多糖类化妆品原料的研究与开发

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广东药学院

研究背景：衰老及相关疾病

疾病种类

- 恶性肿瘤
- 神经退行性疾病

药物种类

- 多糖、寡糖、糖缀合物
- 蛋白、多肽、肽缀合物

疾病模型

- 酵母（单细胞）
- 秀丽线虫（无脊椎动物）
- 斑马鱼（脊椎动物）
- 哺乳动物及哺乳动物细胞（尤其是人细胞）

相信进化论…

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A quest for longevity…

500 years ago, the Spanish explorer Ponce de León drank his way around the Florida coast during his expedition to find the legendary fountain of youth.

Finkel T (2003) *Nature* 425: 132–133.

Long-live animals

Anti-aging medicinal herbs…





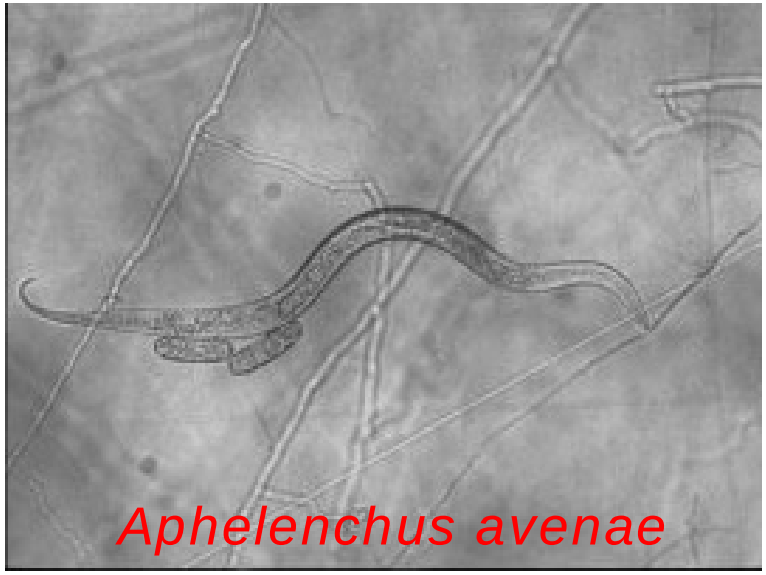


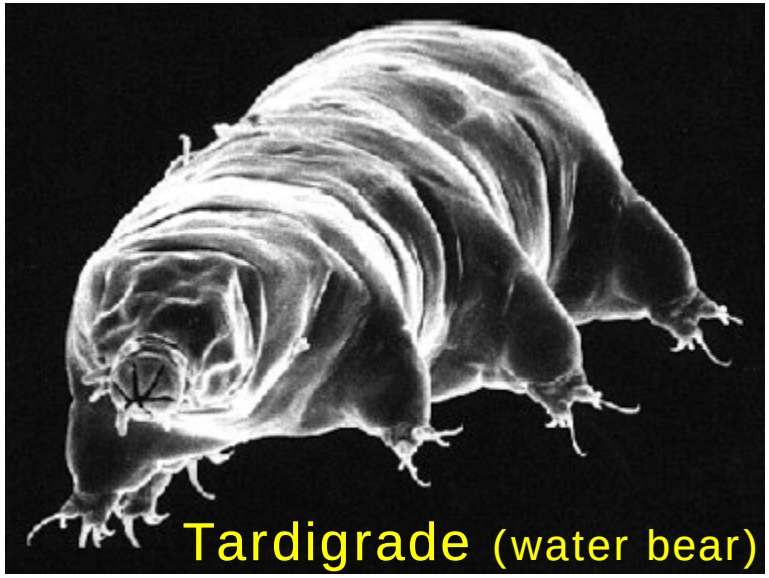




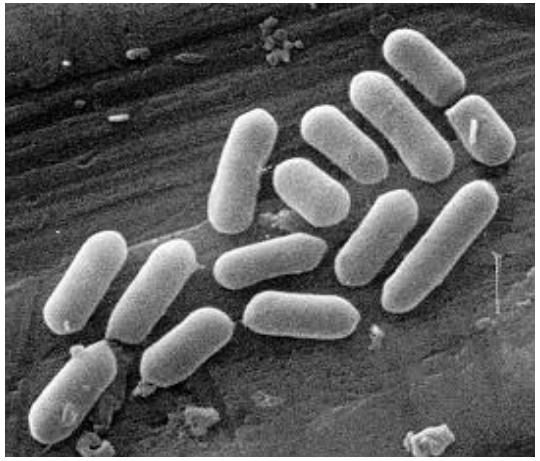
Regenerative animals

Anhydrobiotes

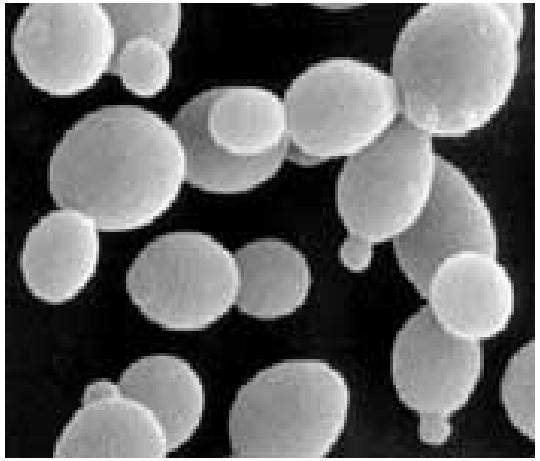




Anhydrobiotes



Bacteria



Yeast

Resurrection plant
Selaginella lepydophylla

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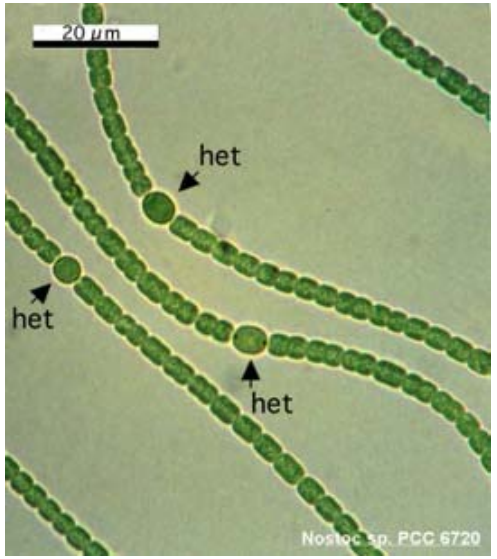
Anhydrobiotes

Nostoc flagelliforme

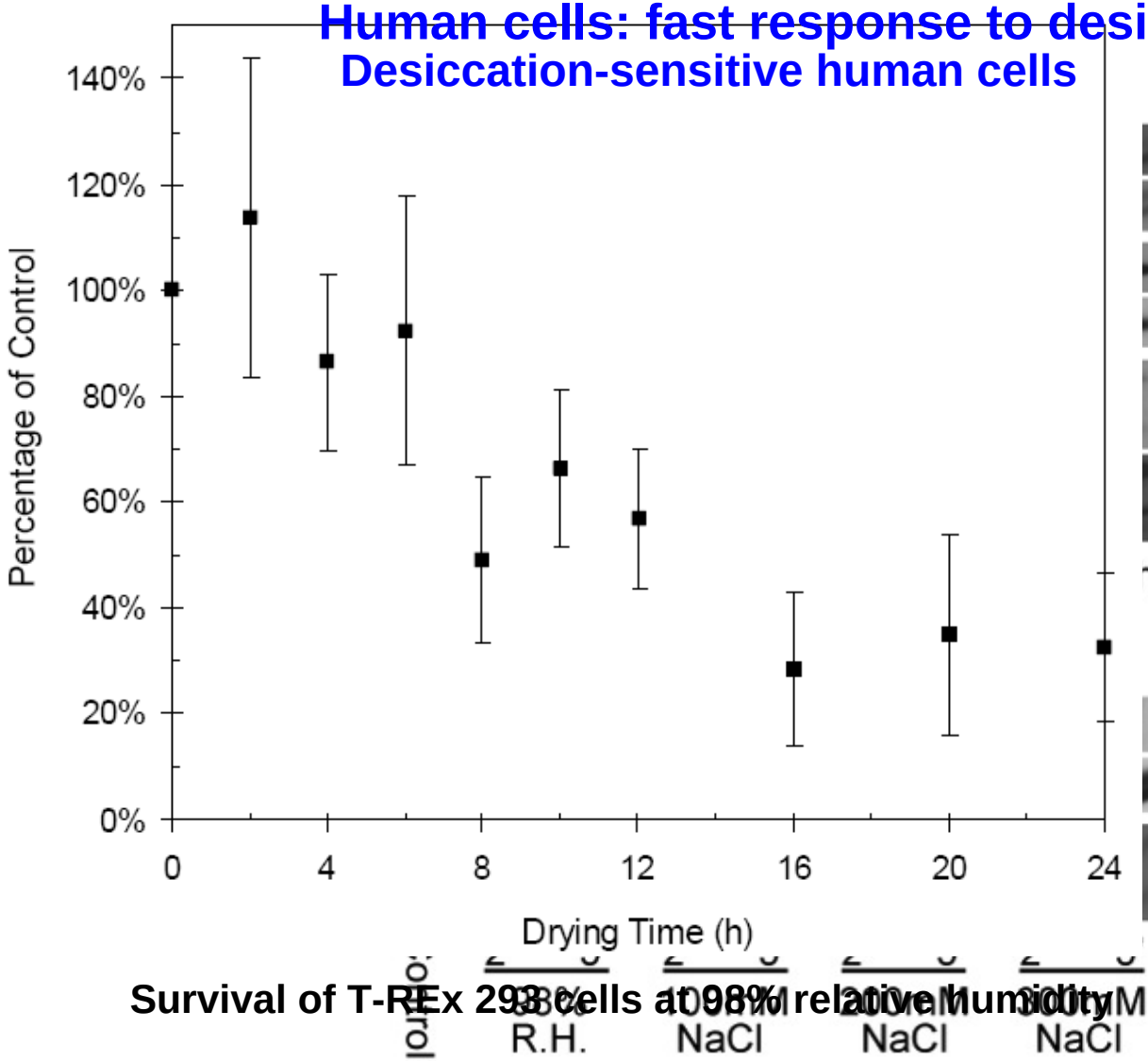
Nostoc sphaeroides

Nostoc commune

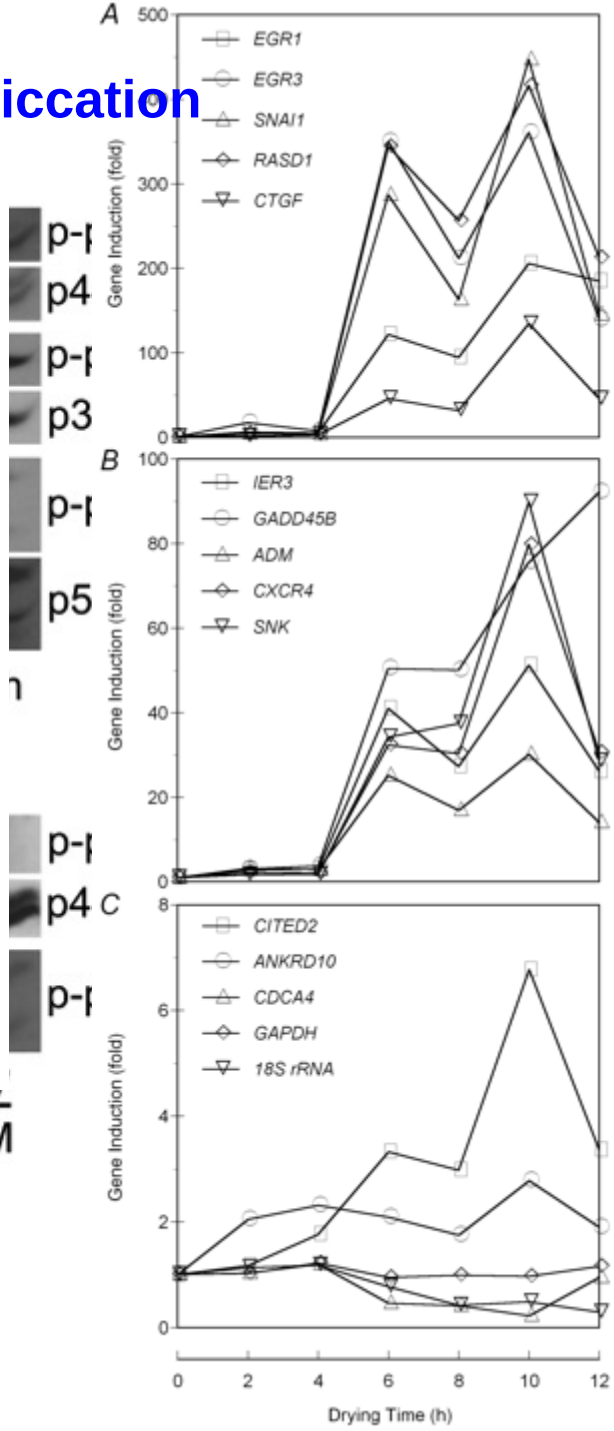


Human cells: fast response to desiccation

Desiccation-sensitive human cells

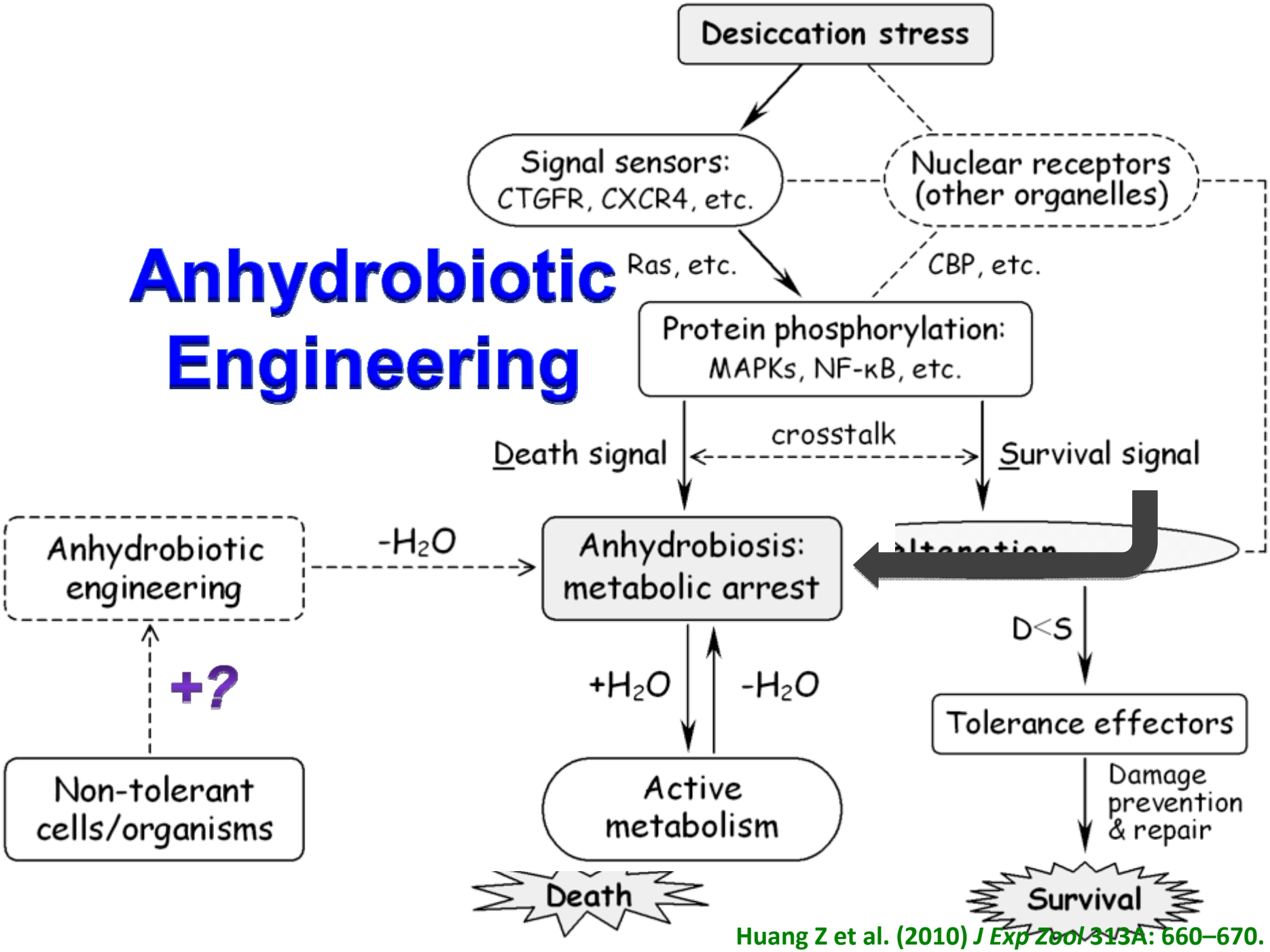


Survival of T-REx 293 cells at 98% relative humidity



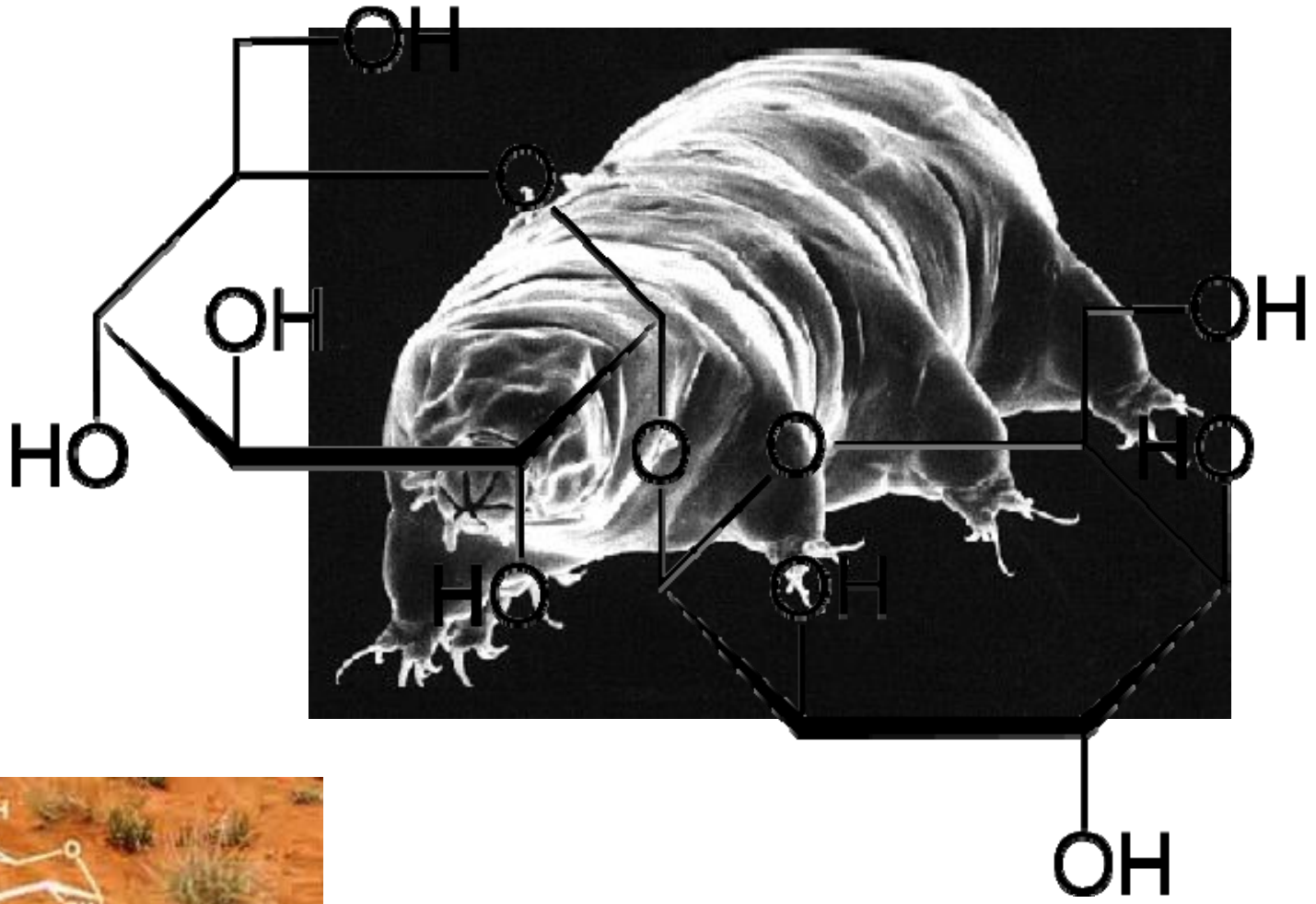
Huang Z & Tunnacliffe A (2004) *J Physiol* 558: 181–191.
Huang Z & Tunnacliffe A (2005) *FEBS Lett* 579: 4973–4977.
Huang Z & Tunnacliffe A (2007) *Methods Enzymol* 428: 269–277.

