

# OMICS INTERNATIONAL



OMICS International through its Open Access Initiative is committed to make genuine and reliable contributions to the scientific community. OMICS International signed an agreement with more than 1000 International Societies to make healthcare information Open Access.

# OMICS Journals are welcoming Submissions

OMICS International welcomes submissions that are original and technically so as to serve both the developing world and developed countries in the best possible way.

OMICS Journals are poised in excellence by publishing high quality research. OMICS International follows an Editorial Manager® System peer review process and boasts of a strong and active editorial board.

Editors and reviewers are experts in their field and provide anonymous, unbiased and detailed reviews of all submissions. The journal gives the options of multiple language translations for all the articles and all archived articles are available in HTML, XML, PDF and audio formats. Also, all the published articles are archived in repositories and indexing services like DOAJ, CAS, Google Scholar, Scientific Commons, Index Copernicus, EBSCO, HINARI and GALE.

**For more details please visit our website:**

**<http://omicsonline.org/Submitmanuscript.php>**



福建医科大学  
FUJIAN MEDICAL UNIVERSITY



# The role of Nrf2/ARE system and epigenetic in the neurotoxicity

Huangyuan LI (Ph.D, M.D., Professor)

[fmulhy@163.com](mailto:fmulhy@163.com)

School of Public Health  
Fujian Medical University  
Fuzhou, China

# Outline

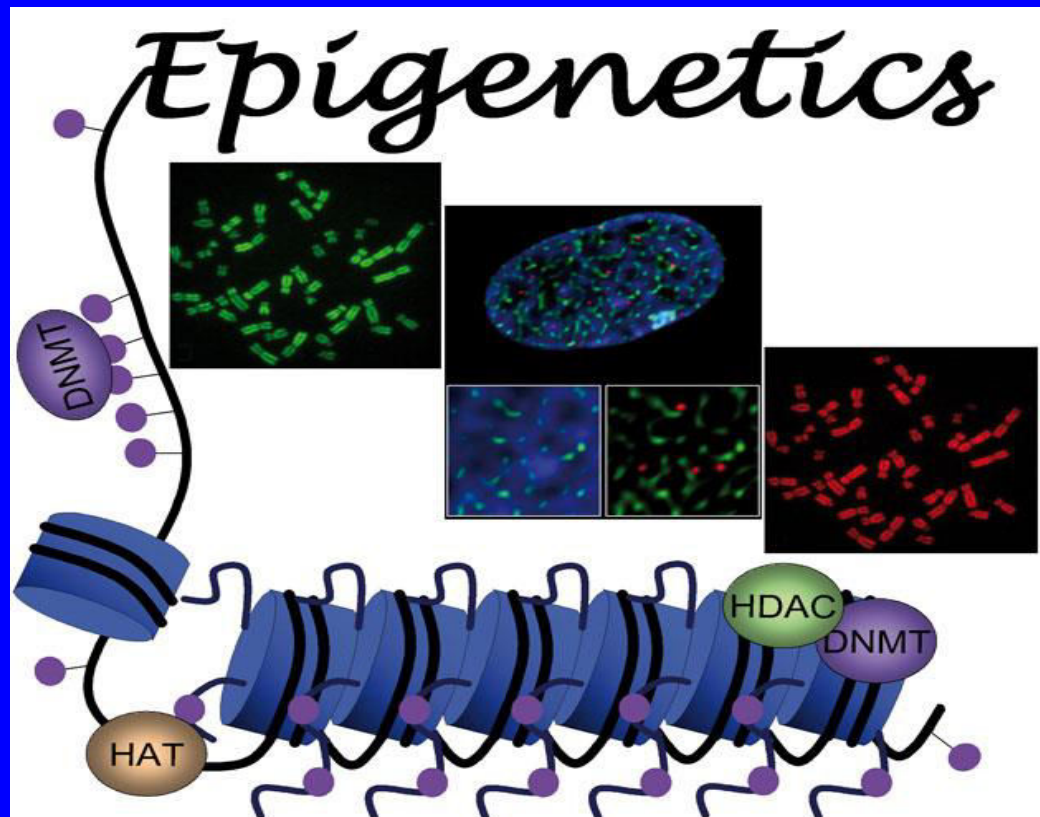
- I . Introduction to the research fields of **Epeigenetic Toxicology** in our team.
- II . The role of **Nrf2/ARE system** in the neurotoxicity induced by environmental chemical, **deltamethrin (DM)**, **manganese (Mn)** and **paraquat (PQ)**.
- III. The role of **non-coding RNA (ncRNA)** in the neurotoxicity induced by **paraquat (PQ)**.
- IV. The role of **Histone acetylation** in the neurotoxicity induced by **manganese (Mn)** .

