memory as a person with a high score (11, 90th percentile)
  - Lower odor identification score was associated with lower function at baseline in each cognitive domain
  - Lower score was also associated with more rapid decline in perceptual speed and episodic memory but not with rate of decline in semantic memory, working memory, or visuospatial ability.

Wilson RS, Arnold SE, Tang Y, Bennett DA. 2006. **Odor identification** and decline in different cognitive domains in old age. Neuroepidemiology. 2006;26(2):61-7. http://www.ncbi.nlm.nih.gov/pubmed/16352908

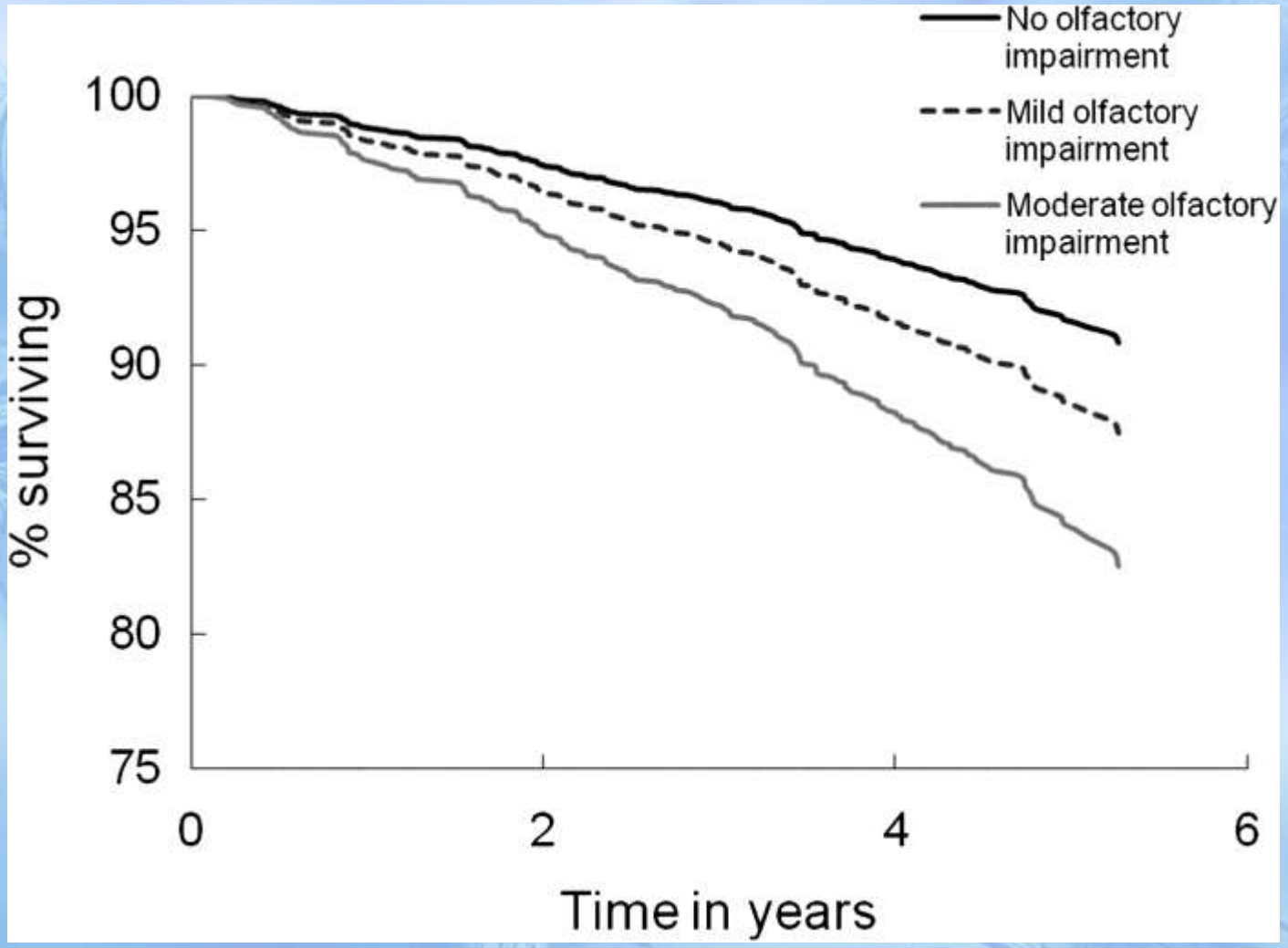
Dysfunctional odor identification

- Neurodegenerative diseases such as Alzheimer's and Parkinson's disease
  - Mesholam RI, Moberg PJ, Mahr RN, Doty RL. 1998. Olfaction in **neurodegenerative** disease: a meta-analysis of olfactory functioning in Alzheimer's and Parkinson's diseases. Arch Neurol. 1998 Jan;55(1):84-90. http://www.ncbi.nlm.nih.gov/pubmed/9443714
- **Schizophrenia**
  - Nguyen AD, Shenton ME, Levitt JJ. 2010. Olfactory dysfunction in schizophrenia: a review of **neuroanatomy** and psychophysiological measurements. Harv Rev Psychiatry. 2010 Oct;18(5):279-92. http://www.ncbi.nlm.nih.gov/pubmed/20825265
- Depression
