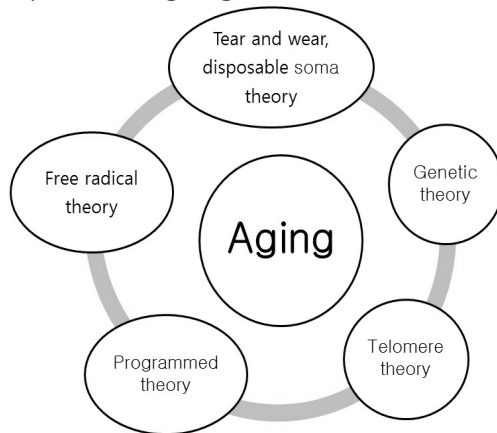


## 장수 유전자 SIRT1 (허혈성 뇌졸중과 운동)

이 재 민

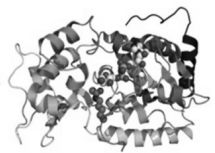
경희대학교

### Lifespan – aging



### Sirtuins

- **Sirtuin** or Silent information regulator (**Sir2**) proteins are a class of proteins
- **Promote an increased life span**
- Sirtuin 1 (SIRT1), a member of the sirtuin family of nicotinamide adenine dinucleotide (NAD<sup>+</sup>)-dependent deacetylases
- **Mammals contain seven sirtuins (SIRT1-7)**