**Part I .**

**Introduction to the research fields of  
Epeigenetic Toxicology in our team.**

***Epigenetics*** refers to heritable alterations in gene expression that do not entail changes in nucleotide sequence.

---



## Environmental Exposure

Environmental endocrine disruptors

cadmium

n-hexane

bis(2-ethylhexyl)phthalate

Neurotoxic chemical

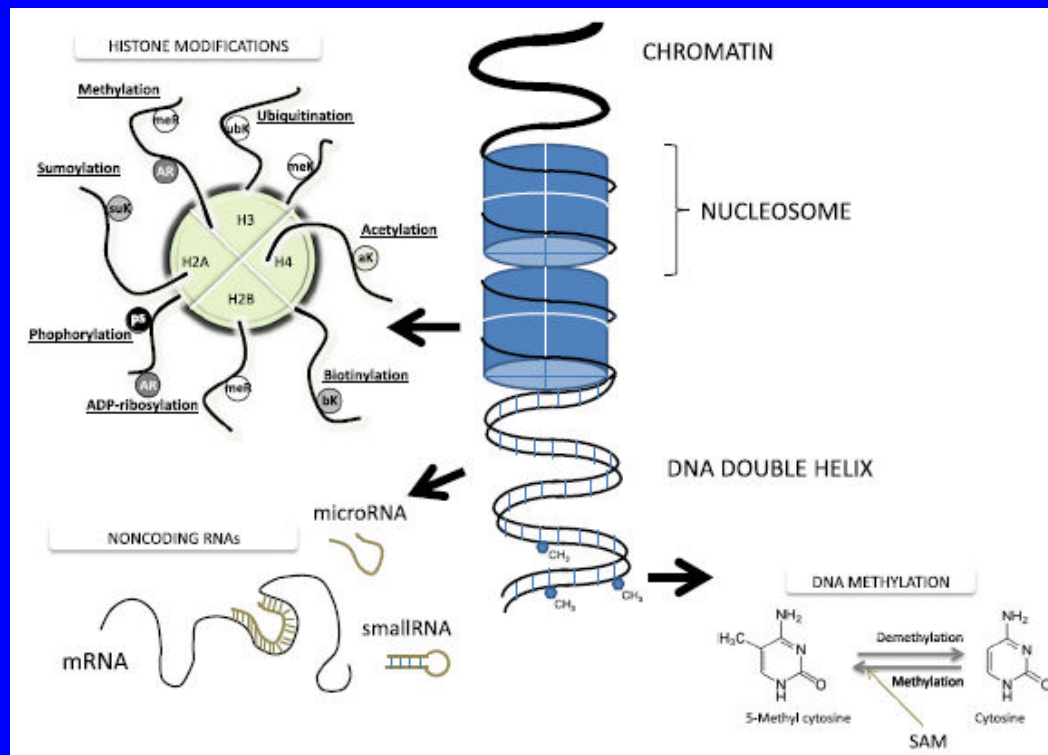
paraquat (PQ)

manganese (Mn)

Epi-genetic  
Modification  
Alteration

Gene  
Expression  
Pattern  
Alteration

Reproductive  
toxicity  
Neurotoxicity  
Cancer



## **Part II.**

**The role of Nrf2/ARE system in the neurotoxicity induced by environmental chemical, deltamethrin (DM), manganese (Mn) and paraquat (PQ).**