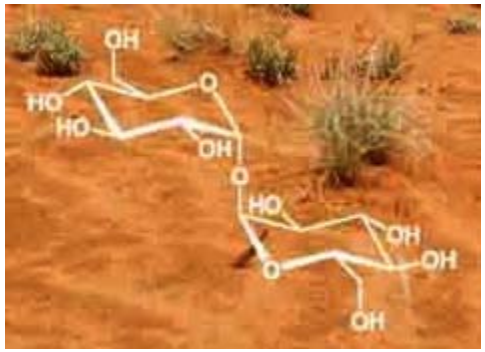
Anhydrobiotic Engineering

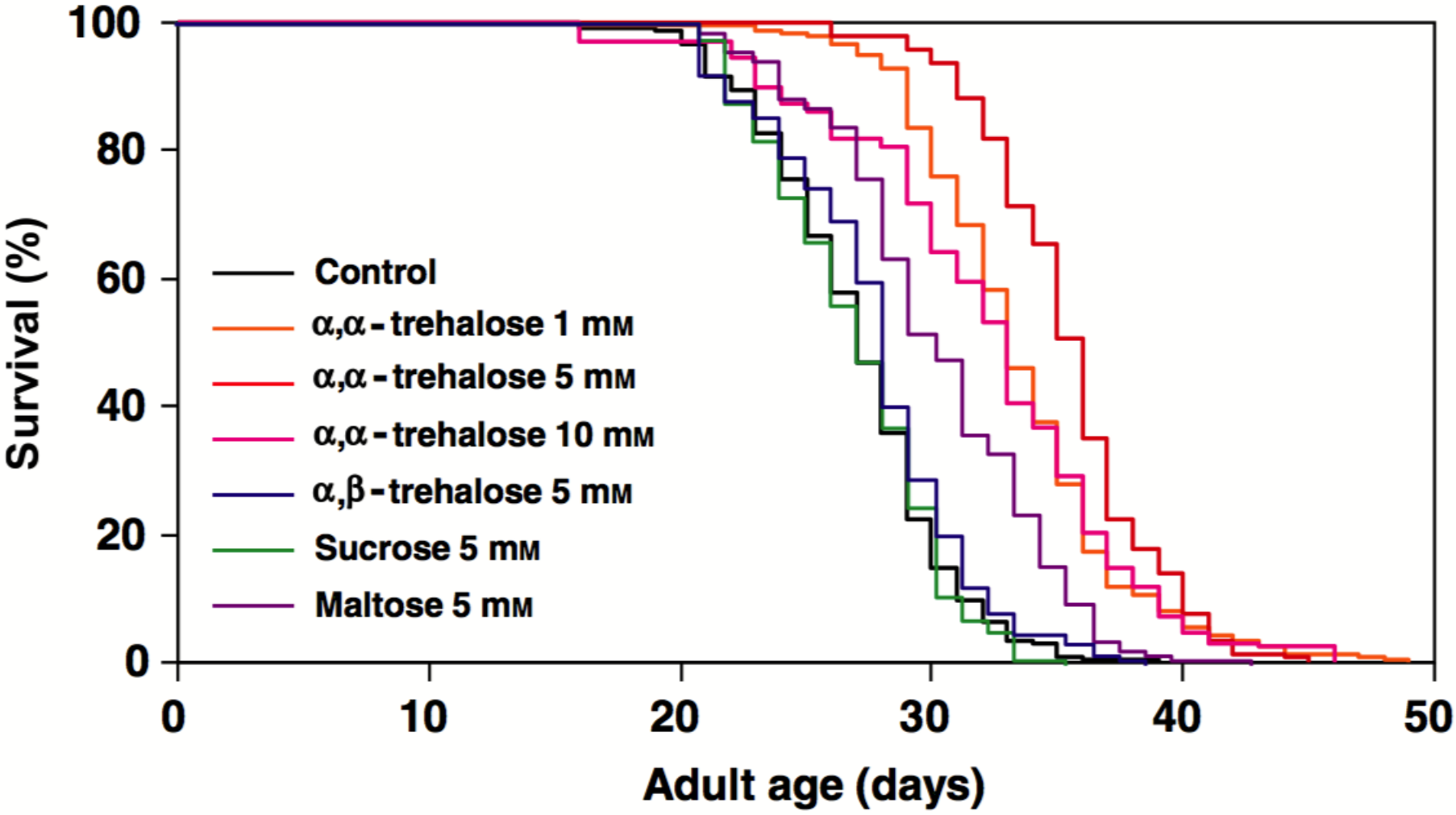


Huang Z et al. (2010) *J Exp Zool* 313A: 660–670.

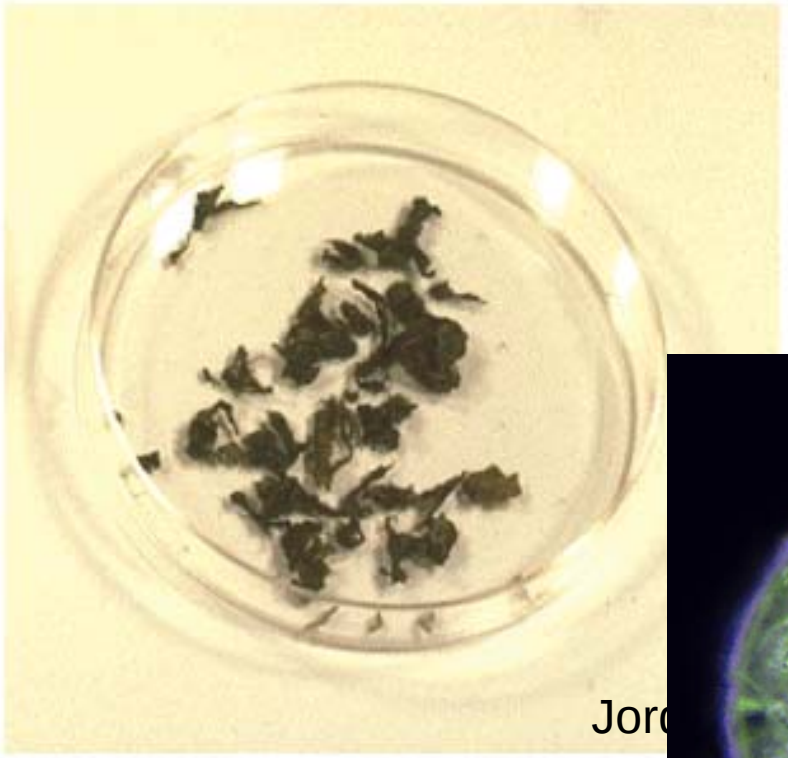
Trehalose

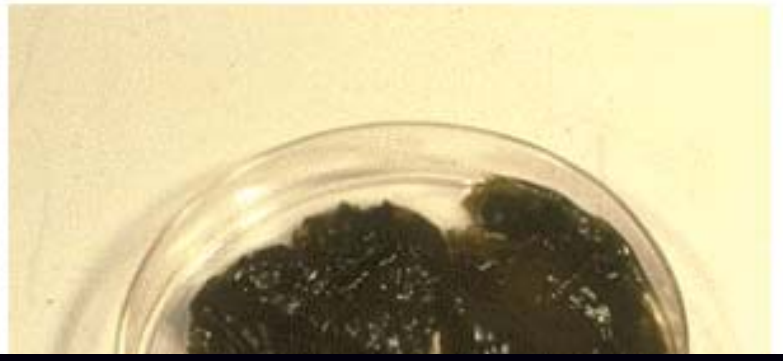


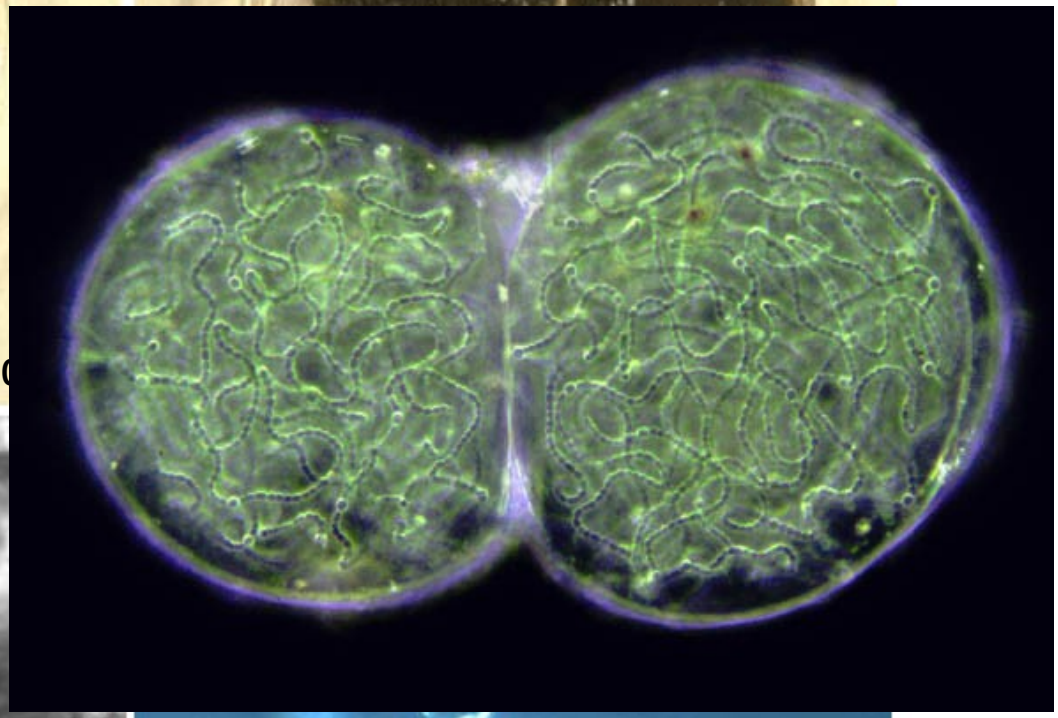


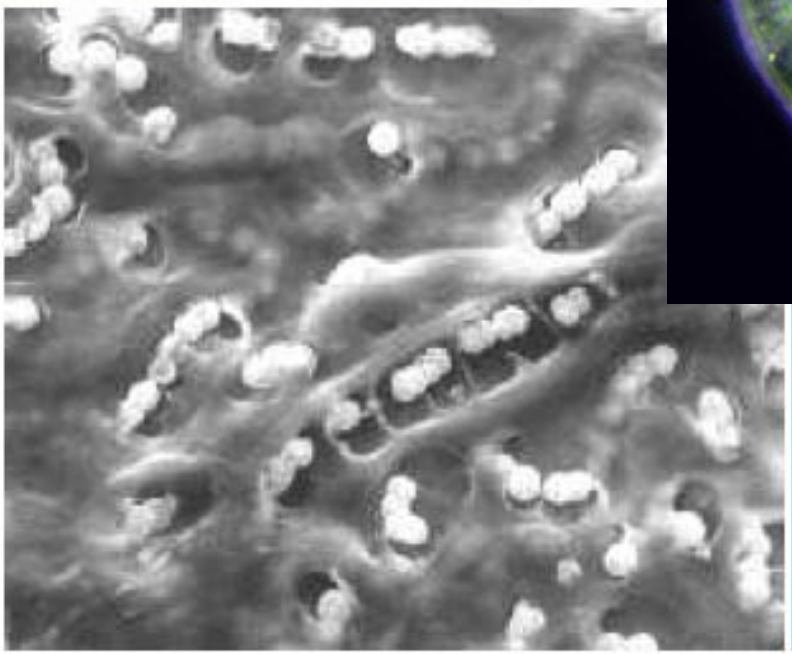


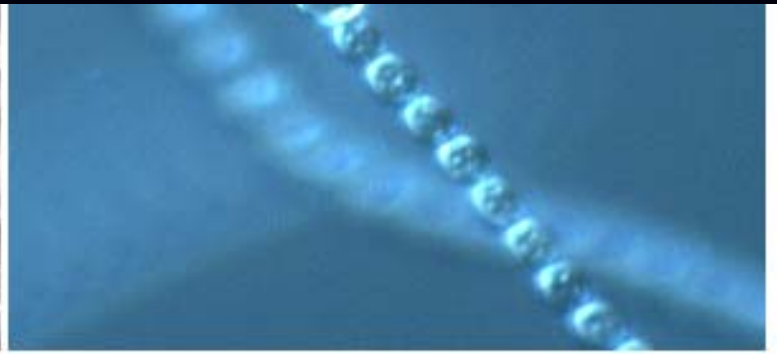
Honda Y et al. (2010) *Aging Cell* 9: 558–569.





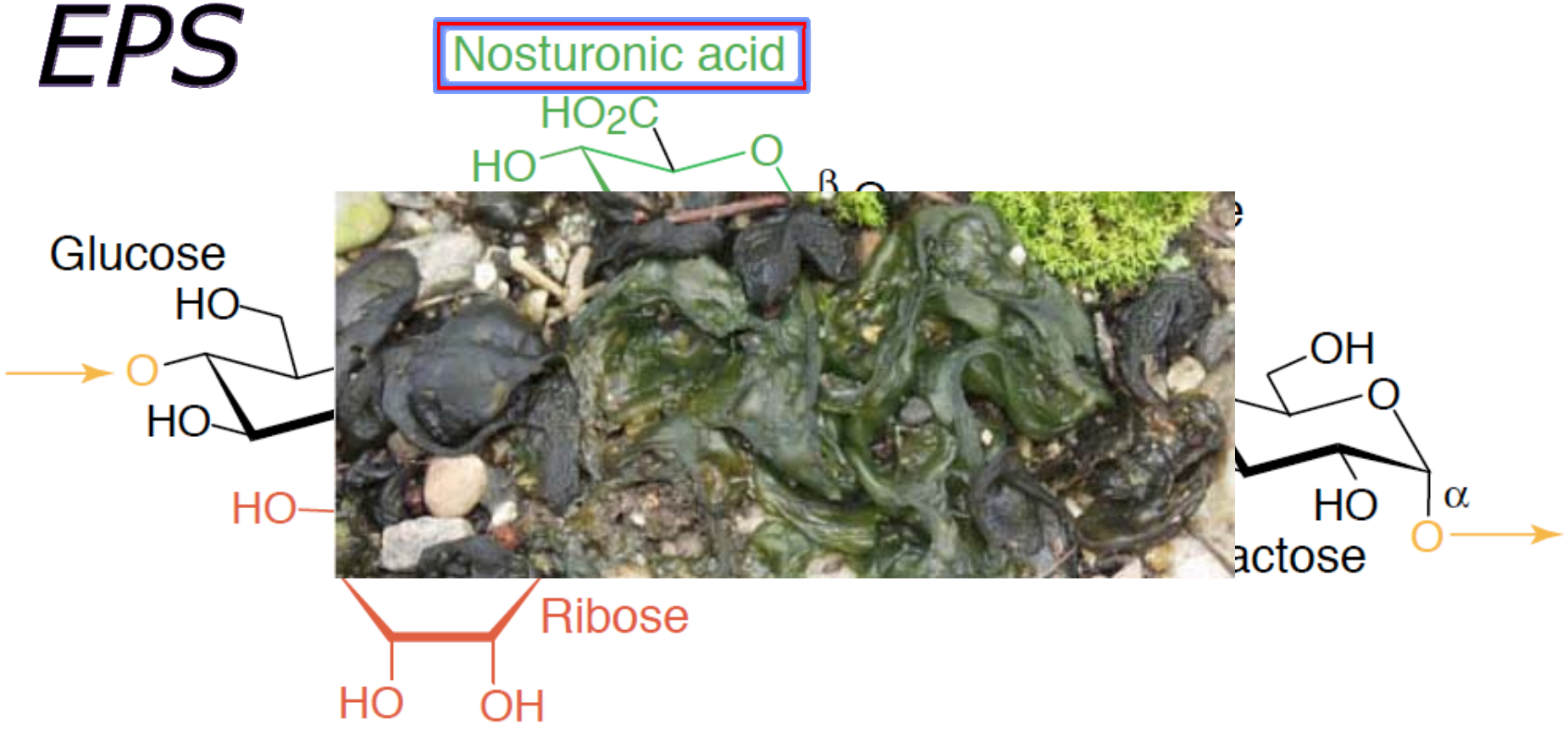






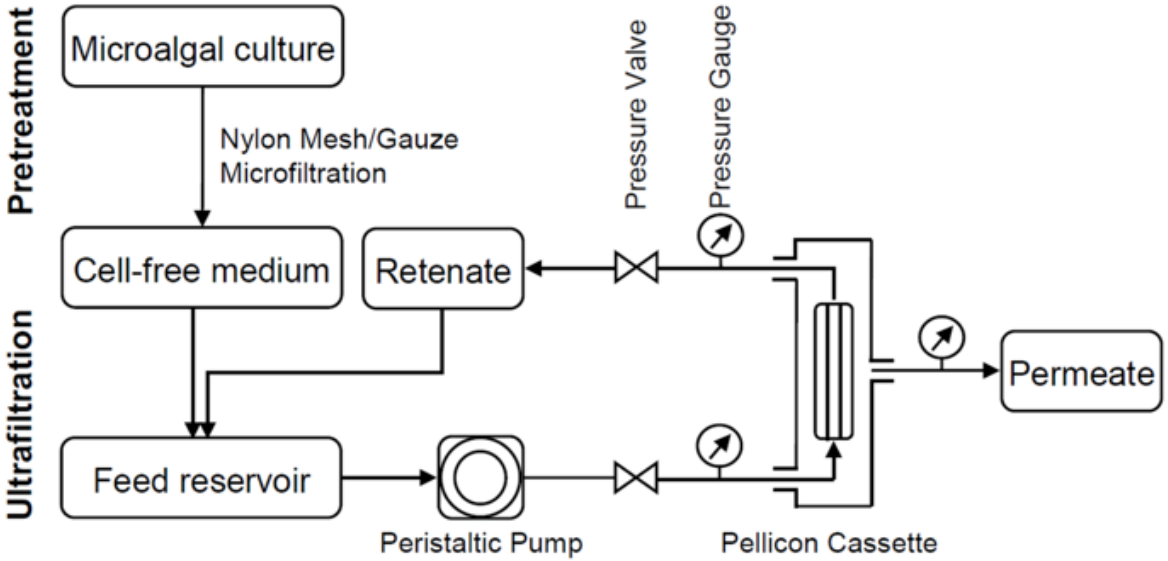
Nostoc polysaccharides

EPS



Huang Z et al. (1998) *J Phycol* 34: 962–968.
Helm RF et al. (2000) *J Bacteriol* 182: 974–982.
Huang Z et al. (2000) *Carbohydr Res* 328: 77–83.
Brüll LP et al. (2000) *J Phycol* 36: 871–881.