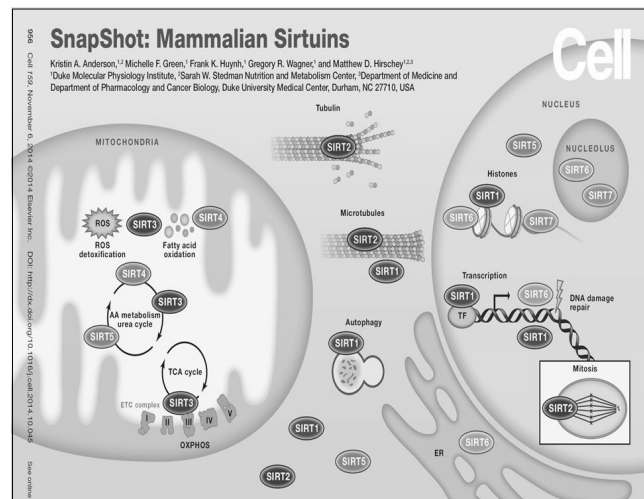


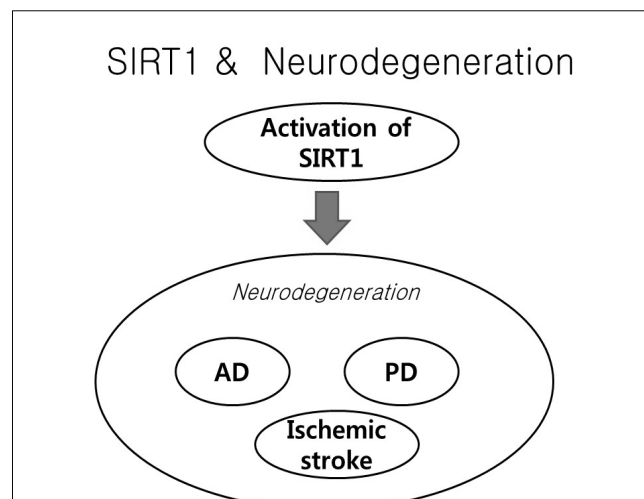
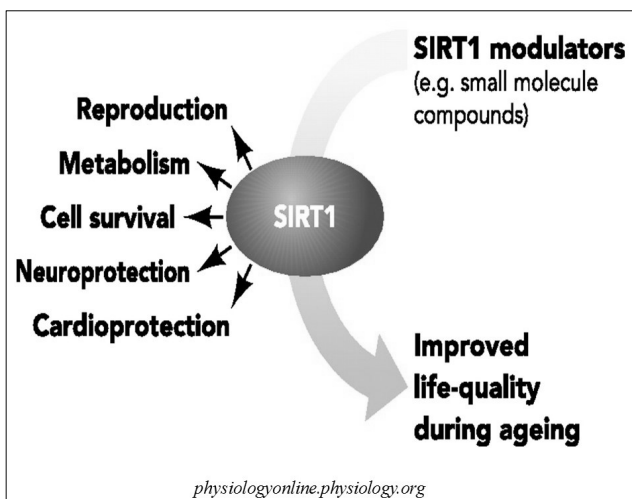
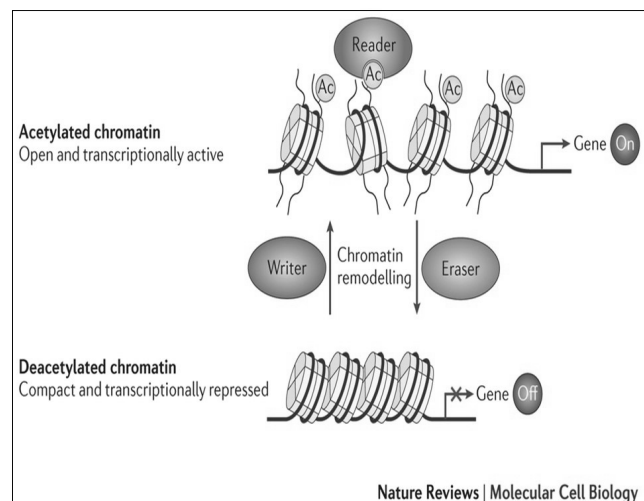
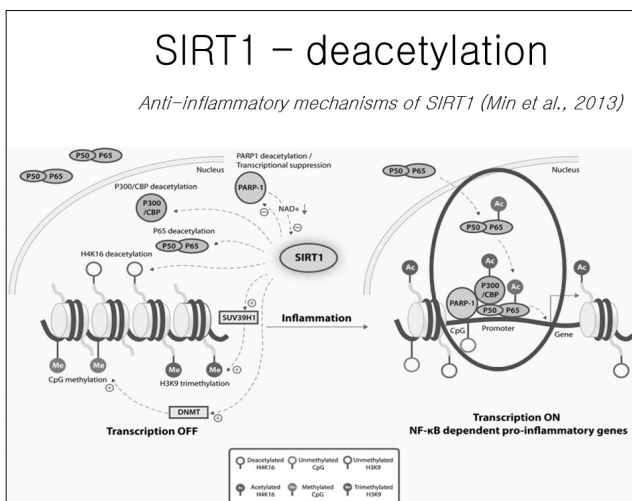
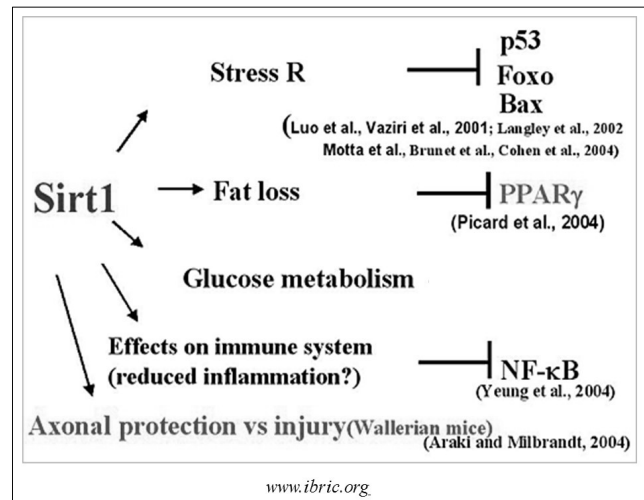
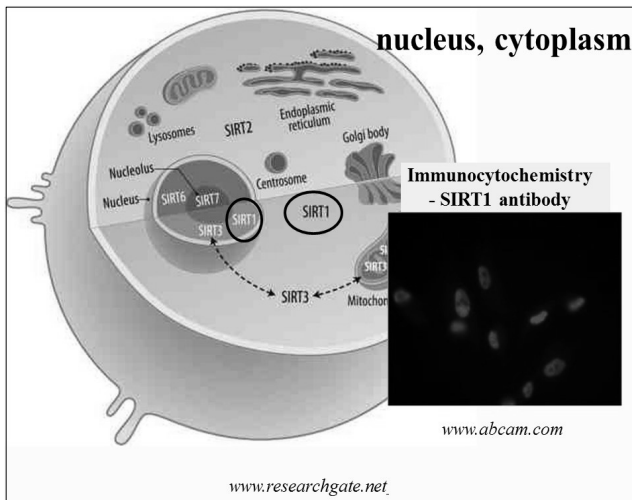
<https://en.wikipedia.org/wiki/Sirtuin>