# 1. Introduction

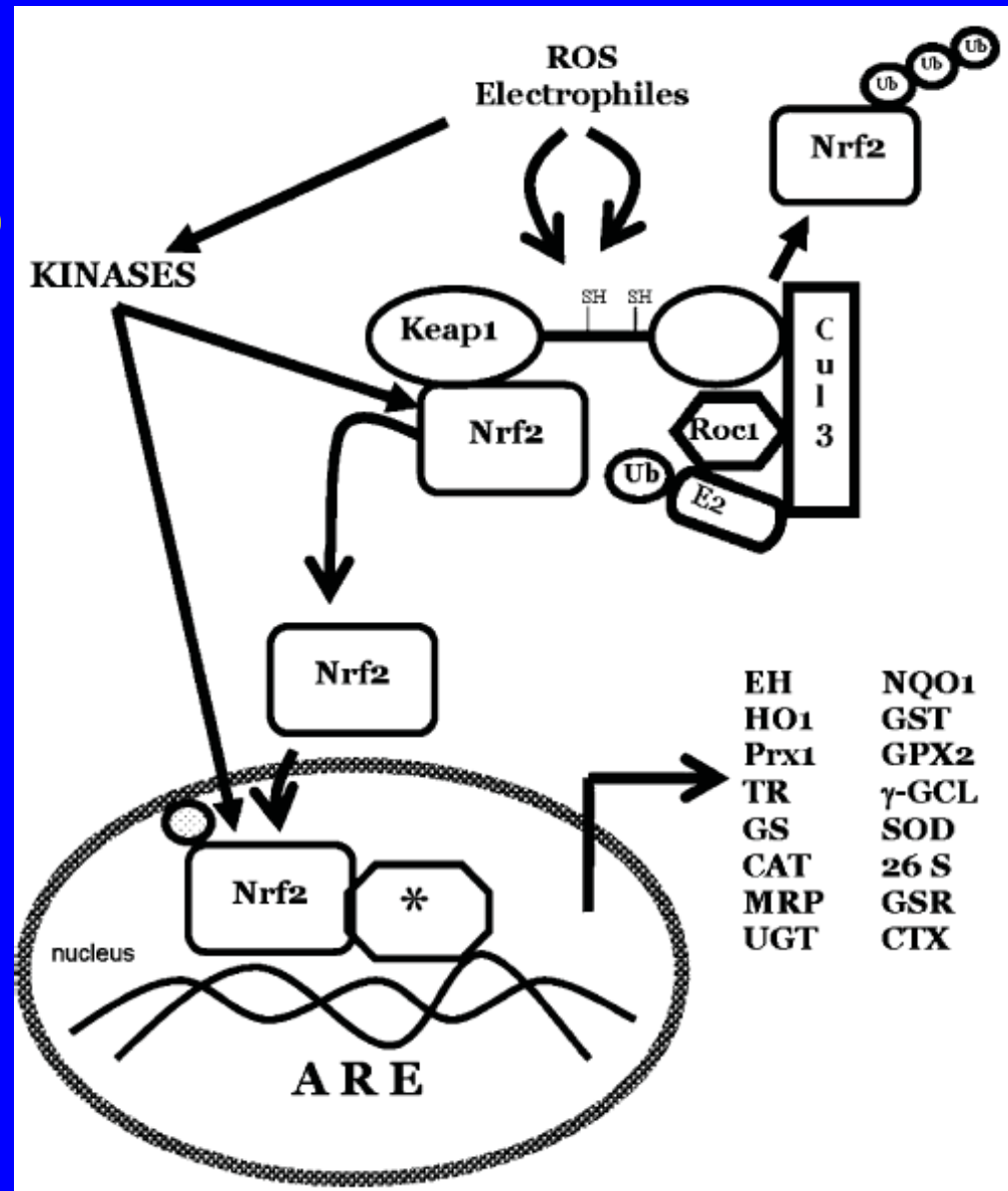
## Nrf2: Nuclear factor E 2(NF-E2) p45-related factor 2

a member of the NF-E2 family of nuclear basic leucine zipper transcriptional activators

## Keap1: Kelch-like ECH-associated protein 1

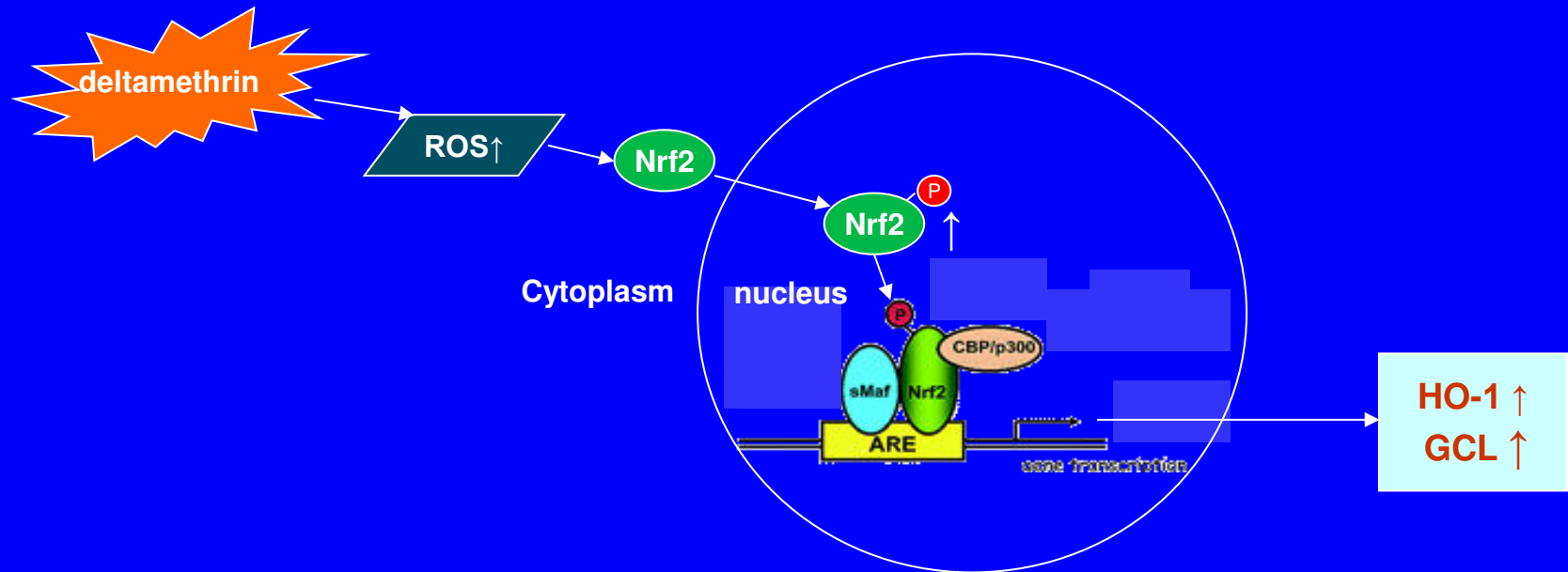
a cytoplasmic protein homologous to the Drosophila actin binding protein Kelch