Pilot-scale EPS isolation from algal cultures

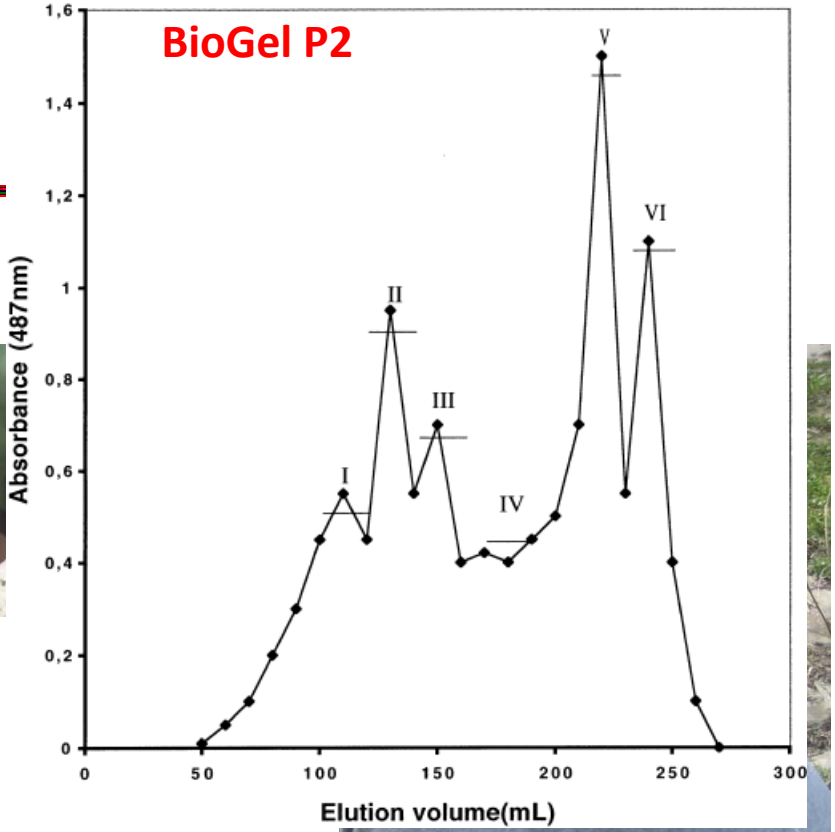


Li H et al. (2011) *Proc Biochem* 46: 1104–1109.

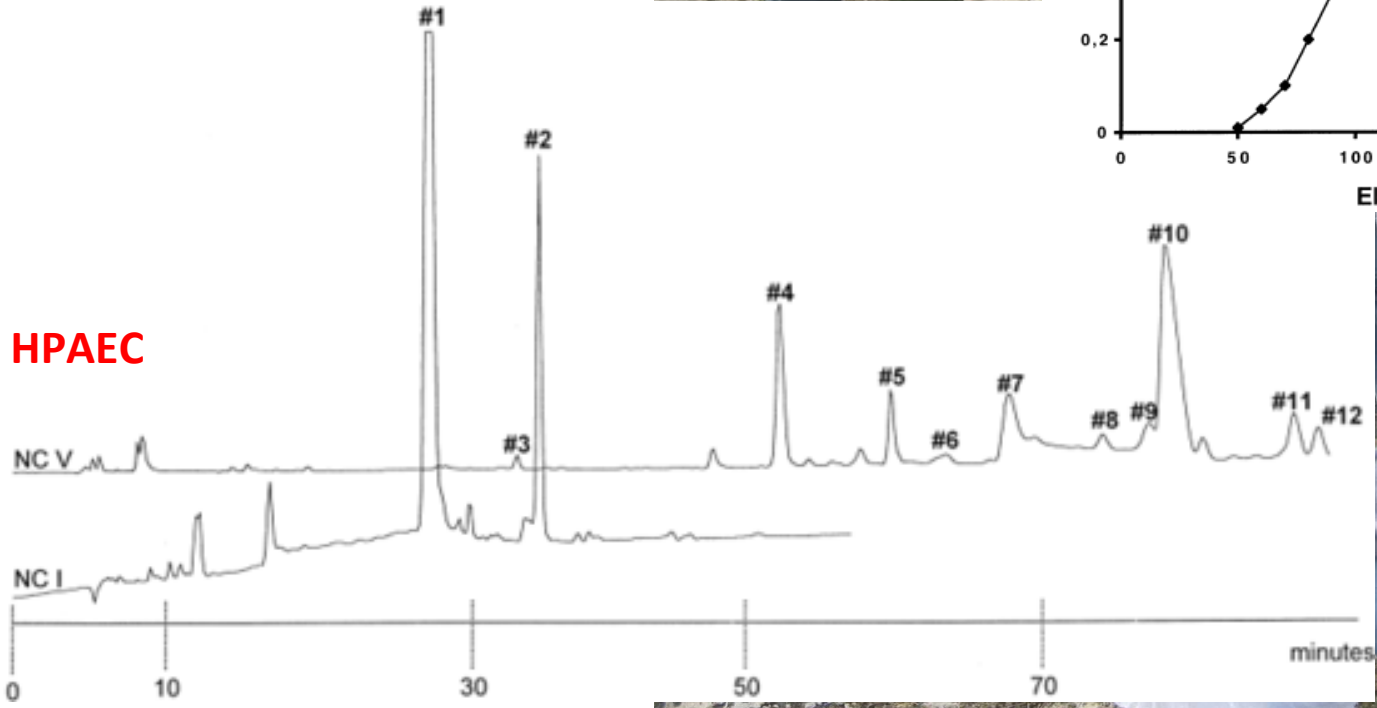
Nostoc polysaccharides

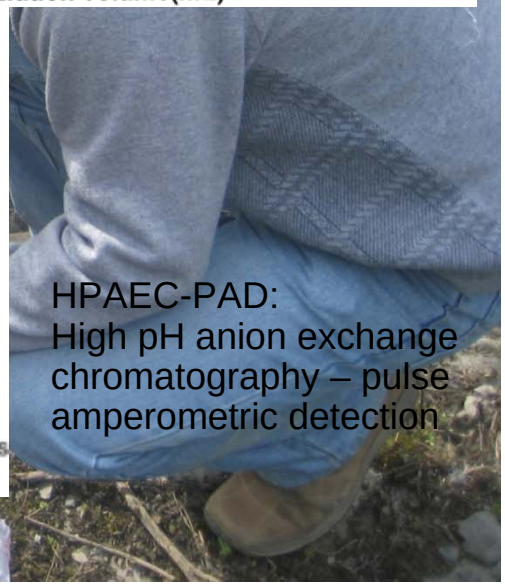
Weak acid hydrolysate of the polysaccharide from field *N. commune* colonies

BioGel P2

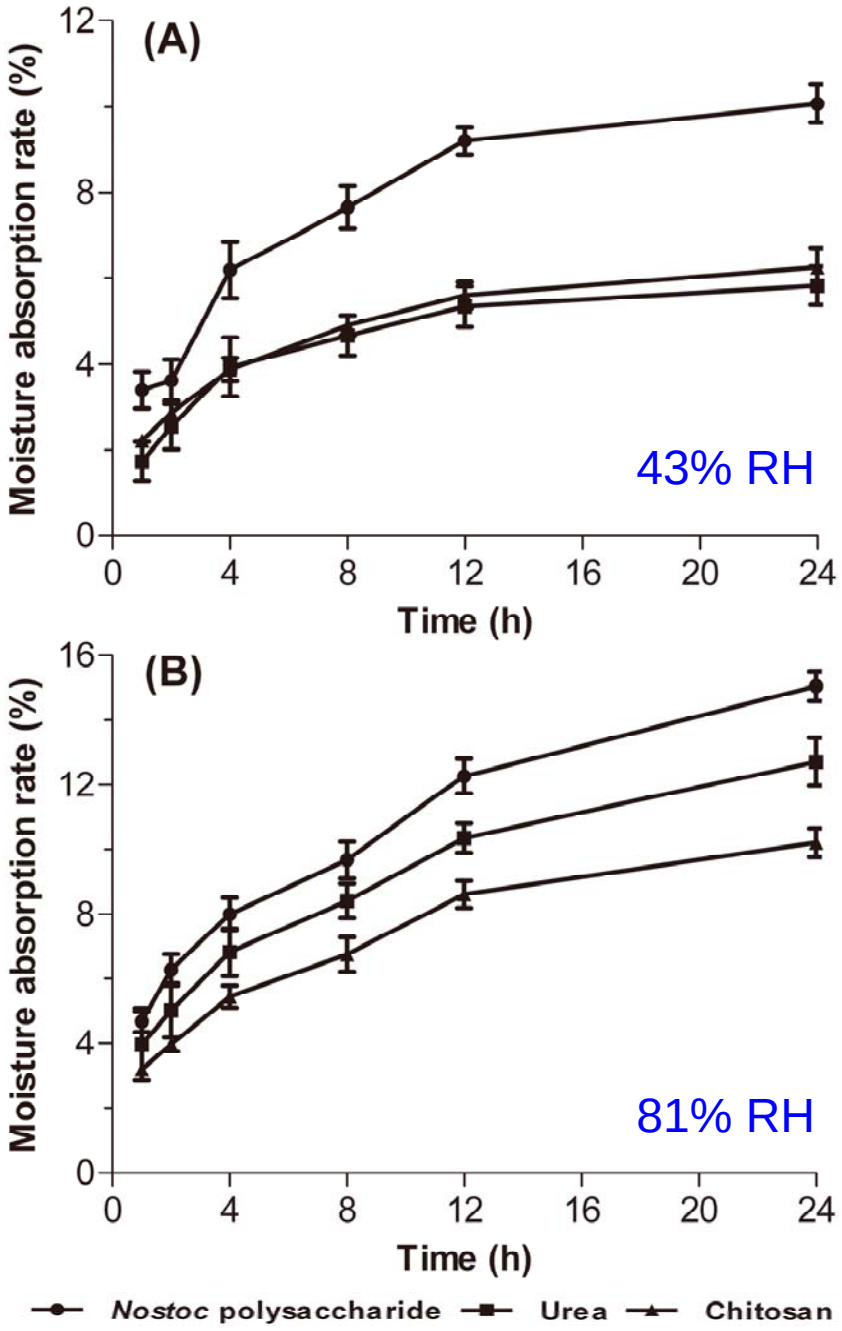


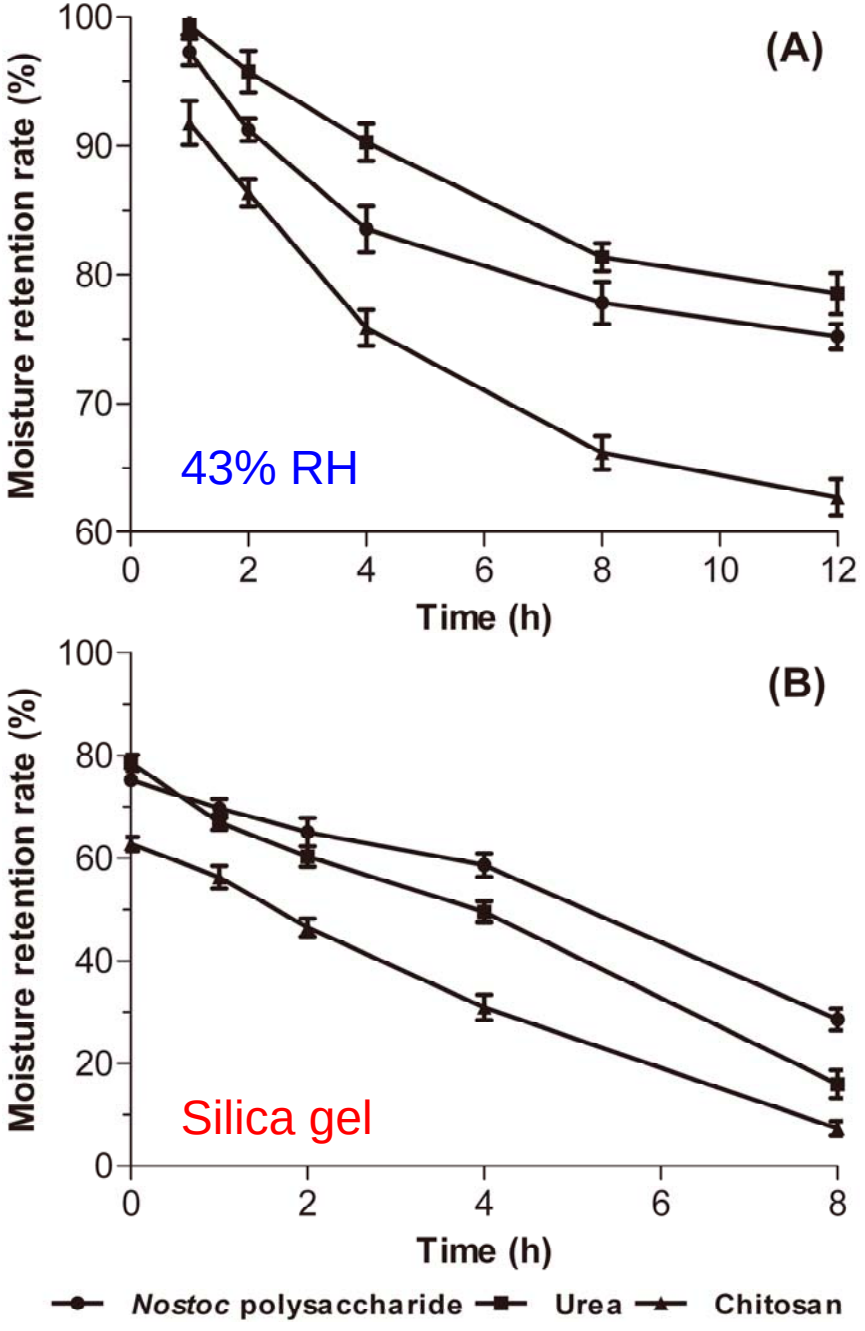
HPAEC



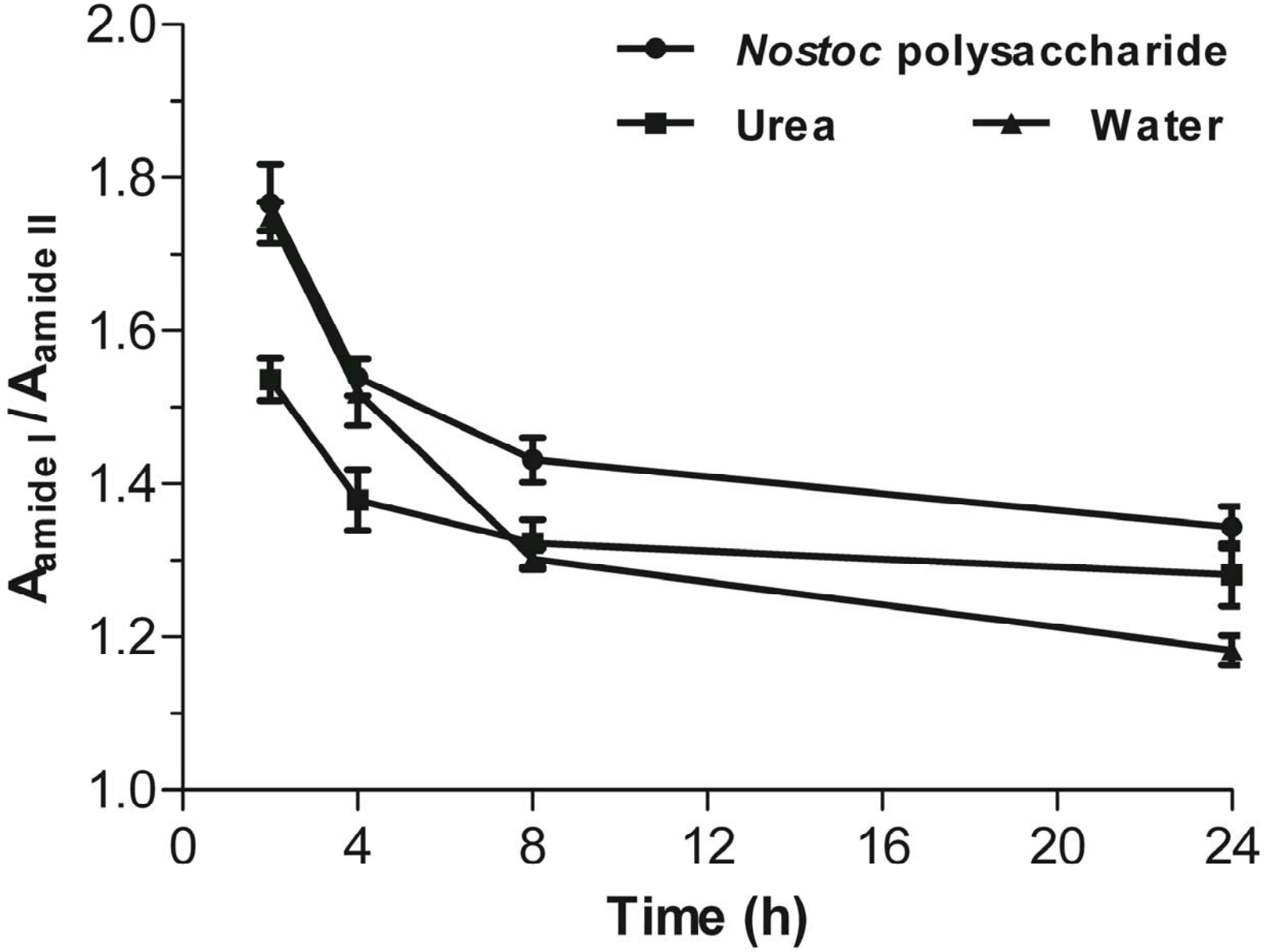


HPAEC-PAD:
High pH anion exchange chromatography – pulse amperometric detection





Li H et al. (2011) *Carbohydr Polym* 83: 1821–1827.



Li H et al. (2011) *Carbohydr Polym* 83: 1821–1827.