### Sirtuins localization & function



No	location			enzymatic function	function
	Nucleus	Cytoplasm	Mitochondria		
SIRT1	O	O		Deacetylase	metabolism, inflammation
SIRT2		O		Deacetylase	cell cycle, tumorigenesis Energy expenditure regulation
SIRT3	O		O	Deacetylase	metabolism
SIRT4			O	ADP-ribosyltransferase Weak deacetylase	insulin secretion
SIRT5			O	Weak deacetylase NAD-dependent protein lysine Desuccinylase	ammonia detoxification
SIRT6	O			Weak Deacetylase, ADP-ribosyltransferase	DNA repair, metabolism, TNF secretion
SIRT7	O			Deacetylase	DNA transcription





Brain Research Journal of Medical and Biological Research (2013) 40: 659-669, <http://dx.doi.org/10.1556/1544-3113.121903>  
ISSN 1544-3113

### SIRT1 negatively regulates amyloid-beta-induced inflammation via the NF- $\kappa$ B pathway

L. Cao<sup>1\*</sup>, C. Liu<sup>1\*</sup>, F. Wang<sup>2</sup> and H. Wang<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, Tenth People's Hospital, School of Medicine, Affiliates of Tongji University, Shanghai, China  
<sup>2</sup>Department of Ophthalmology, Shanghai Tenth People's Hospital, Shanghai, China

- Sirtuin 1 (SIRT1) regulates inflammation via inhibition of nuclear factor-kappa B (NF- $\kappa$ B) signaling
- MMP-9 has been reported to modify barrier function by disrupting TJ proteins
- SIRT1 activation could inhibit A $\beta$ -induced expression of MMP-9



Free Radical Biology and Medicine

Volume 41, Issue 12, 15 December 2006, Pages 1781–1794



Original Contribution

### Protection by EGb 761 against $\beta$ -amyloid-induced neurotoxicity: Involvement of NF- $\kappa$ B, SIRT1, and MAPKs pathways and inhibition of amyloid fibril formation

Fanny Longpré<sup>a</sup>, Philippe Garneau<sup>a</sup>, Yves Christen<sup>b</sup>, Charles Ramassamy<sup>a,c</sup>

- A $\beta$  peptide-induced toxicity is mediated through oxidative stress and is associated with an activation of intracellular signaling (such as the transcription factor NF- $\kappa$ B and MAPK pathways)
- **EGb 761** can also activate SIRT1 (EGb 761 is a well-known antioxidant)
- The synthesis of p65 and its nuclear translocation induced by A $\beta$ <sub>25-35</sub> are inhibited in the presence of EGb 761

The EMBO Journal (2007) 26, 3169–3179 | © 2007 European Molecular Biology Organization | All Rights Reserved | 0950-4189/07  
[www.embojournal.org](http://www.embojournal.org)

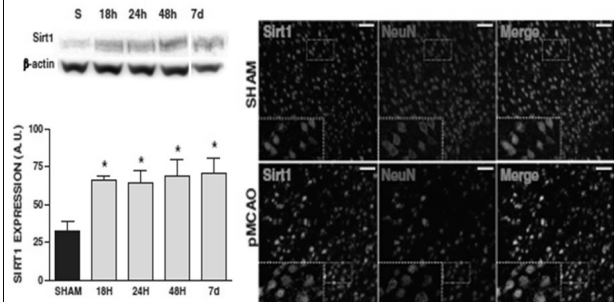
THE  
EMBO  
JOURNAL

### SIRT1 deacetylase protects against neurodegeneration in models for Alzheimer's disease and amyotrophic lateral sclerosis