  - Gopinath B, Anstey KJ, Sue CM, Kifley A, Mitchell P. 2011. Olfactory impairment in older adults is associated with **depressive** symptoms and poorer quality of life scores. Am J Geriatr Psychiatry. 2011 Sep;19(9):830-4. http://www.ncbi.nlm.nih.gov/pubmed/21422904

Dysfunctional odor identification

- HIV infection
  - Mueller C, Temmel AF, Quint C, Rieger A, Hummel T. Olfactory function in **HIV**-positive subjects. Acta Otolaryngol. 2002 Jan;122(1):67-71. http://www.ncbi.nlm.nih.gov/pubmed/11878282
- Posttraumatic stress disorder (PTSD)
  - Vasterling JJ, Brailey K, Sutker PB. Olfactory identification in combat-related posttraumatic stress disorder. J Trauma Stress. 2000 Apr;13(2):241-53. http://www.ncbi.nlm.nih.gov/pubmed/10838673
- Addiction
  - Podskarbi-Fayette R, Rydzewski B, Lipińska M. 2005. [Smell and taste in drug addicts]. Otolaryngol Pol. 2005;59(4):585-90. Polish. http://www.ncbi.nlm.nih.gov/pubmed/16273867

Age-sex adjusted Kaplan–Meier survival curves by severity of olfactory impairment among Blue Mountains Eye Study participants aged 60 years and older.



Gopinath B et al. J Gerontol A Biol Sci Med Sci 2012;67A:204-209

Gopinath B, Sue CM, Kifley A, Mitchell P. 2012. The association between olfactory impairment and total **mortality** in older adults. J Gerontol A Biol Sci Med Sci. 2012 Feb;67(2):204-9. http://www.ncbi.nlm.nih.gov/pubmed/22080501