***Nostoc commune*: harboring UV-A/B absorbing pigments; survival in areas of extreme UV radiation as well.**

证书号第835402号

发明专利证书

发明名称：念珠藻多糖在营养保湿型化妆品中的应用

发明人：黄泽波;许娟;刘永梅;李海峰;刘永平;李章伟

专利号：ZL 2009 1 0063907.1

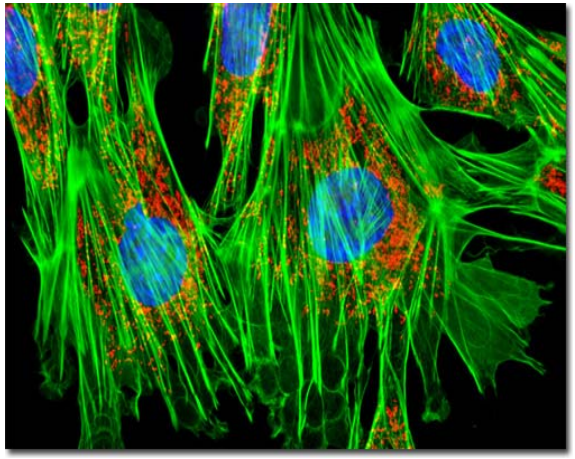
专利申请日：2009年09月08日

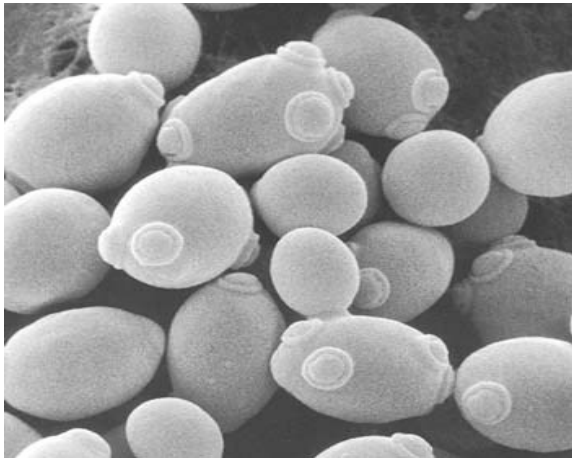
专利权人：武汉大学

授权公告日：2011年09月07日

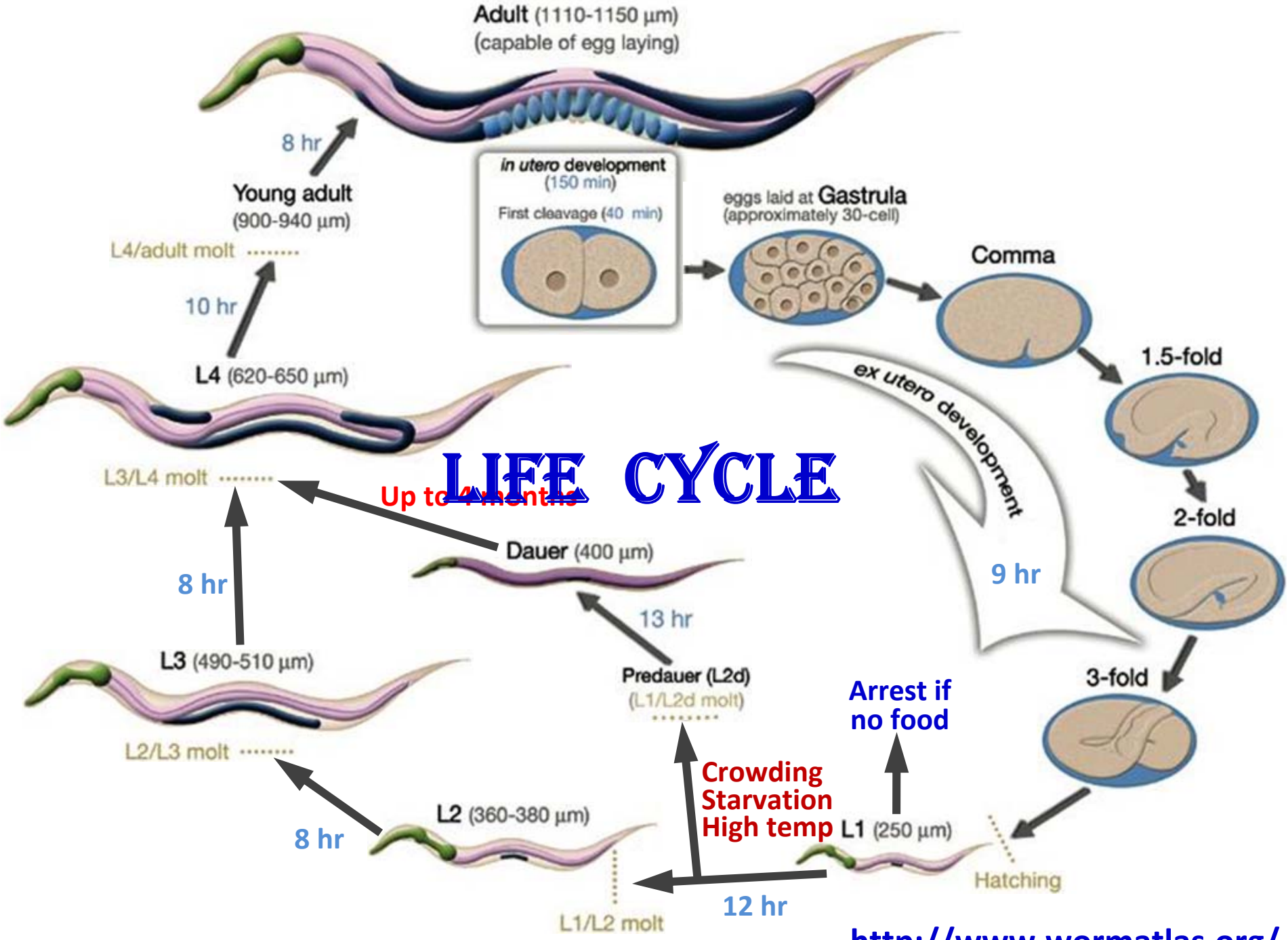
In vivo screening

Functional assays in living cells and organisms

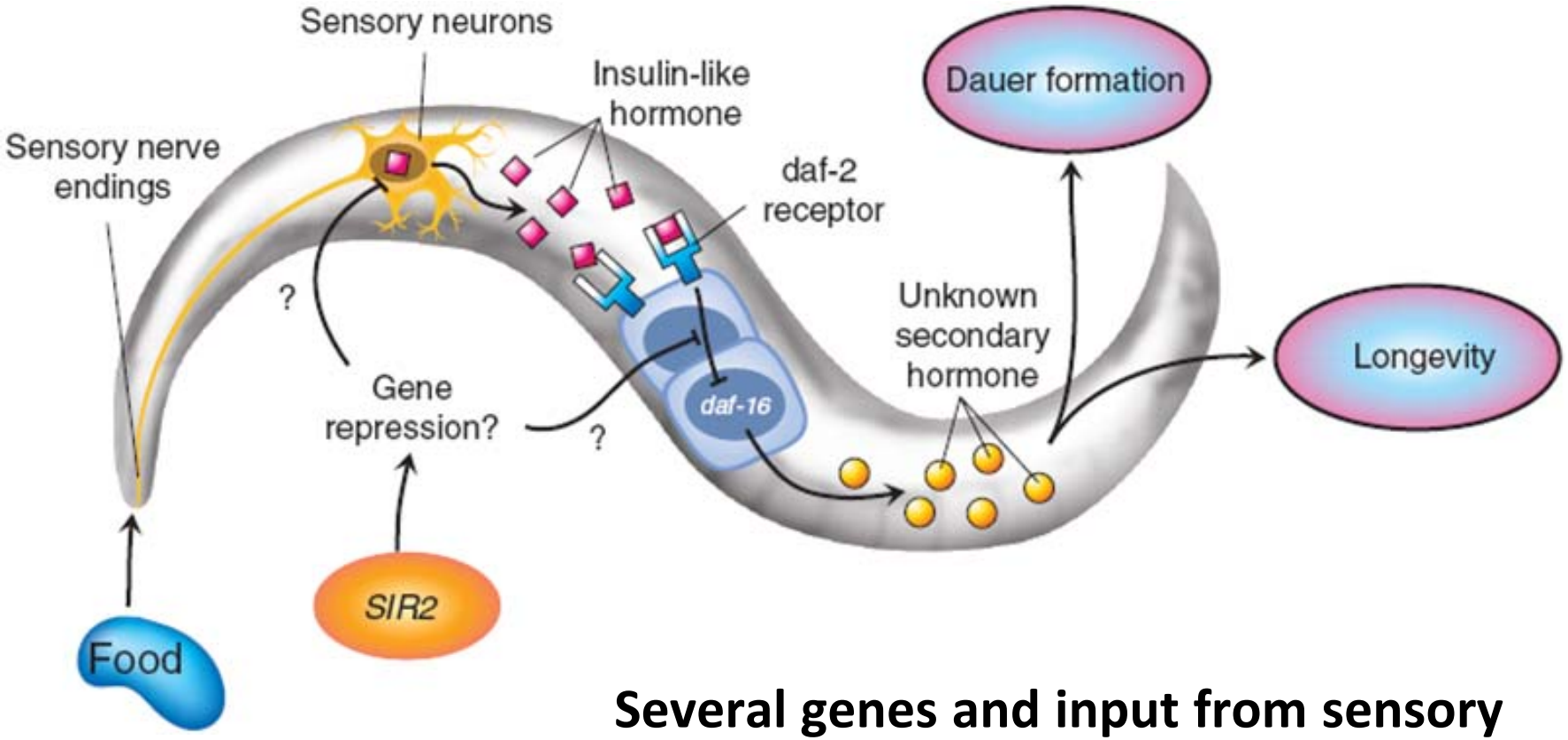




well-characterised models


Adult (1110-1150 µm)
(capable of egg laying)
8 hr
Young adult
(900-940 µm)
L4/adult molt
10 hr
L4 (620-650 µm)
L3/L4 molt
8 hr
L3 (490-510 µm)
L2/L3 molt
8 hr
L2 (360-380 µm)
L1/L2 molt
12 hr
L1 (250 µm)
Hatching
Arrest if
no food
Crowding
Starvation
High temp
Predauer (L2d)
(L1/L2d molt)
13 hr
Dauer (400 µm)
Up to 4 months
in utero development
(150 min)
First cleavage (40 min)
eggs laid at Gastrula
(approximately 30-cell)
Comma
1.5-fold
2-fold
3-fold
ex utero development
9 hr
LIFE CYCLE
http://www.wormatlas.org/

C. elegans: ageing signalling

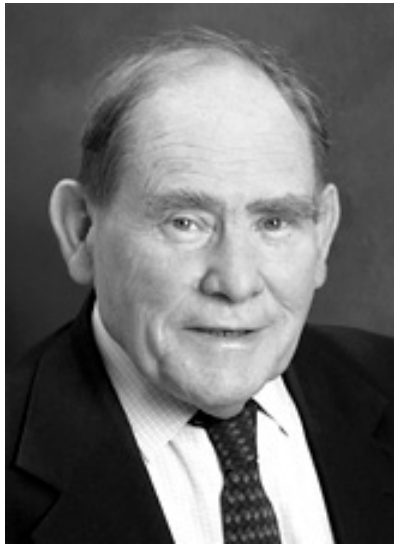


Several genes and input from sensory organs and the reproductive system influence the pace of ageing.

Leslie M (2001) *Science Aging Knowledge Environment* (1): oa1.

C. elegans and Nobel Prize

The Nobel Prize in Physiology or Medicine 2002



Sydney Brenner

H. Robert Horvitz

John E. Sulston

…for their discoveries concerning 'genetic regulation of organ development and programmed cell death'

C. elegans and Nobel Prize

The Nobel Prize in Physiology or Medicine 2006

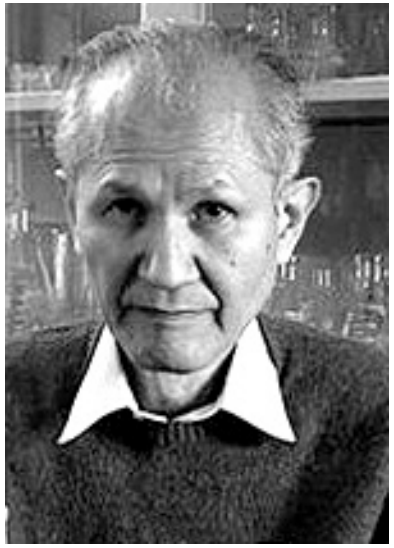
Andrew Z. Fire

Craig C. Mello

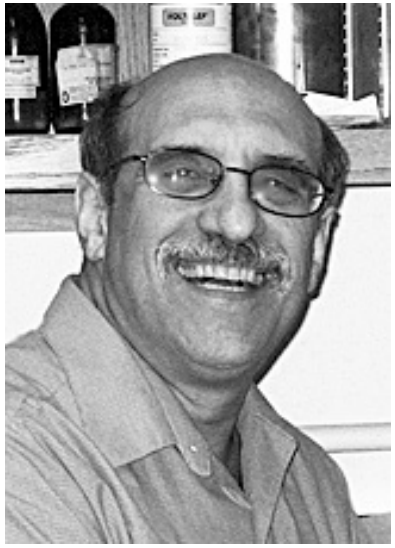
…for their discovery of RNA interference – gene silencing by double-stranded RNA

C. elegans and Nobel Prize

The Nobel Prize in Chemistry 2008



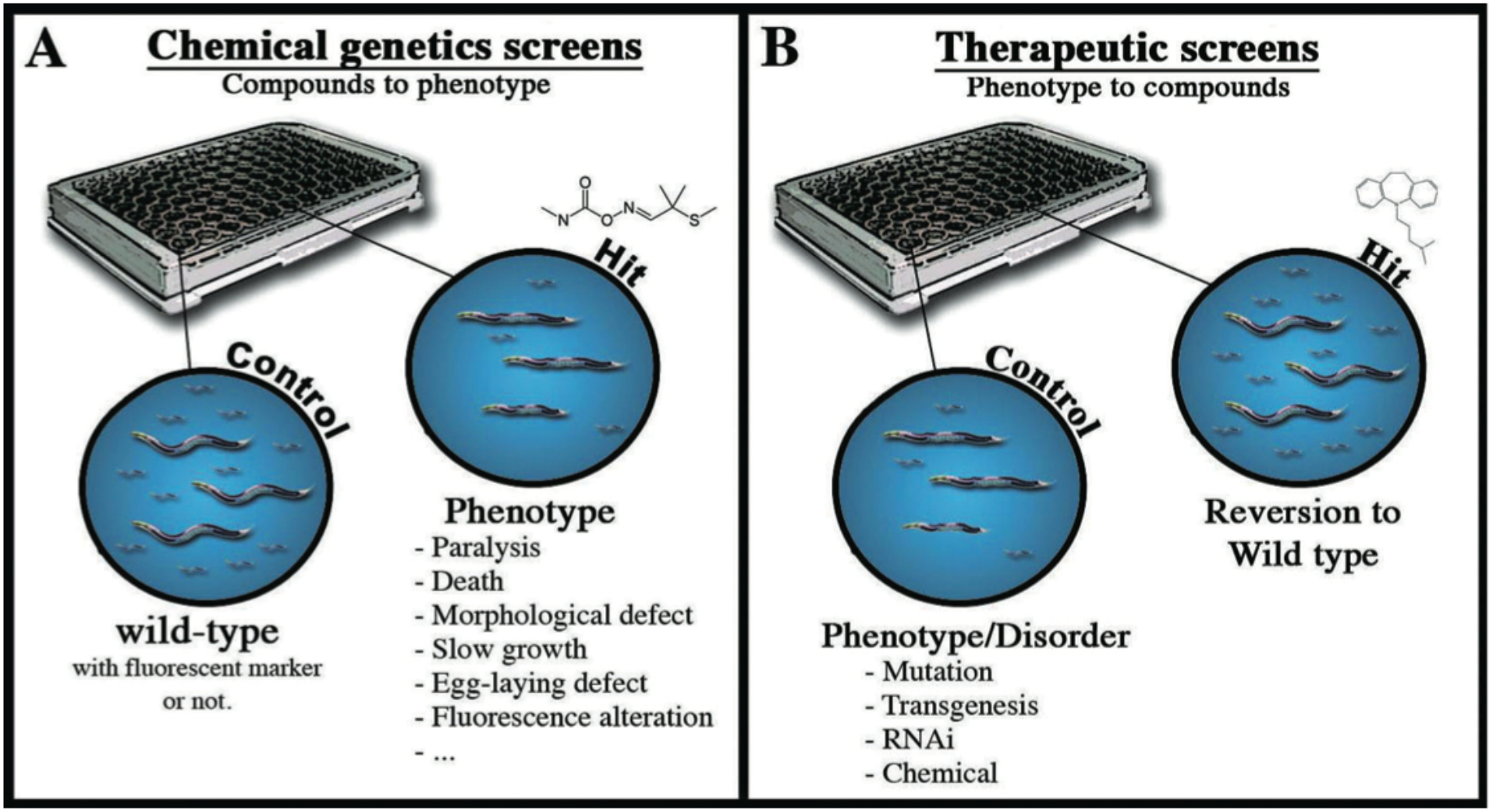
Osamu Shimomura



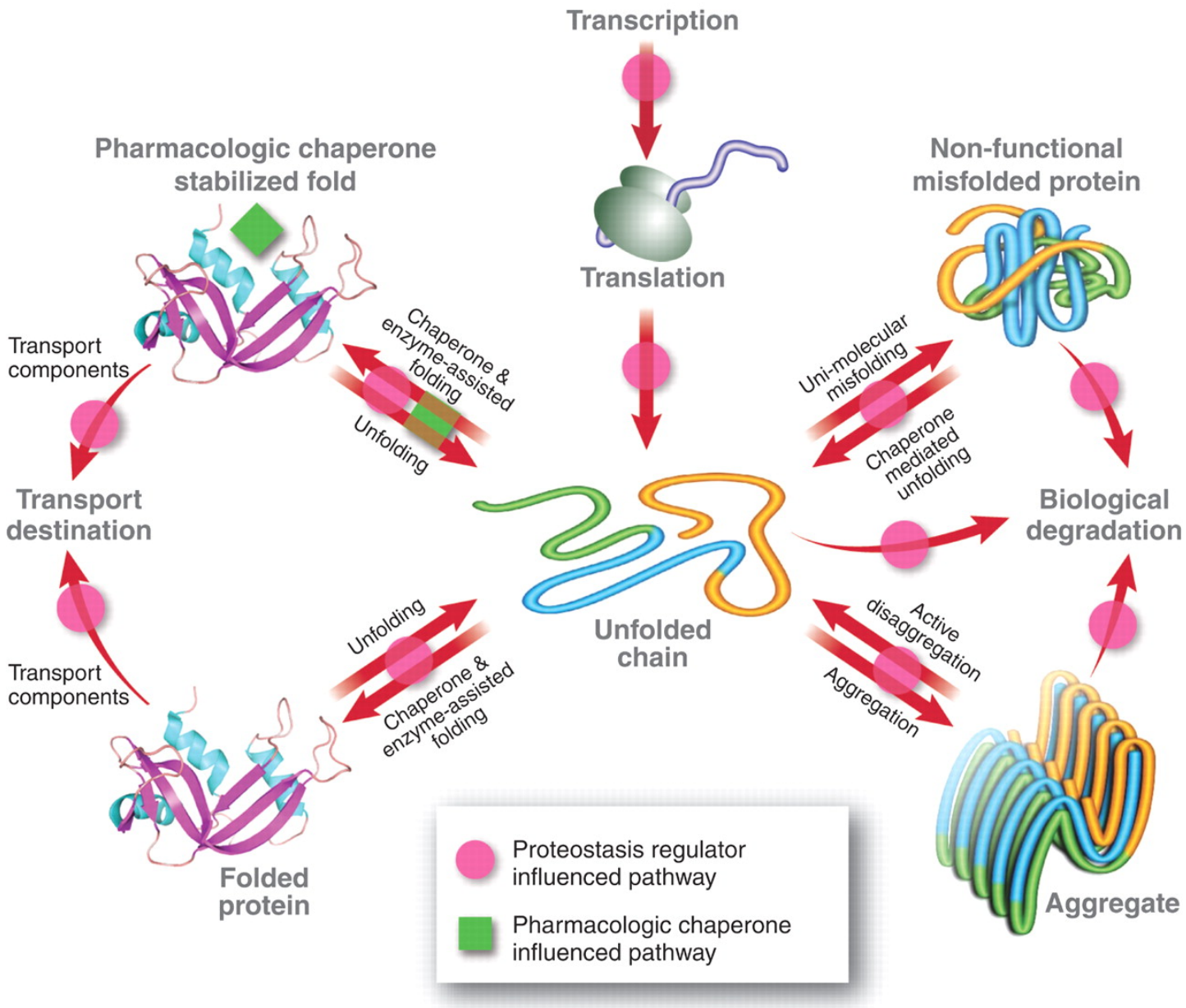
Martin Chalfie

Roger Y. Tsien

… for the discovery and development of the green fluorescent protein, GFP



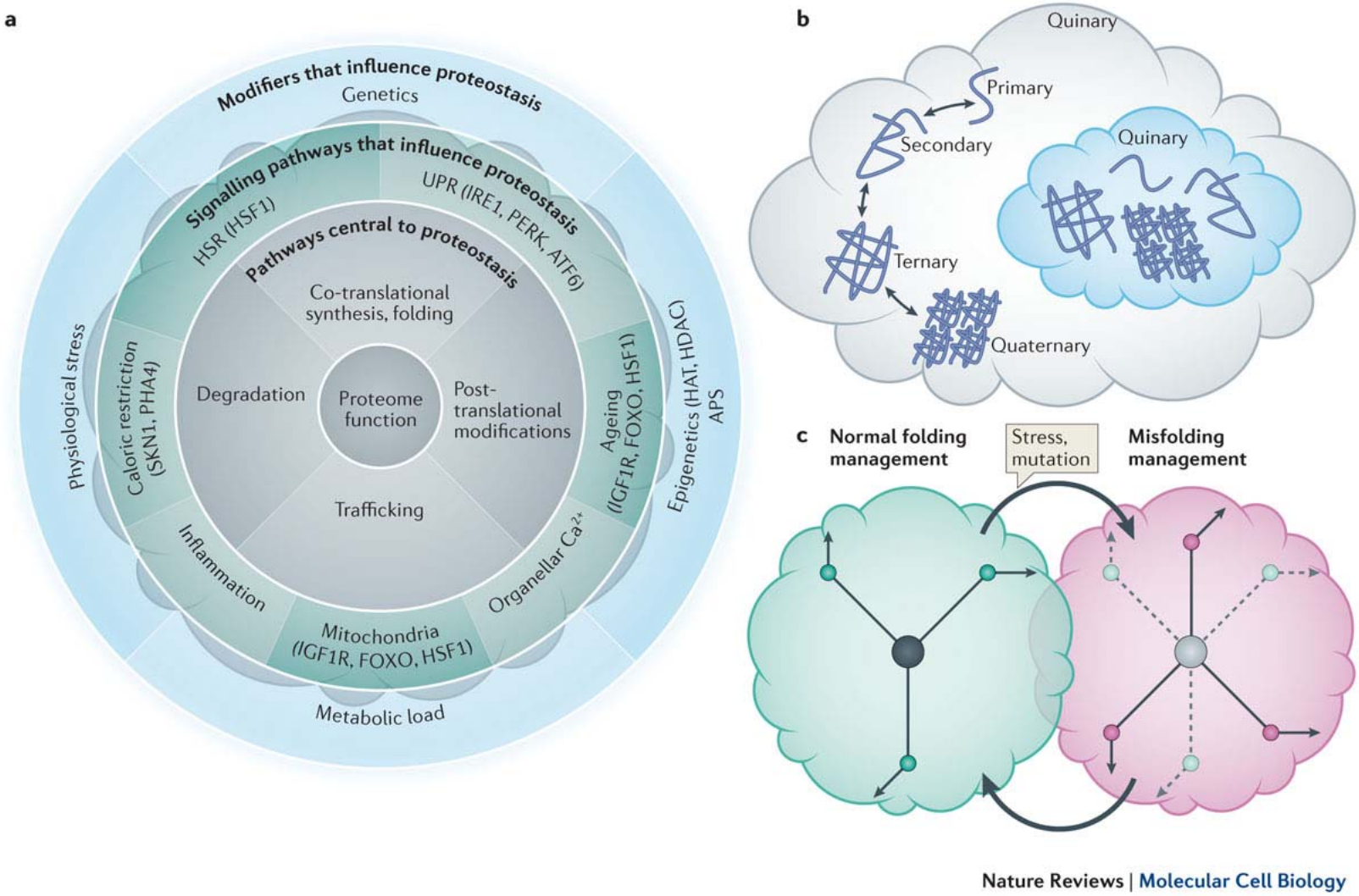
Giacomotto J & Ségalat L (2010) *Br J Pharmacol* 160: 204–216.