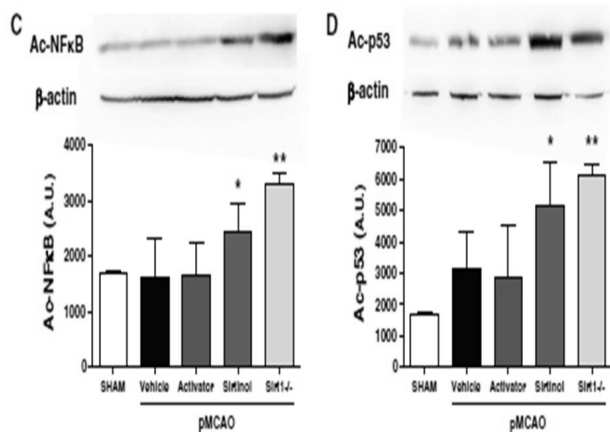
- **Levels of SIRT1 in models of neurodegeneration**
  - ✓ SIRT1 levels may increase as a protective response to neurodegenerative conditions
- **Resveratrol-mediated SIRT1 activation protects against p25**
  - ✓ Overexpression of p25: display massive degeneration of forebrain with features of AD

### Silent Information Regulator 1 Protects the Brain Against Cerebral Ischemic Damage

Macarena Hernández-Jiménez, PhD<sup>\*</sup>; Olivia Hurtado, PhD<sup>\*</sup>; María I. Cuartero, MSc; Iván Ballesteros, PhD; Ana Moraga, MSc; Jesús M. Pradillo, PhD; Michael W. McBurney, PhD; Ignacio Lizasoain, PhD, MD; María A. Moro, PhD



(Hernández-Jiménez et al., 2013).



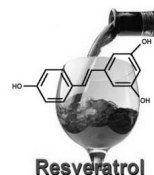
(Hernández-Jiménez et al., 2013).

## Activation of SIRT1

### Caloric restriction



### Resveratrol



### Resveratrol

[supplement-geek.com](http://supplement-geek.com)

### Exercise



[saiadonline.com](http://saiadonline.com)

## Resveratrol



Neuroscience

Volume 310, 3 December 2015, Pages 641–649



**Resveratrol decreases the insoluble A $\beta$ 1–42 level in hippocampus and protects the integrity of the blood–brain barrier in AD rats**

H.F. Zhao<sup>a,\*</sup>, N. Li<sup>a,\*</sup>, Q. Wang<sup>a</sup>, X.J. Cheng<sup>a</sup>, X.M. Li<sup>a</sup>, T.T. Liu<sup>a</sup>

- Resveratrol decreases the insoluble A $\beta$ 1–42 level in the hippocampus in AD rats.
- Resveratrol protects the integrity of the blood–brain barrier in AD rats



Brain Research Bulletin

Volume 121, March 2016, Pages 255–262



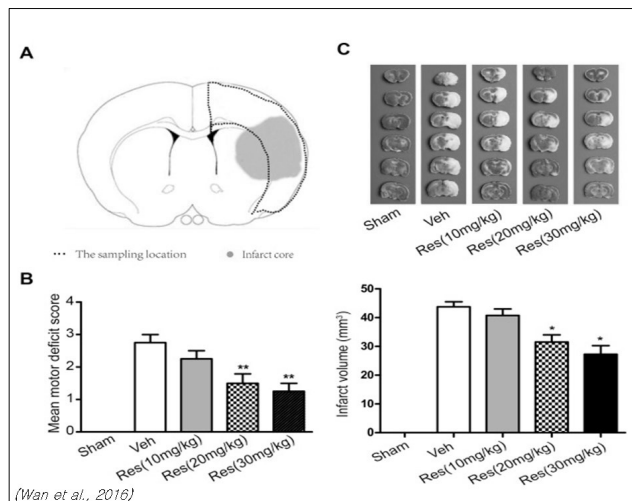
Research report

**Resveratrol provides neuroprotection by inhibiting phosphodiesterases and regulating the cAMP/AMPK/SIRT1 pathway after stroke in rats**