the Journals of gerontology Series a

Odor identification Score (OIS) and mortality in old age

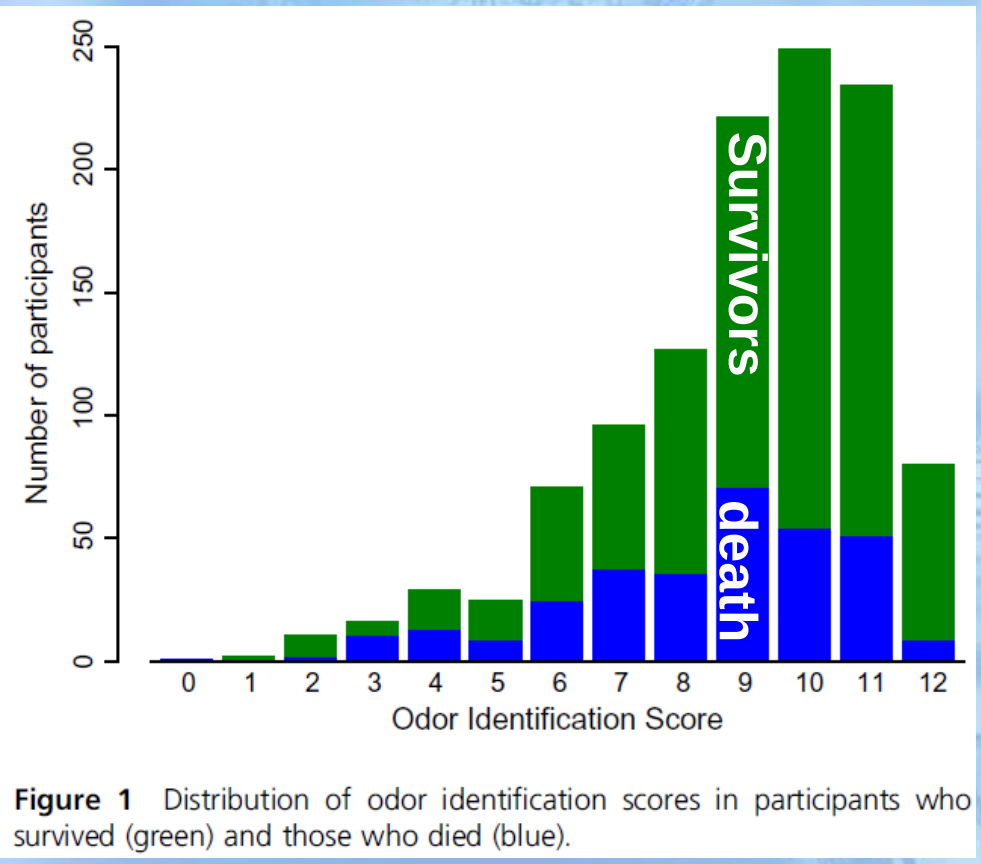


Figure 1 Distribution of odor identification scores in participants who survived (green) and those who died (blue).

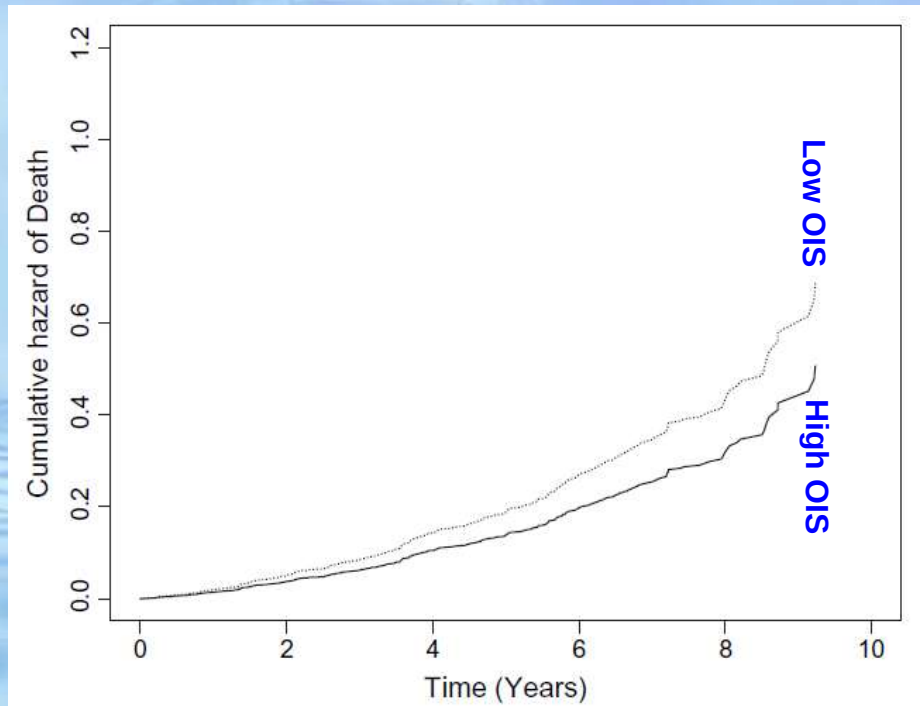
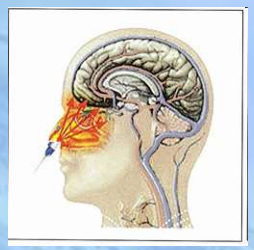