Protein homeostasis

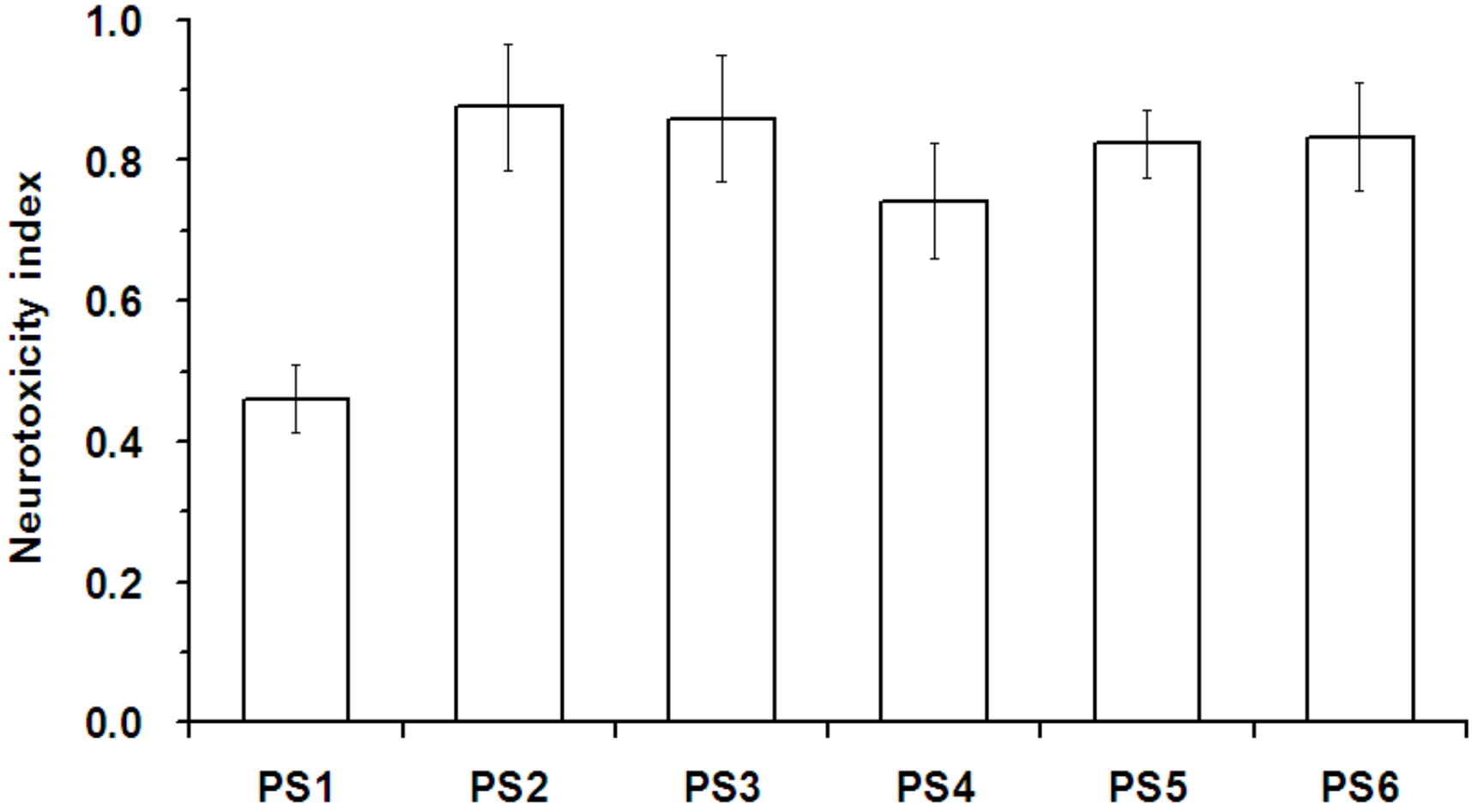
Balch WE et al. (2008) *Science* 319: 916–919.

Proteostasis network functioning as a cloud



Powers ET & Balch WE (2013) *Nat Rev Mol Cell Biol* 14: 237-248.

Polysaccharides from anti-aging herbs: neuroprotective screening



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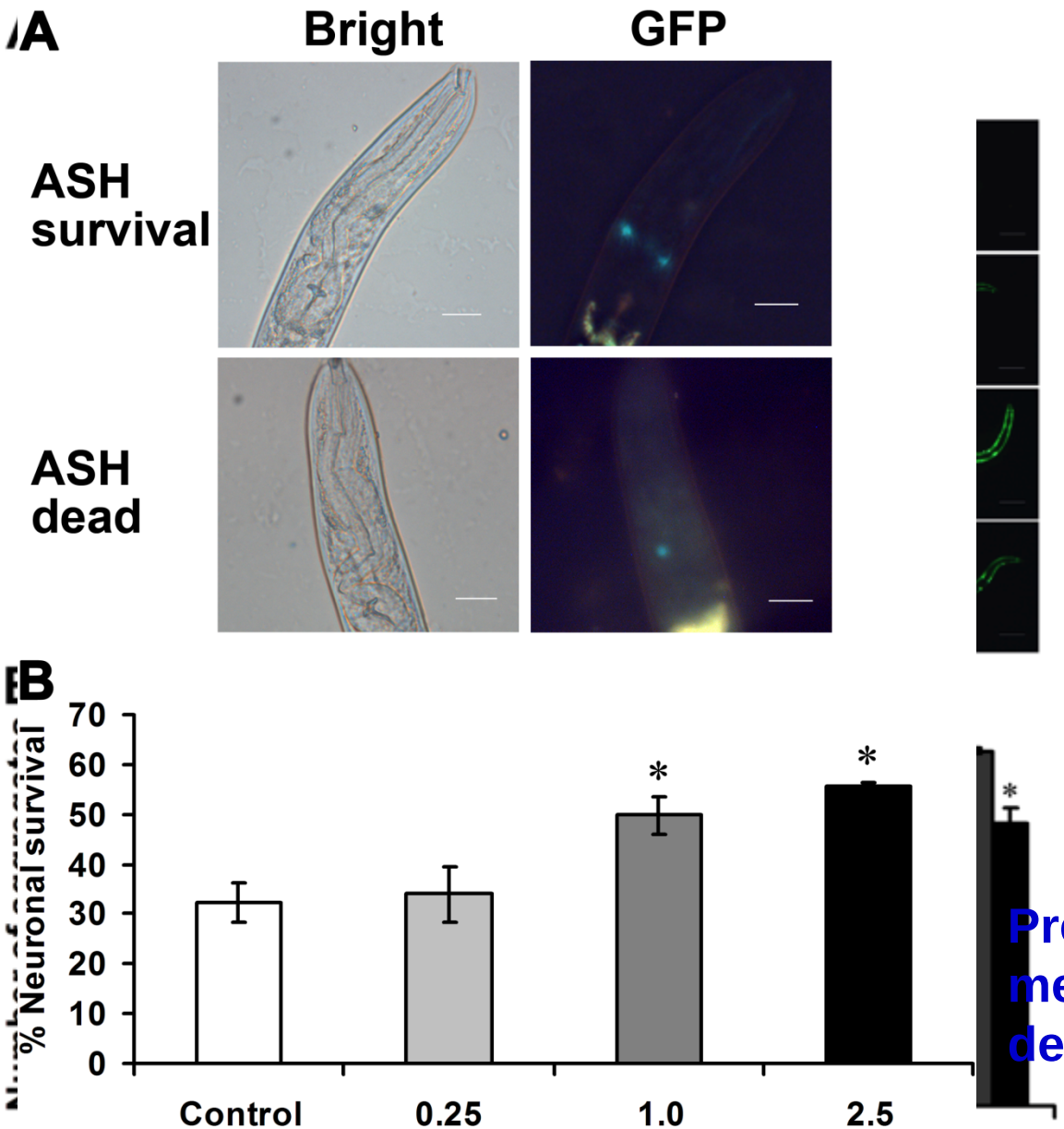
Zhang H et al. (2012) *Biochem J* 441: 417–424.



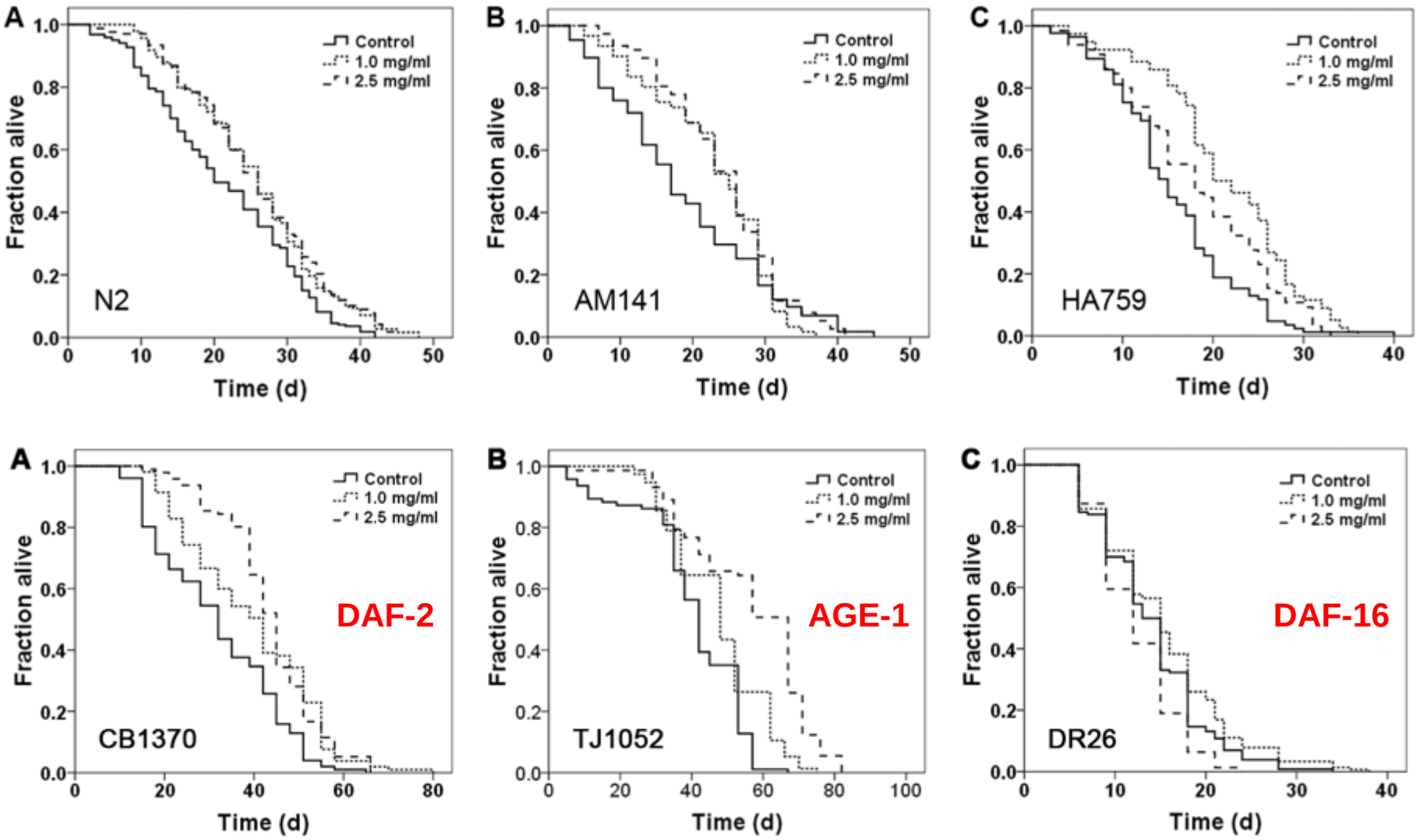
Reduction of polyQ40 aggregation in *C. elegans* AM141

Polysaccharide from *Astragalus membranaceus*

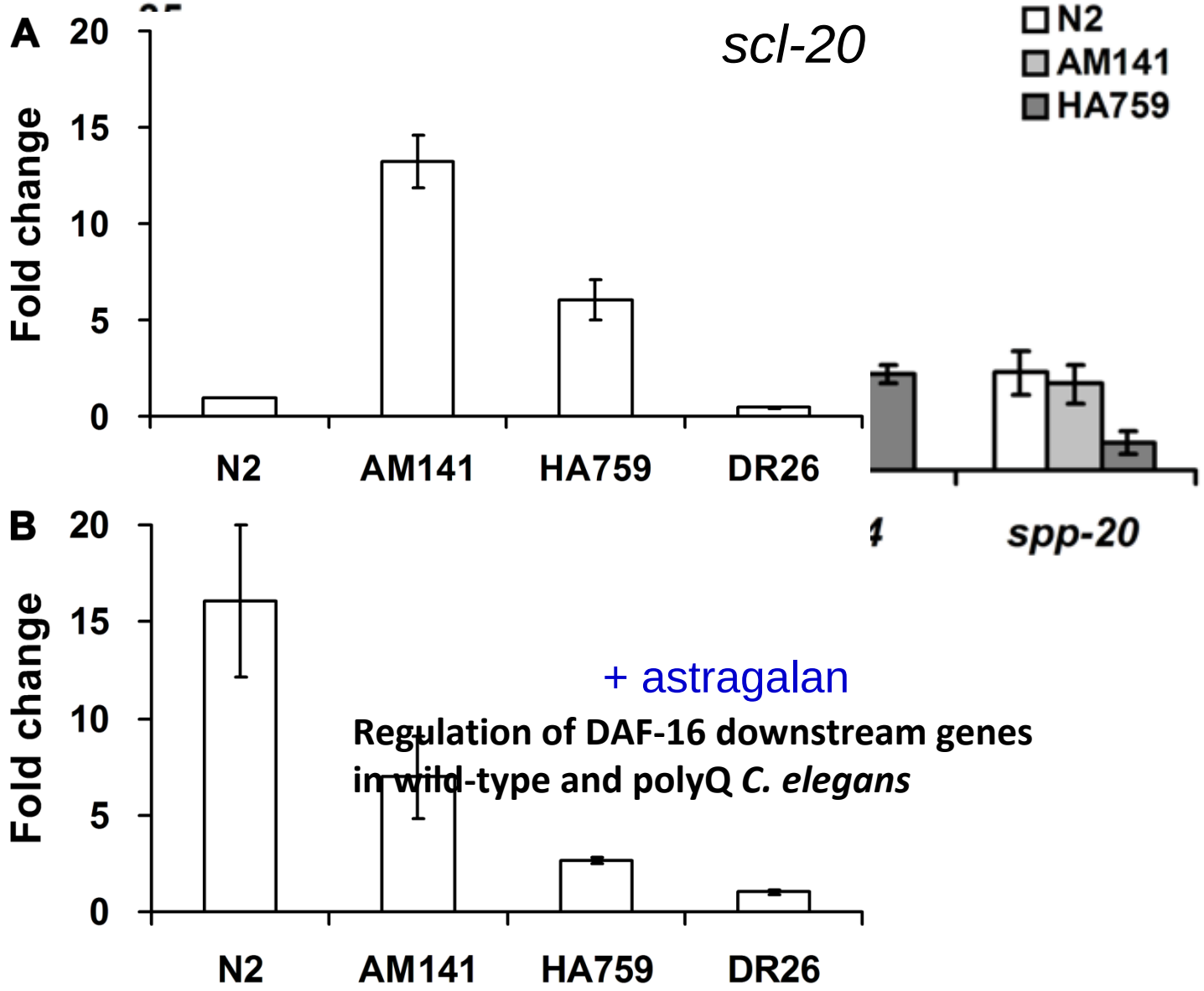
Prevention of polyQ150-mediated ASH neuronal death in *C. elegans* HA759

Zhang H et al. (2012) *Biochem J* 441: 417–424.

Lifespan-extending effect of astragalan in *C. elegans*



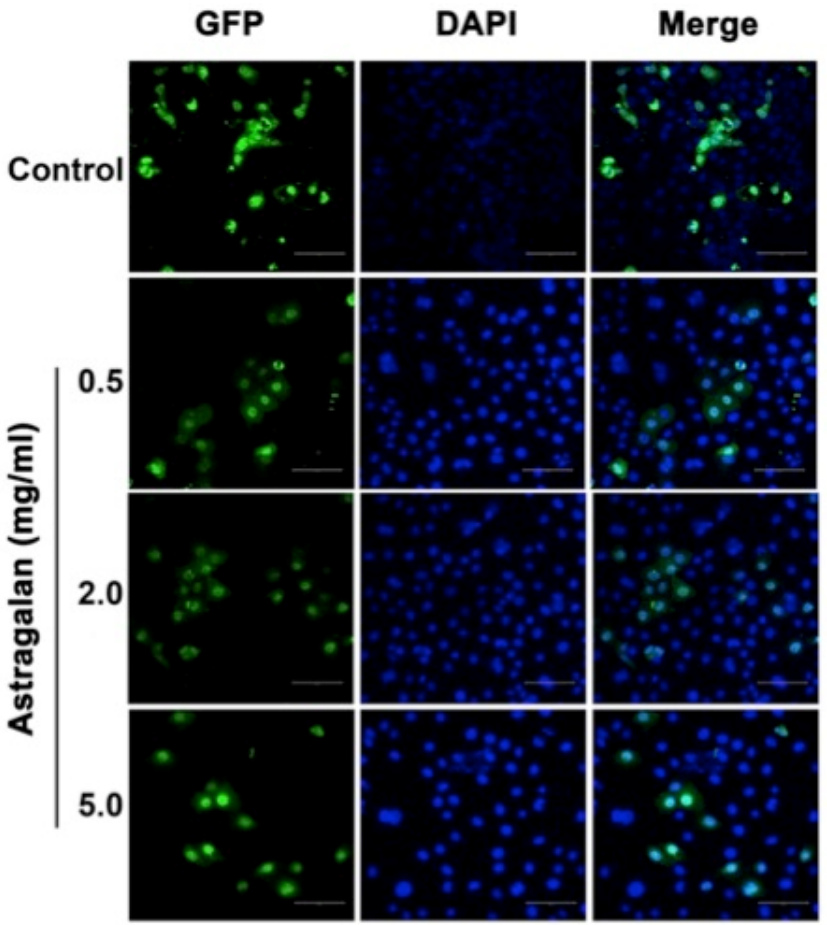
Zhang H et al. (2012) *Biochem J* 441: 417–424.