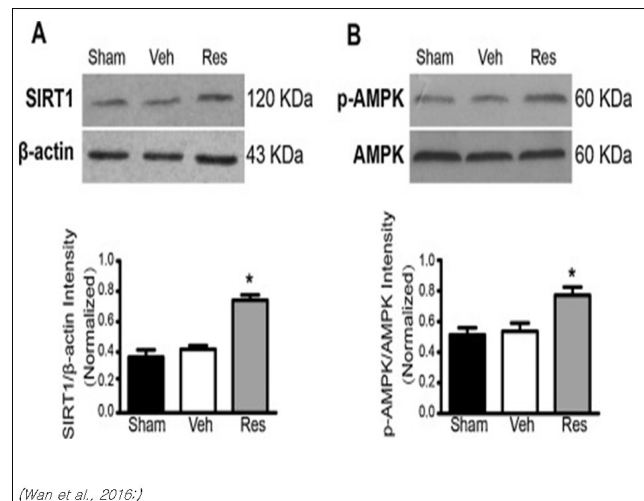
Dan Wan<sup>a,b,c</sup>, Yehan Zhou<sup>a,b,c</sup>, Ke Wang<sup>a,c</sup>, Yongying Hou<sup>a,c</sup>, Ruihang Hou<sup>a,c</sup>, Xufeng Ye<sup>a,b,c</sup>

Show more

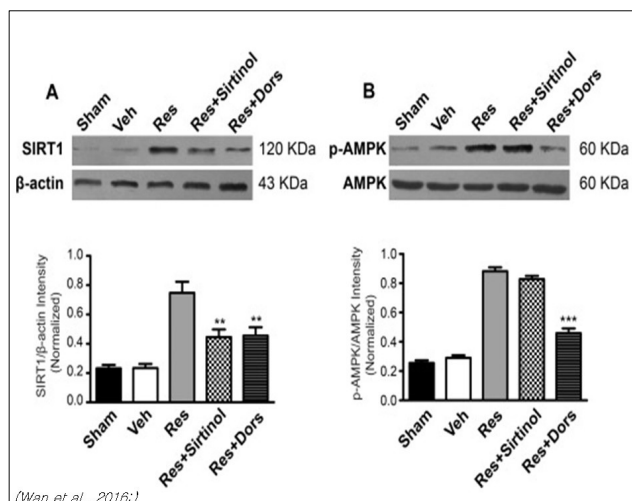
- Resveratrol significantly reduced the harmful effects of cerebral ischemic injury
- Levels of ATP, p-AMPK, SIRT1, and cAMP were increased by resveratrol



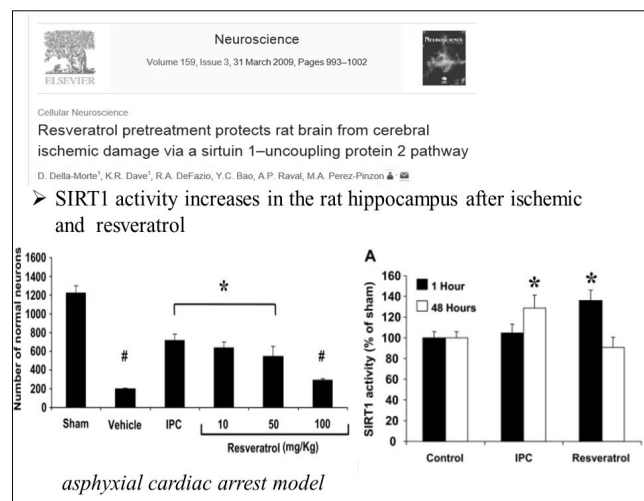
(Wan et al., 2016)



(Wan et al., 2016)



(Wan et al., 2016)



asphyxial cardiac arrest model