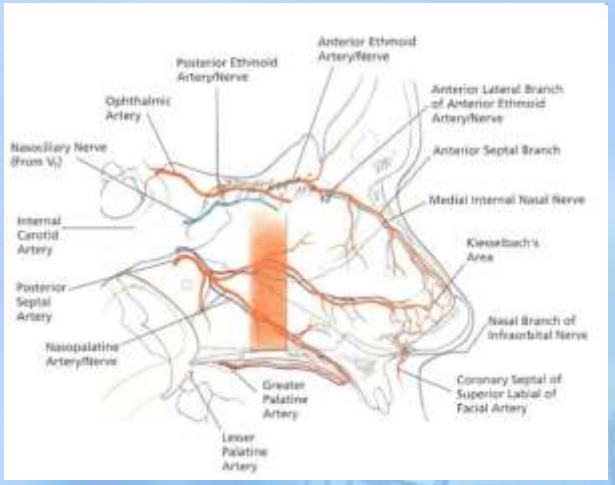
Figure 2 Cumulative risk of death associated with a low (dotted line, 10th percentile) compared with high (solid line, 90th percentile) odor identification score, adjusted for age, sex, and education.

Wilson RS, Yu L, Bennett DA. 2011. Odor identification and mortality in old age. Chem Senses. 2011 Jan;36(1):63-7. http://www.ncbi.nlm.nih.gov/pubmed/20923931

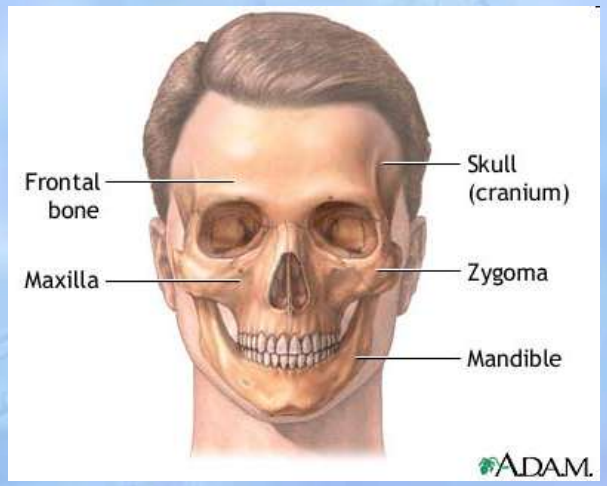
Olfaction might be recovered/enhanced with ILIT

- Numerous central nervous system disorders may be associated with olfactory dysfunction.
  - According to dPBM, ILIT might recover CNS disorders at least through olfaction recovery.
- Olfaction has been found to represent longevity. The stronger the olfaction, the longer the longevity.
  - According to iPBM, ILIT might extend the longevity at least through olfaction promotion .