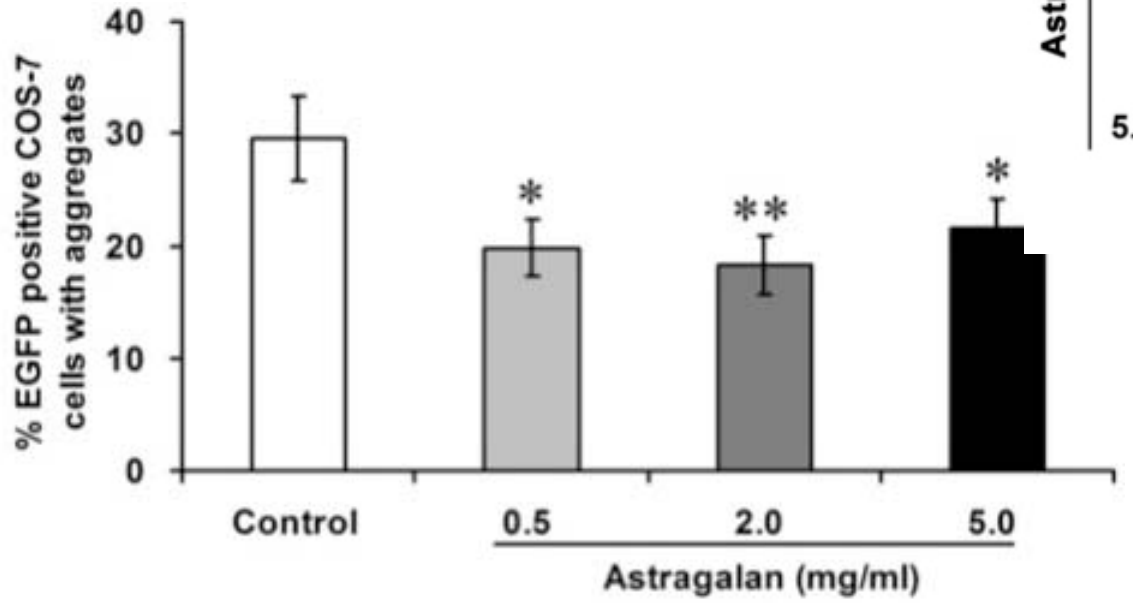


scl-20 (*dct-2*) encodes a predicted SCP-like extracellular protein homologous to mammalian GliPR1 and functions to regulate both lifespan and tumor cell proliferation.

Zhang H et al. (2012) *Biochem J* 441: 417–424.

Reduction of HDQ74 aggregation by astragalan in COS-7 cells





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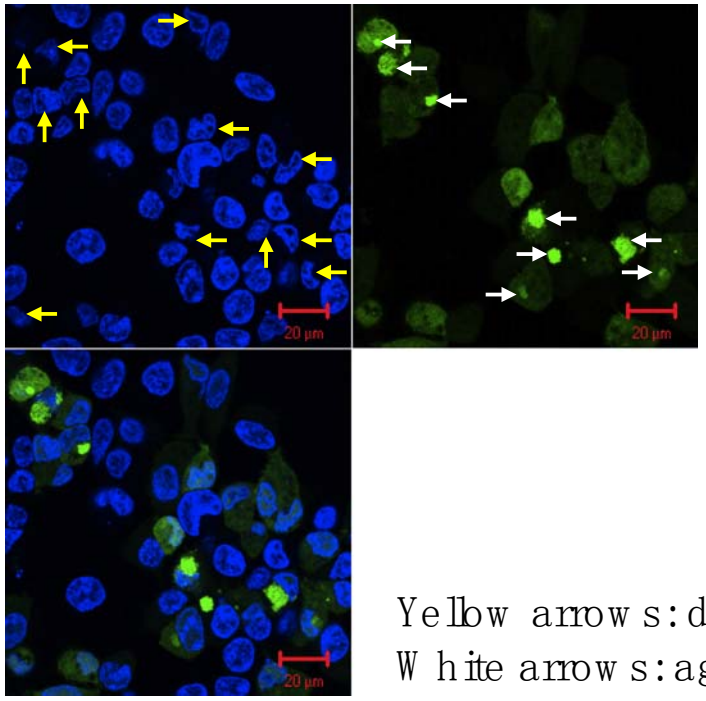
Zhang H et al. (unpublished data).

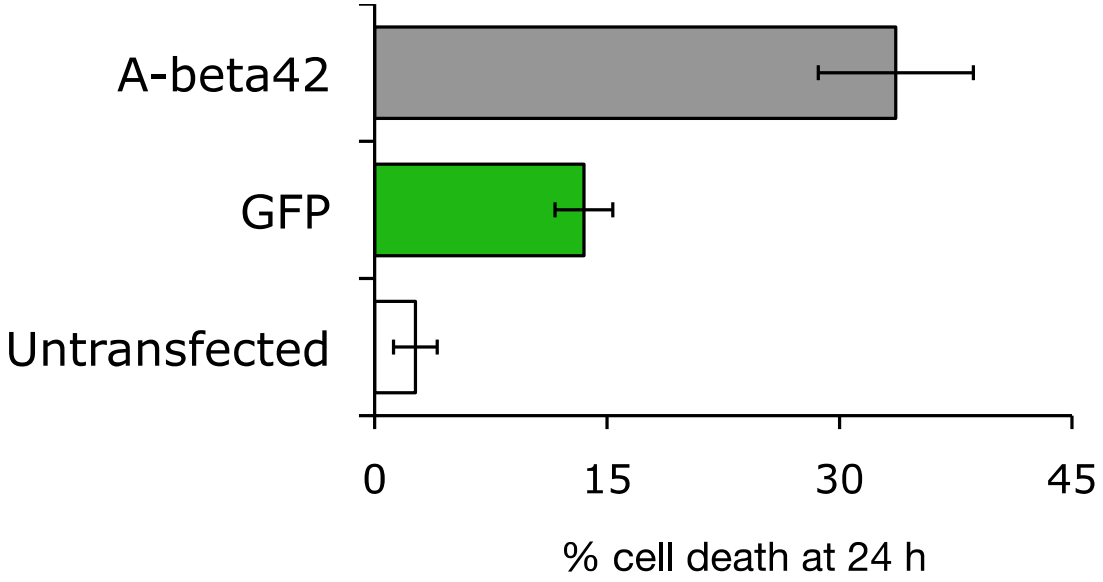
Polysaccharides for effect on intracellular $A\beta_{42}$-EGFP aggregation

sample	source of polysaccharide (Latin name)	source of polysaccharide (Chinese name)	% aggregation relative to untreated cells	standard deviation
	none (control: $A\beta_{42}$-EGFP only)		100	2
PS1	*Astragalus membranaceus* (Fisch.) Bge.	Huang Qi	112	3
PS2	*Achyranthes bidentata* Bl.	Niu Xi	89	1
PS4	*Cuscuta chinensis* Lam.	Tu Si Zi	131	3
PS5	*Rubia cordifolia* L.	Qian Cao	79	2
PS8	*Viscum coloratum* (Komar.) Nakai	Hu Ji Sheng	107	2
PS9	*Poria cocos* (Schw.) Wolf	Fu Ling	93	2
PS10	*Salvia miltiorrhiza* Bge.	Dan Shen	86	3
PS12	*Adenophora tetraphylla* (Thunb.) Fisch.	Nan Sha Shen	106	5
PS13	*Schisandra chinensis* (Turcz.) Baill.	Wu Wei Zi	101	2
PS14	*Rheum palmatum* L.	Da Huang	90	6
PS15	*Polygonum multiflorum* Thunb.	He Shou Wu	115	6

Chakrabortee S et al. (2012) *Biochem J* 442: 507–515.

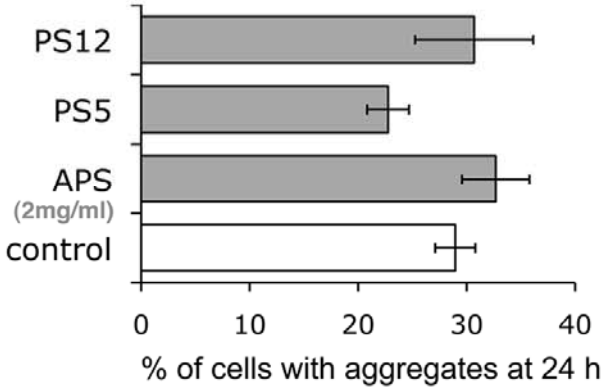
Mammalian cells expressing A β 42-GFP

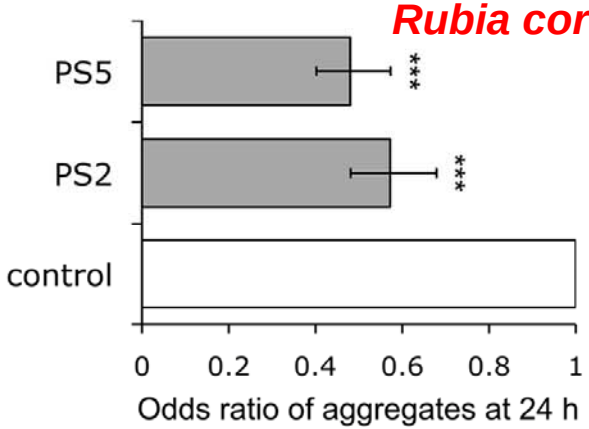


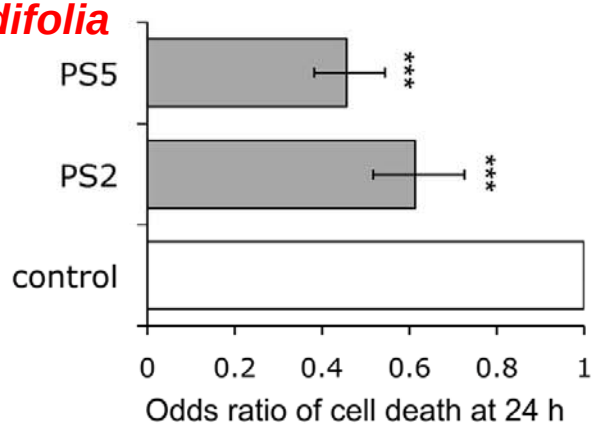


Yellow arrows: dead cells
White arrows: aggregates

Rubia cordifolia

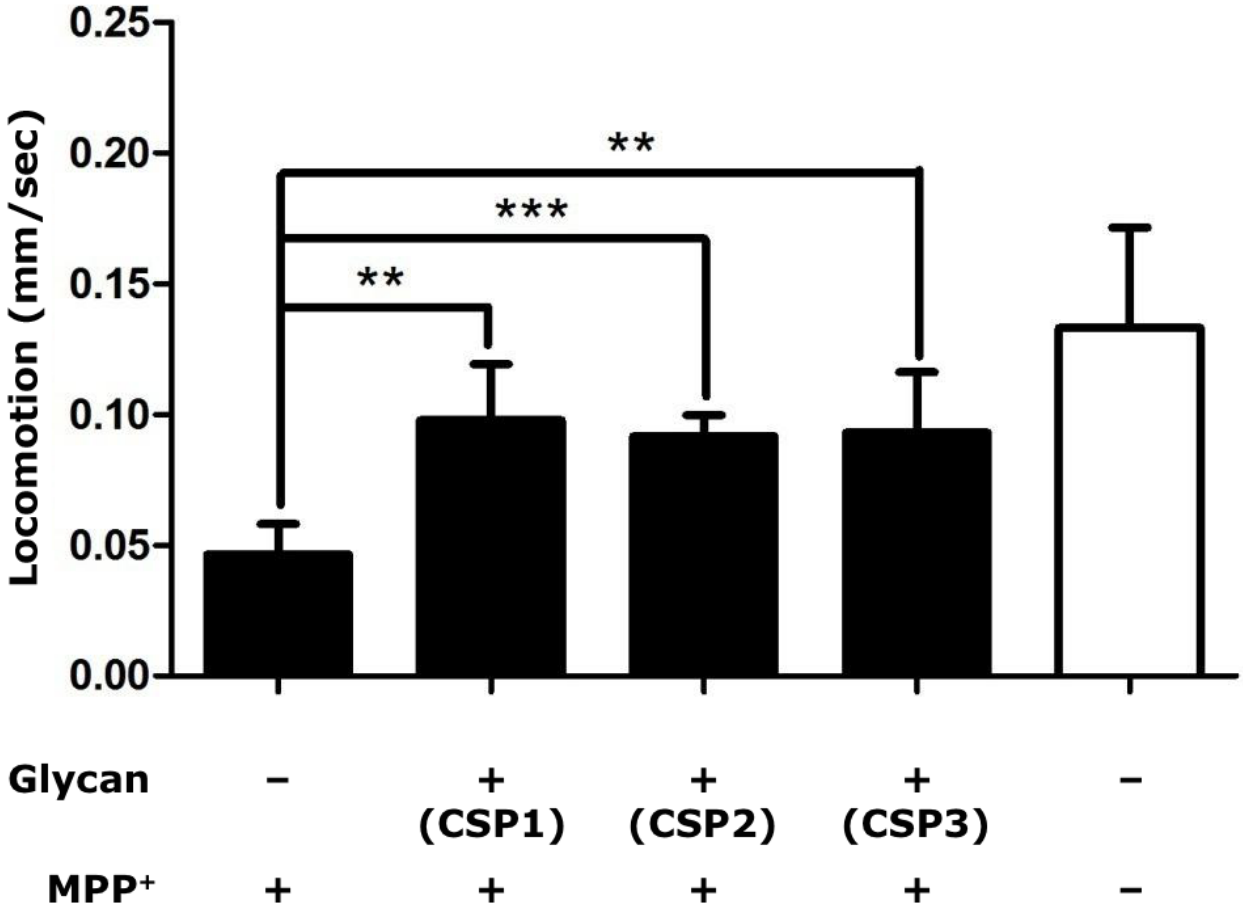






Chakrabortee S et al. (2012) *Biochem J* 442: 507–515.

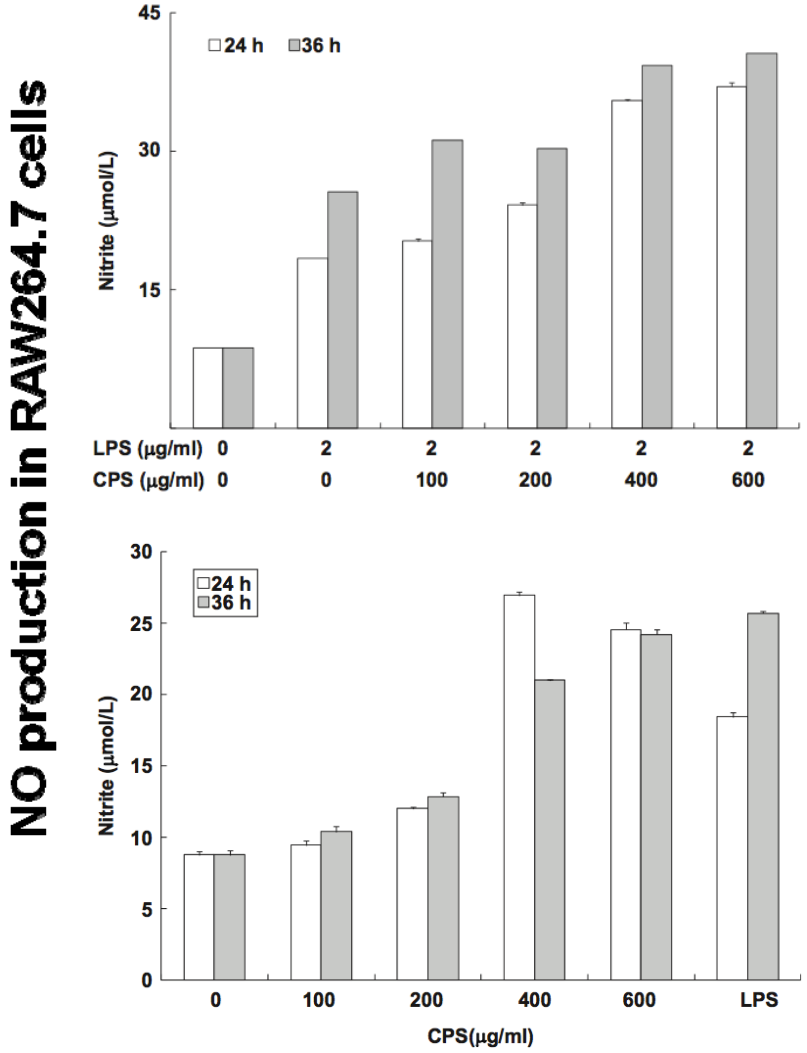
Chaenomeles speciosa polysaccharides

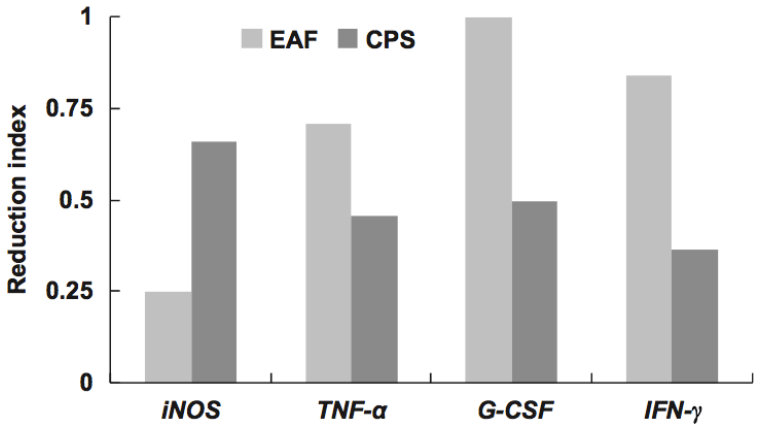


Pharmacologic suppression of MPP$^+$-induced locomotion defect in *C. elegans*

Wang Q et al. (2014) *Rejuvenation Res* 17: (in press).