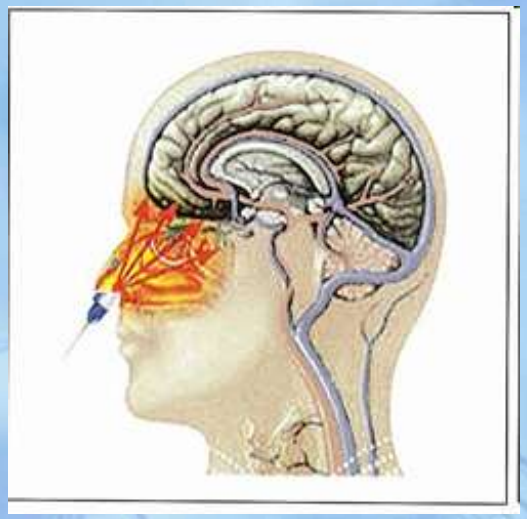


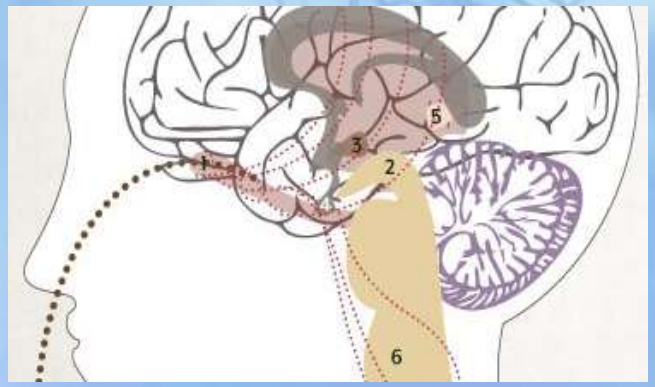


Blood

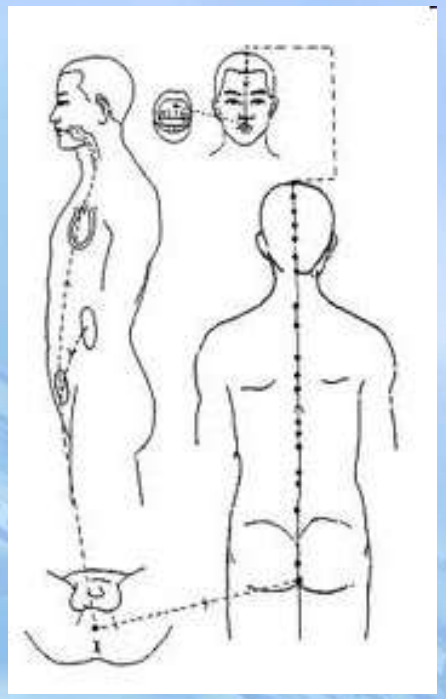


Bone





Olfactory, autonomic and central nervous system



Acupoints and meridians

ILIT: intranasal light therapy

DMN: default mode network

ILIT → **DMN** →

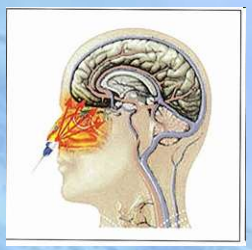
- Cerebral Palsy
- Depression
- Insomnia
- Mild cognitive impairment
- Alzheimer's disease
- Parkinson's disease
- **Schizophrenia**

Clinical applications

Liu CY, Zhu P (ED). 2009. Intranasal low intensity laser therapy. Beijing: People's Military Medical Press.

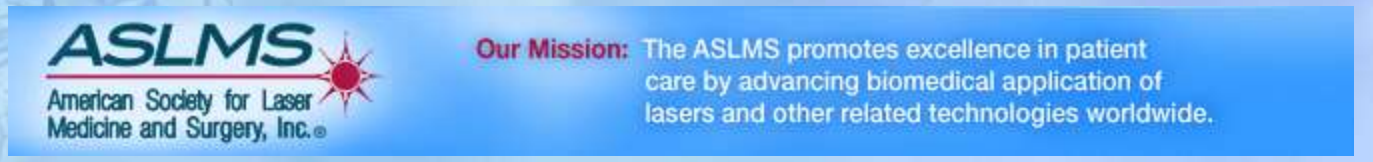
DMN might be recovered/enhanced with ILIT

- Numerous central nervous system disorders may be associated with dysfunctional DMN.
  - According to dPBM, ILIT might recover CNS disorders at least through DMN recovery.
- DMN connectivity has been found to represent cultural intelligence. The stronger the DMN connectivity, the higher the cultural intelligence.
  - According to iPBM, ILIT might extend the cultural intelligence at least through DMN connectivity promotion.



Acknowledgement

- The 2000-2002 summer student research grants of the American Society of Lasers in Surgery and Medicine;



- National Science Foundation of China (60878061, 60478048, 6027812, 60178003 and 69778003).