Chaenomeles speciosa polysaccharide



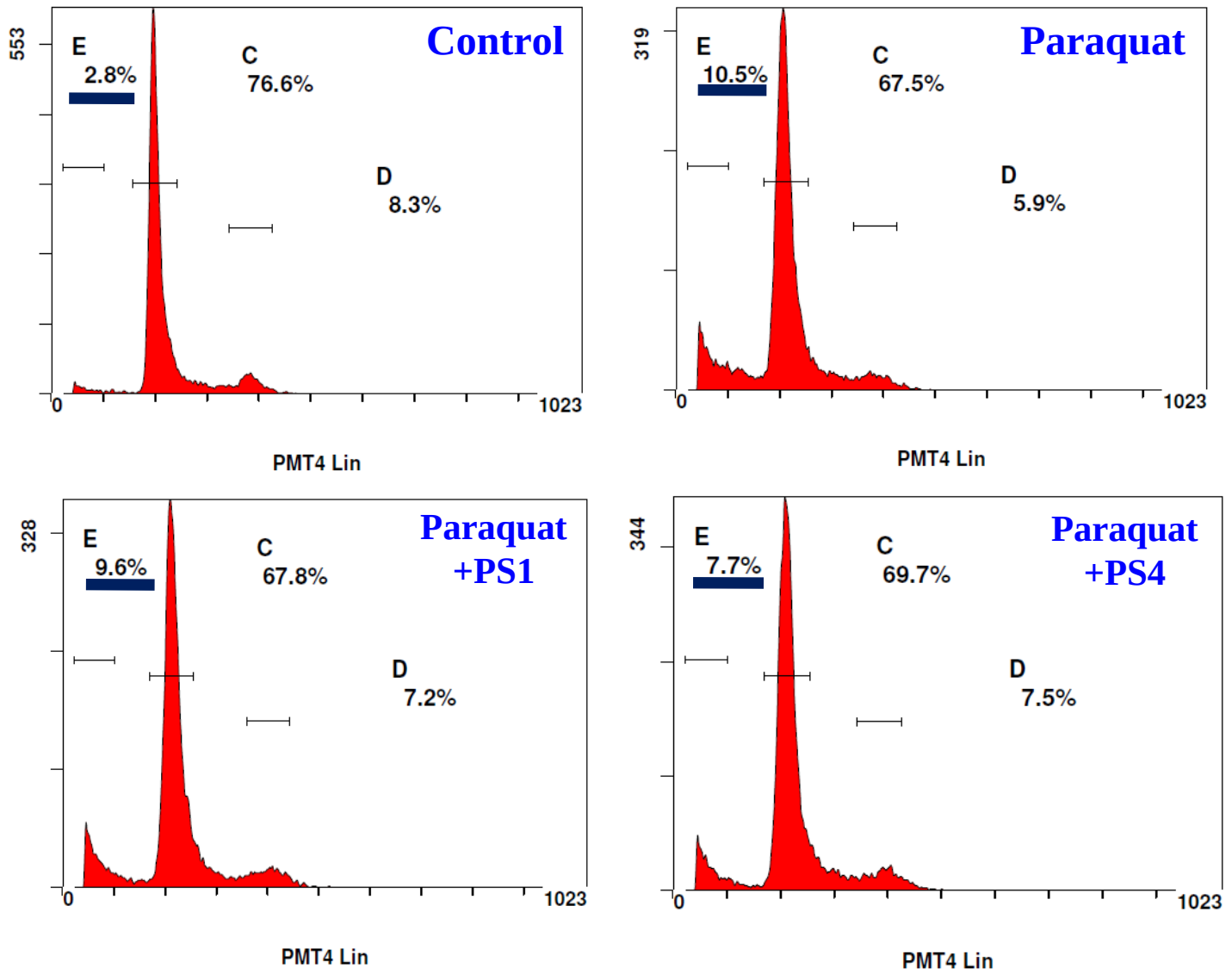


Effect on LPS-induced expression of inflammation-related genes

Modulation of nitric oxide production in macrophage cells

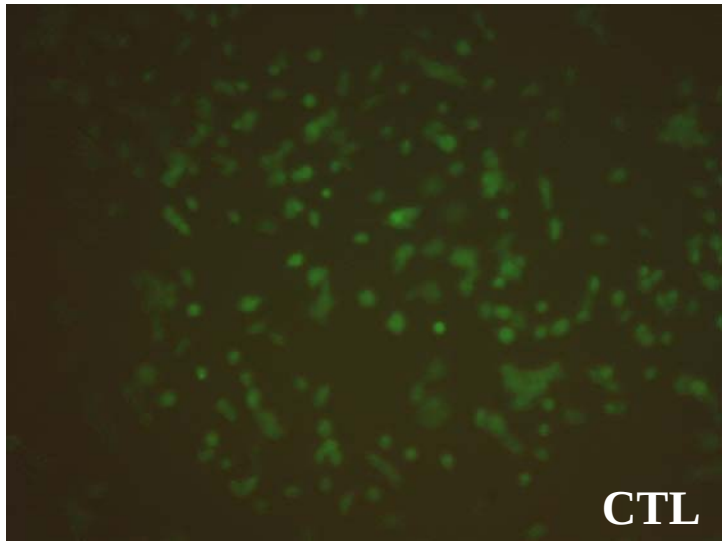
Zhu Q et al. (2012) *J Ethnopharmacol* 144: 441–447.

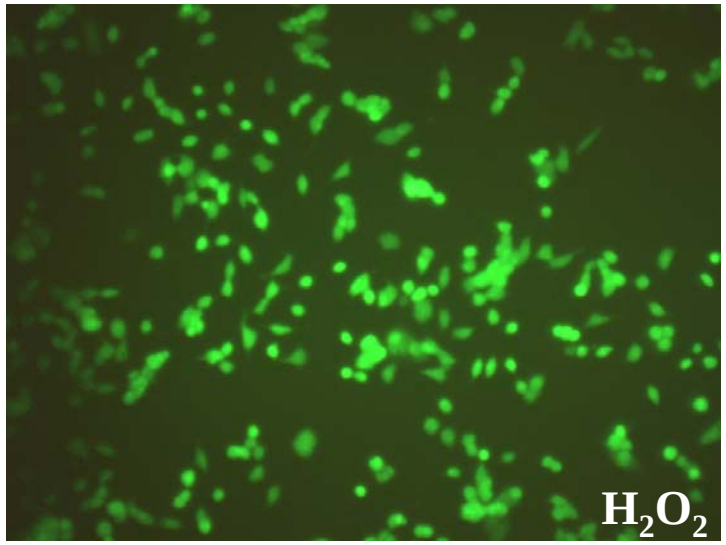
Polysaccharides reduce paraquat-induced apoptosis

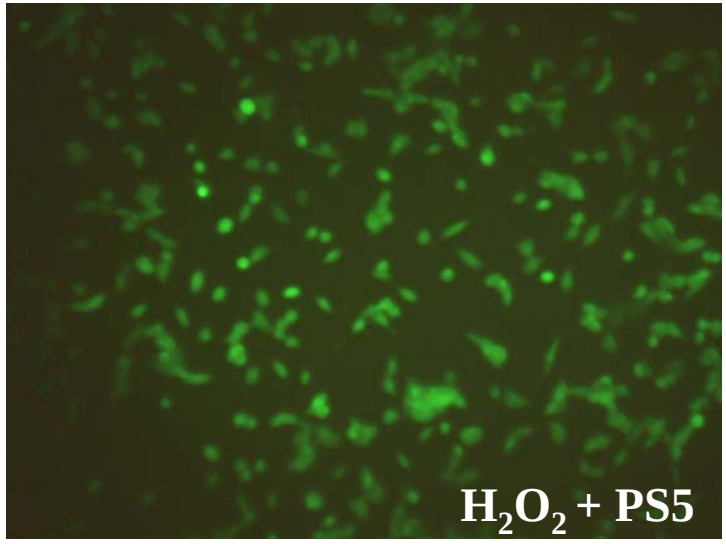


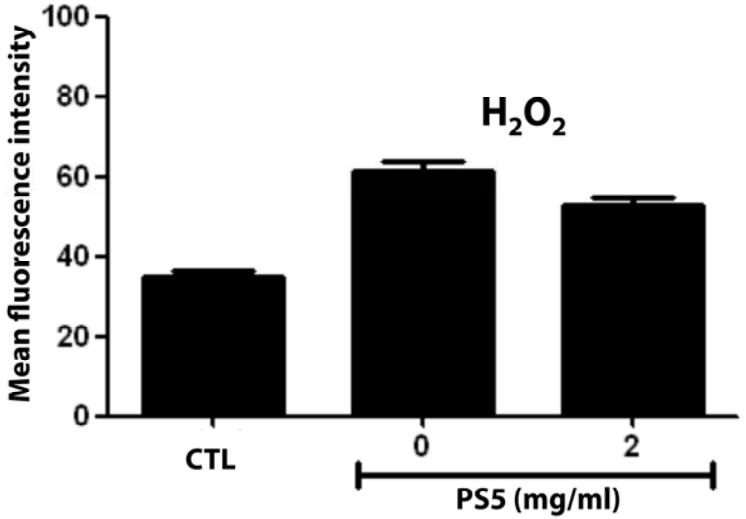
Li H et al. (unpublished data).

Polysaccharides reduce H_2O_2-elevated cellular ROS levels



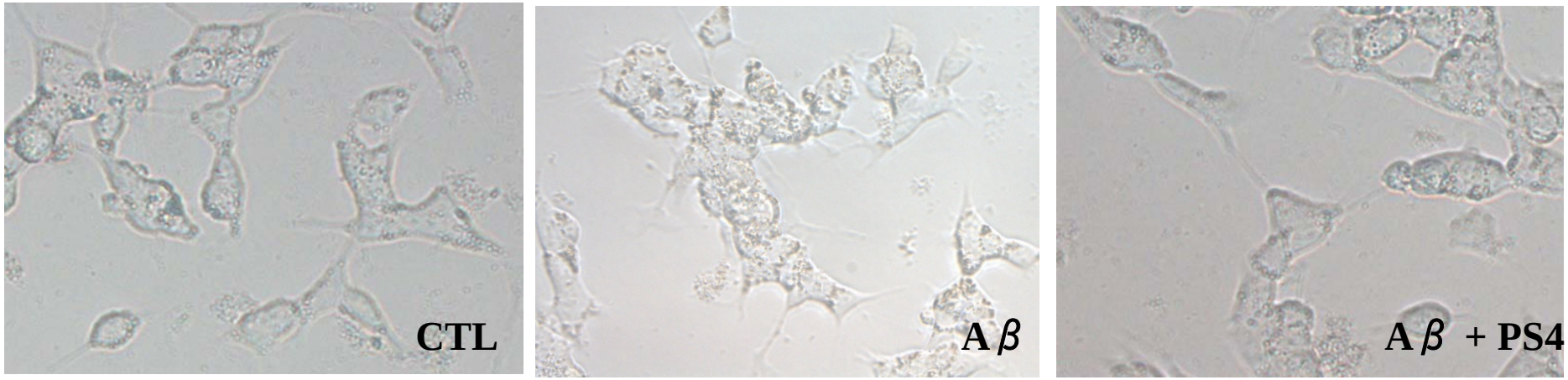


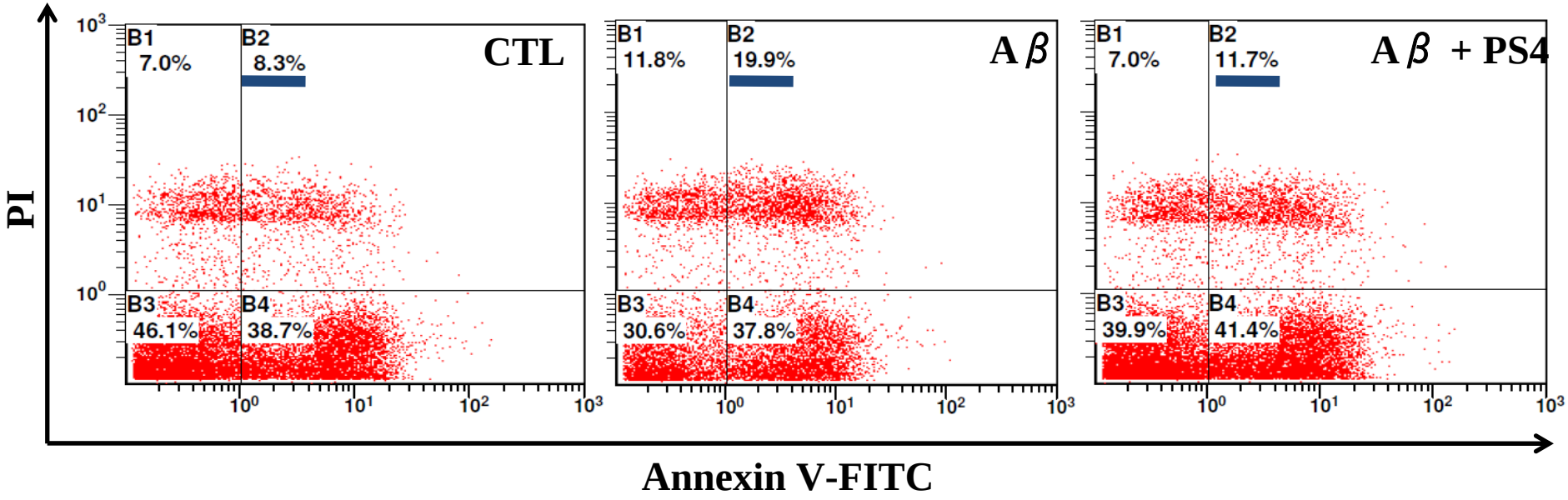




Xiao L et al. (unpublished data).

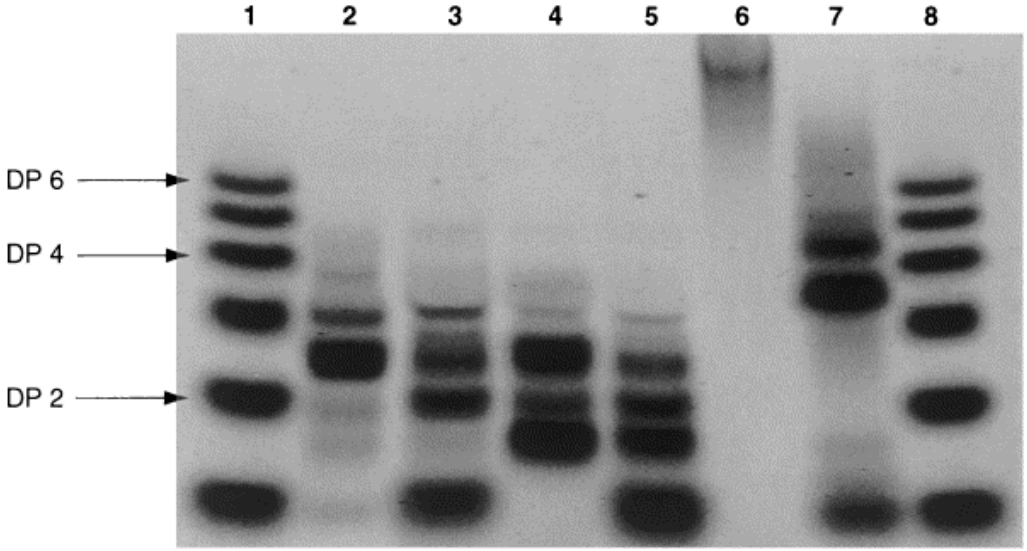
Polysaccharides reduce Aβ-induced apoptosis





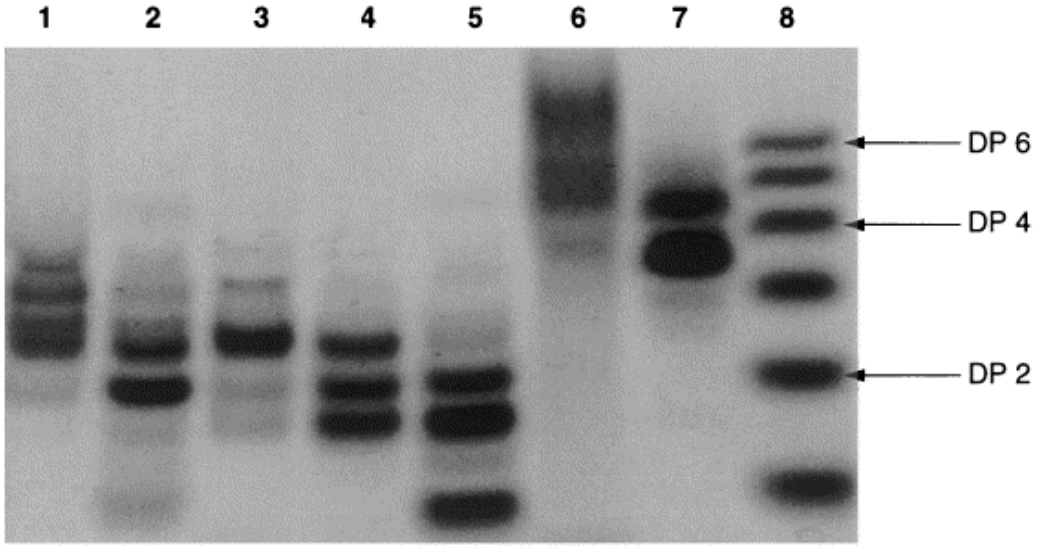
Li H et al. (unpublished data).

Nostoc polysaccharides: Protective functionality of nosturonic acid & D-ribofuranose in native EPS



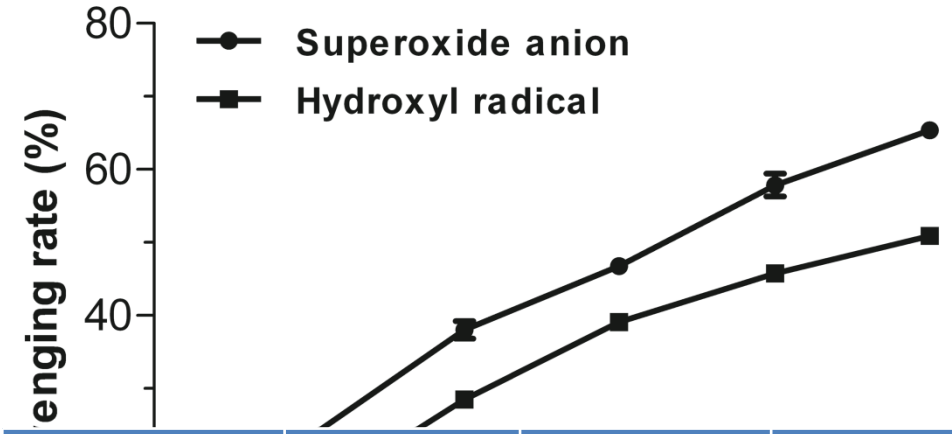
Lane 6: lithium–ethylenediamine treated *Nostoc* EPS after BioGel P2 purification and AA-labeling; **Lane 7**: oligosaccharides after the Driselase digestion and AA-labeling of the Li–EDA-treated glycan of Lane 6

Lane 6 and 7: Li–EDA-treated glycan after Driselase digestion, followed by Bio-Gel P2 purification into high (Lane 6) and low (Lane 7) molecular weight fractions.

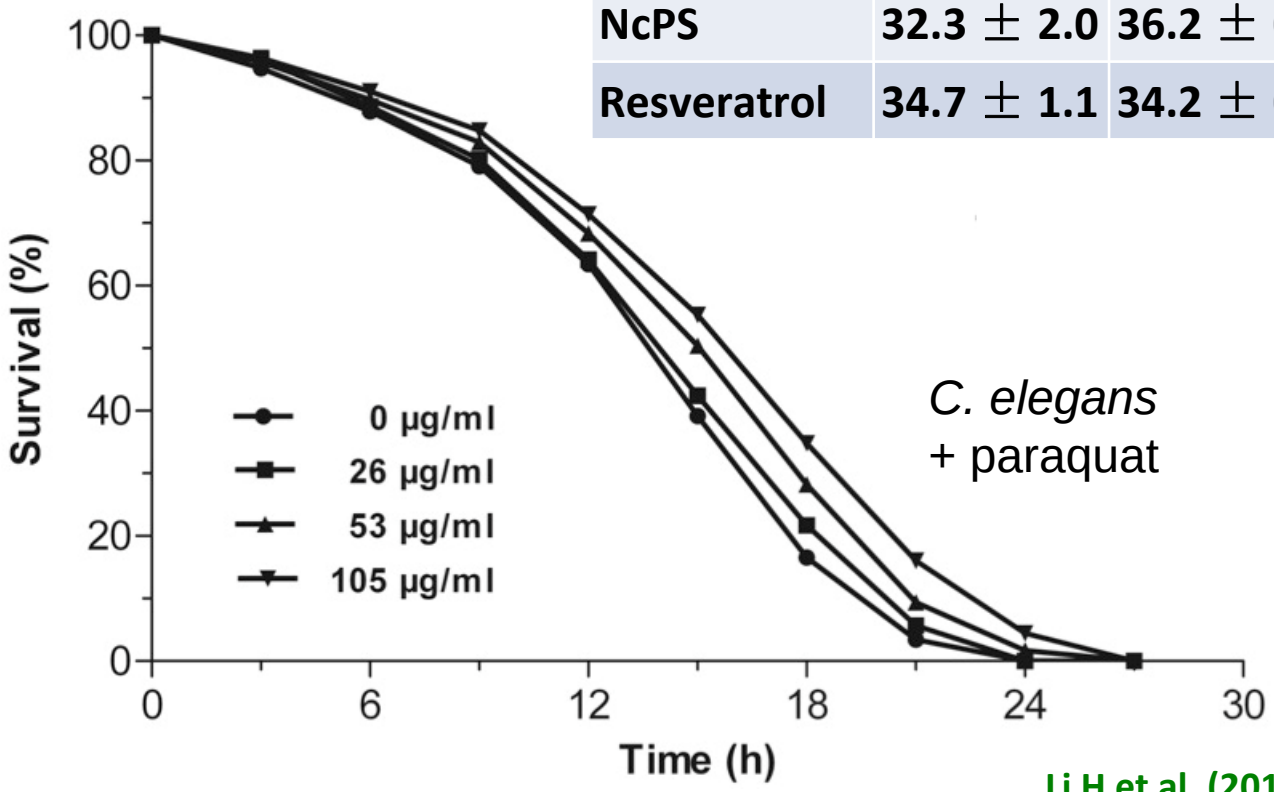


Huang Z et al. (2000) *Carbohydr Res* 328: 77–83.

Nostoc polysaccharide



C. elegans	SOD	CAT	GPX	MDA
Control	24.5 ± 1.8	31.9 ± 0.8	14.7 ± 0.5	2.1 ± 0.2
NcPS	32.3 ± 2.0	36.2 ± 0.7	16.5 ± 0.4	1.9 ± 0.1
Resveratrol	34.7 ± 1.1	34.2 ± 0.9	16.8 ± 0.5	1.9 ± 0.1



C. elegans
+ paraquat

Li H et al. (2011) *Carbohydr Polym* 83: 1821–1827.

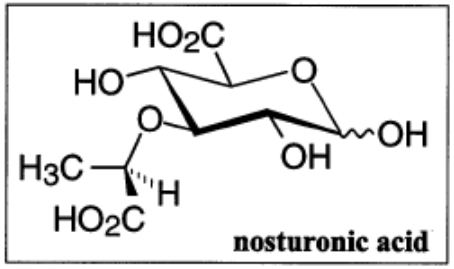
Nostoc polysaccharides

Oligosaccharide strucutres

1 β-D-Glc*p*-(1→4)-D-Xyl*p*

β-D-NosA
1
↓
6

2 β-D-Glc*p*-(1→4)-D-Gal*p*



β-D-NosA
1
↓
6

3 β-D-Glc*p*-(1→4)-α-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→4)-D-Xyl*p*

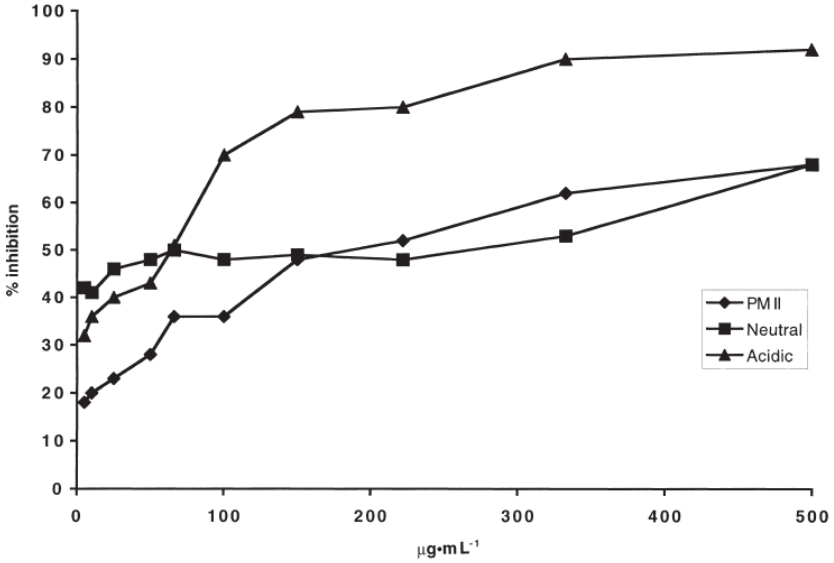
β-D-NosA
1
↓
6

4 β-D-Glc*p*-(1→4)-β-D-Xyl*p*-(1→4)-β-D-Glc*p*-(1→4)-D-Gal*p*

β-D-NosA
1
↓
6

5 β-D-Glc*p*-(1→4)-α-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→4)-D-Xyl*p*
3
↑
1
α-D-Rib*f*

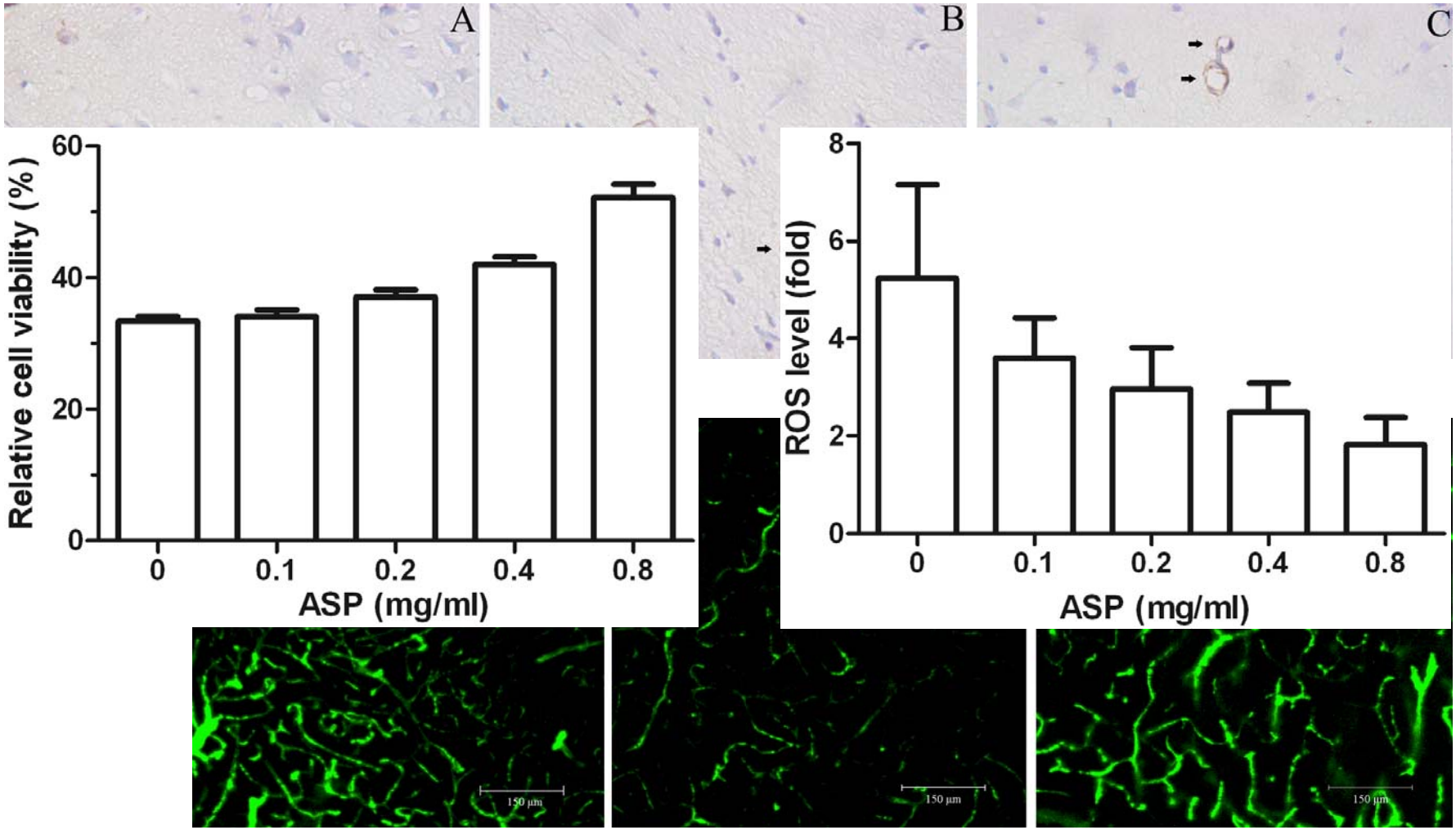
Complement inhibition



Huang Z et al. (2000) *Carbohydr Res* 328: 77–83.
Helm RF et al. (2000) *J Bacteriol* 182: 974–982.
Brüll LP et al. (2000) *J Phycol* 36: 871–881.

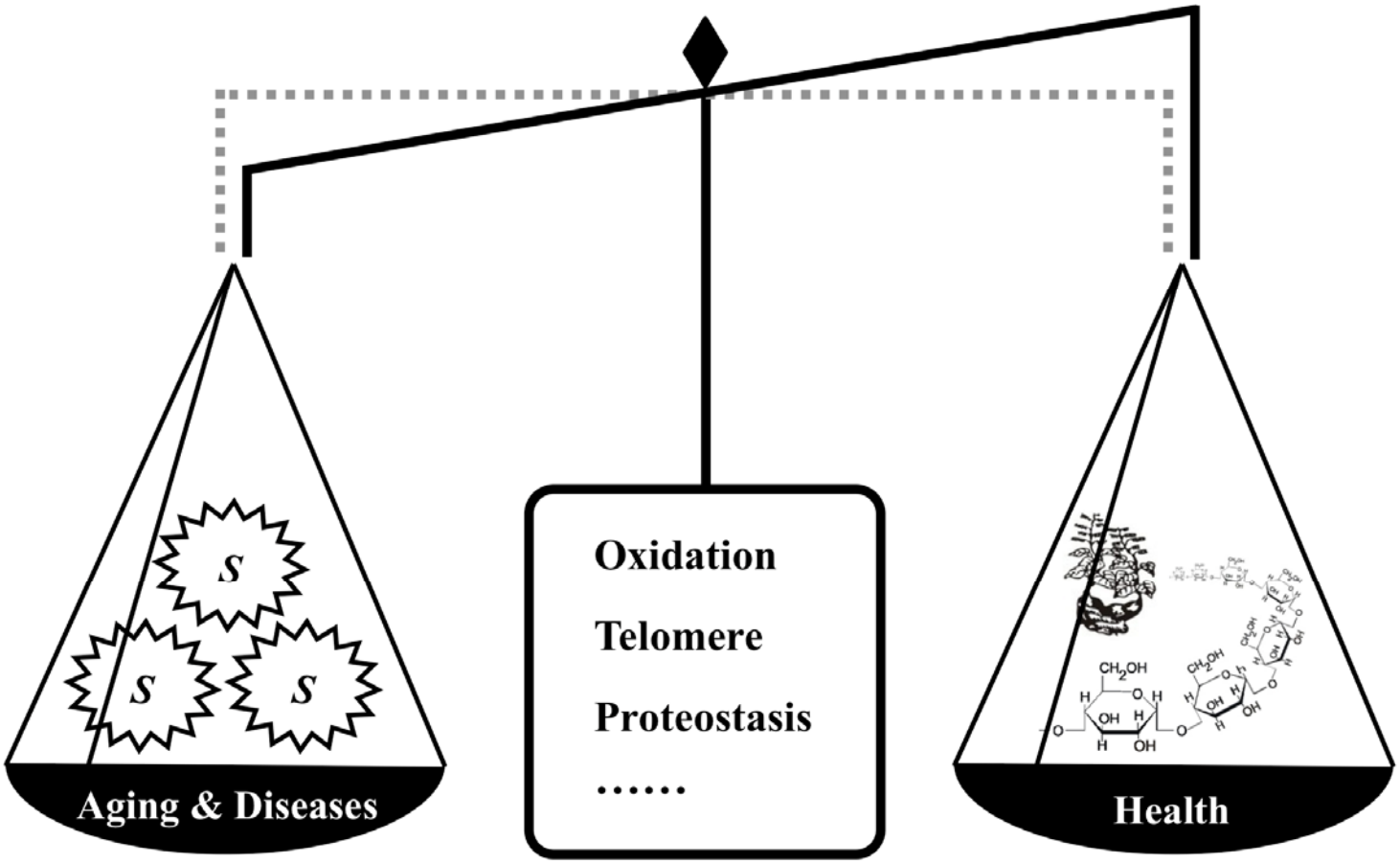
Angelica sinensis polysaccharides:

Ameliorating oxidative stress in PC12 cells & ischemic brain injury in rats



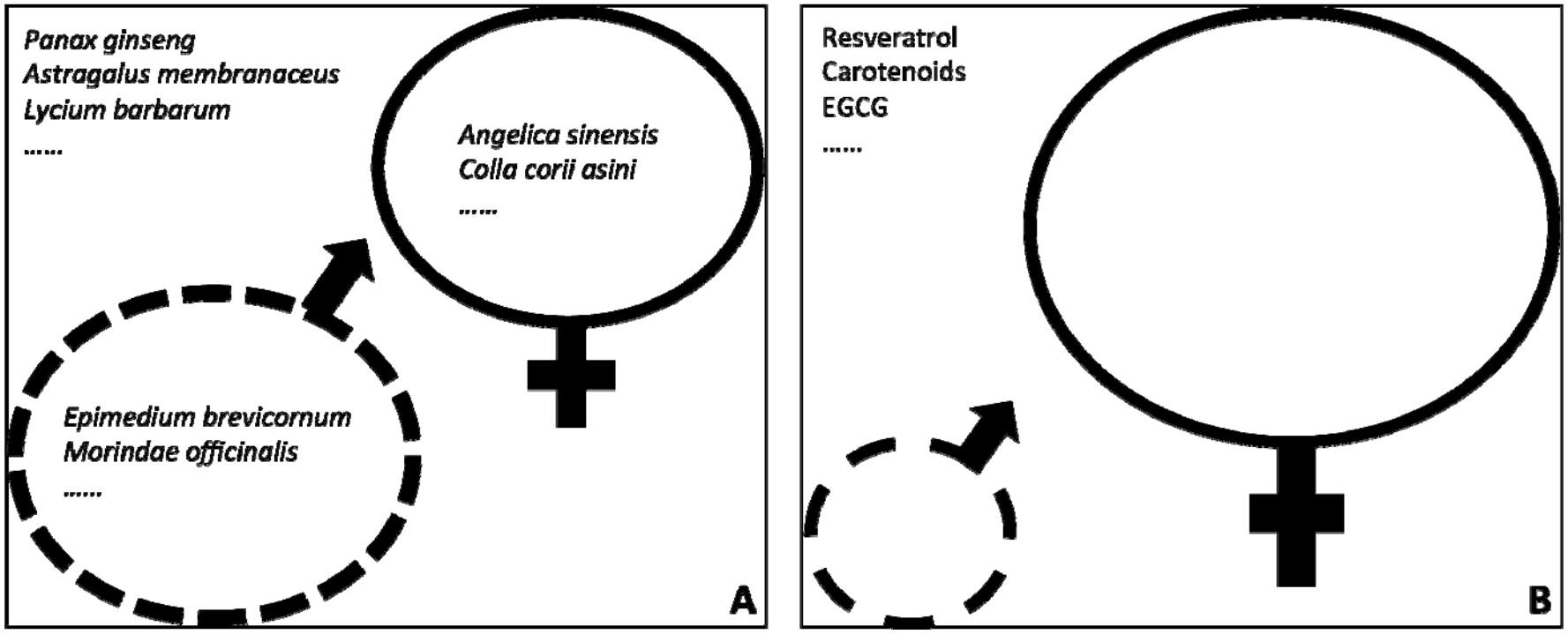
Lei T et al. (2013) *Neural Regen Res* 8: (in press).

Bioactive polysaccharides: mechanisms of action



Li H et al. (2014) *Rejuvenation Res* 17: (in press).

Other anti-aging products



Anti-aging functional beverages sold online in China

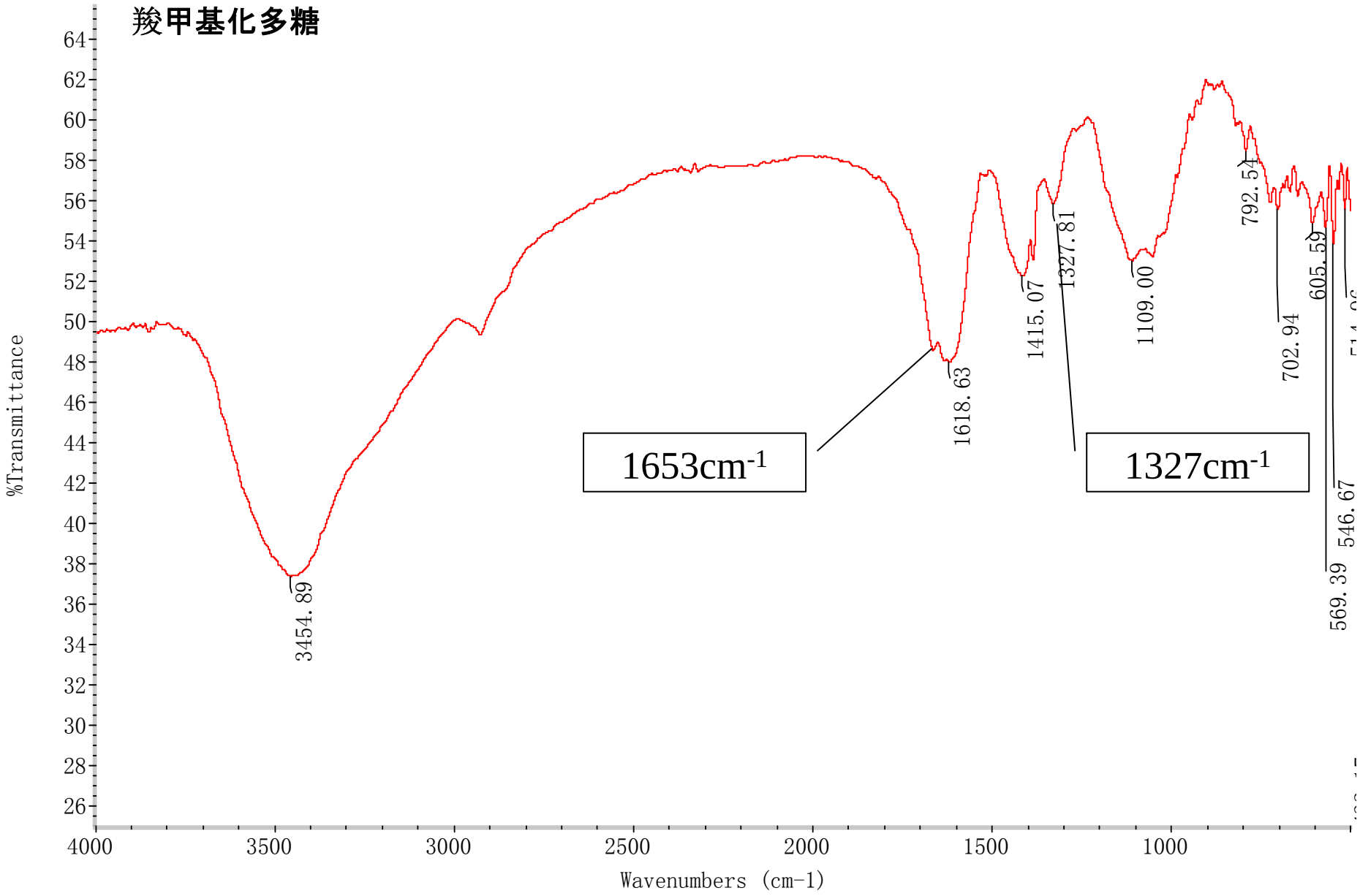
Yang F et al. (2014) *Rejuvenation Res* 17: (in press).

多糖类化妆品原料：透明质酸廉价替代品

- 理想功效
  - 抗衰缓老
  - 抗敏舒颜
  - 润湿保湿
  - 皮肤屏障
  - 美白祛斑
- 主要来源
  - 抗衰老药用植物
  - 药食两用动植物
  - 大型海藻
  - 淡水微藻
  - 荒漠藻类

多糖类化妆品原料：透明质酸廉价替代品

- 除杂修饰
  - 微滤超滤
  - 生物酶法
  - 硫酸酯化
  - 羧甲基化
  - 乙酰化
  - 烷基化
  - 超声波
  - ……
- 目的
  - ✧ 过敏源
  - ✧ 溶解性
  - ✧ 分散度
  - ✧ 质感
  - ✧ 活性
  - ✧ ……


羧甲基化多糖
%Transmittance
Wavenumbers (cm-1)
3454.89
1618.63
1415.07
1327.81
1109.00
792.54
702.94
605.59
569.39
546.67
1653cm-1
1327cm-1

主要问题

- 过敏
- 工艺
- 来源

各2-3种


早安美丽
Morn Belle
清莹保湿洁面乳
3.5 fl.oz 100ml
早安美丽
Morn Belle
水润滋养保湿乳
早安美丽
Morn Belle
均衡润泽爽肤水


早安美丽
Morn Belle
均衡润泽爽肤水
早安美丽
Morn Belle
清莹保湿洁面乳
3.5 fl.oz 100ml

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Prof Jeremy E Turnbull

Shenzhen University
College of Life Sciences
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http://www.863.org.cn

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National Science and Technology Major Project

The Research Council of Norway