## ARE: Antioxidant Response Element



Possible protective mechanism of Nrf2/ARE pathway on cell from cytotoxicity

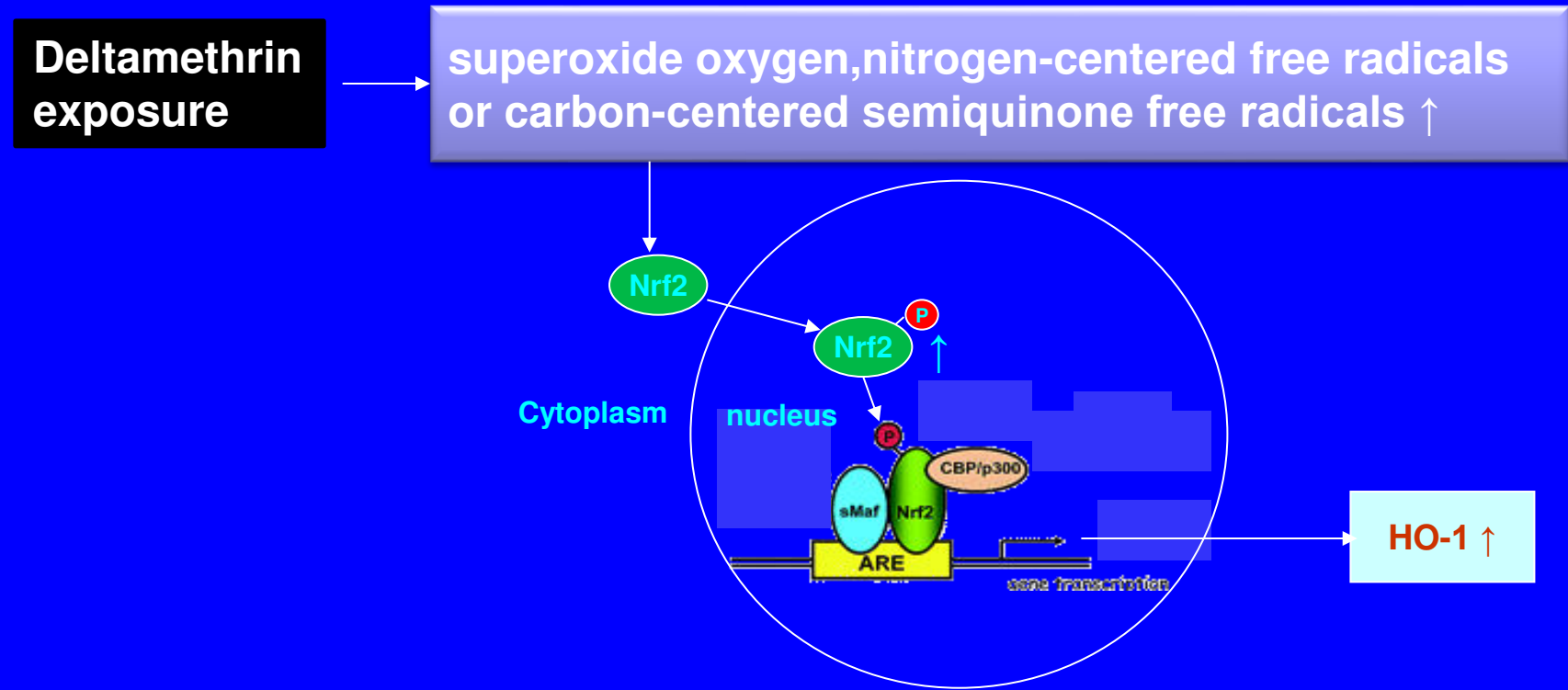
# Finding 1



**Transcription factor Nrf2 activation by deltamethrin in PC12 cells:  
Involvement of ROS**

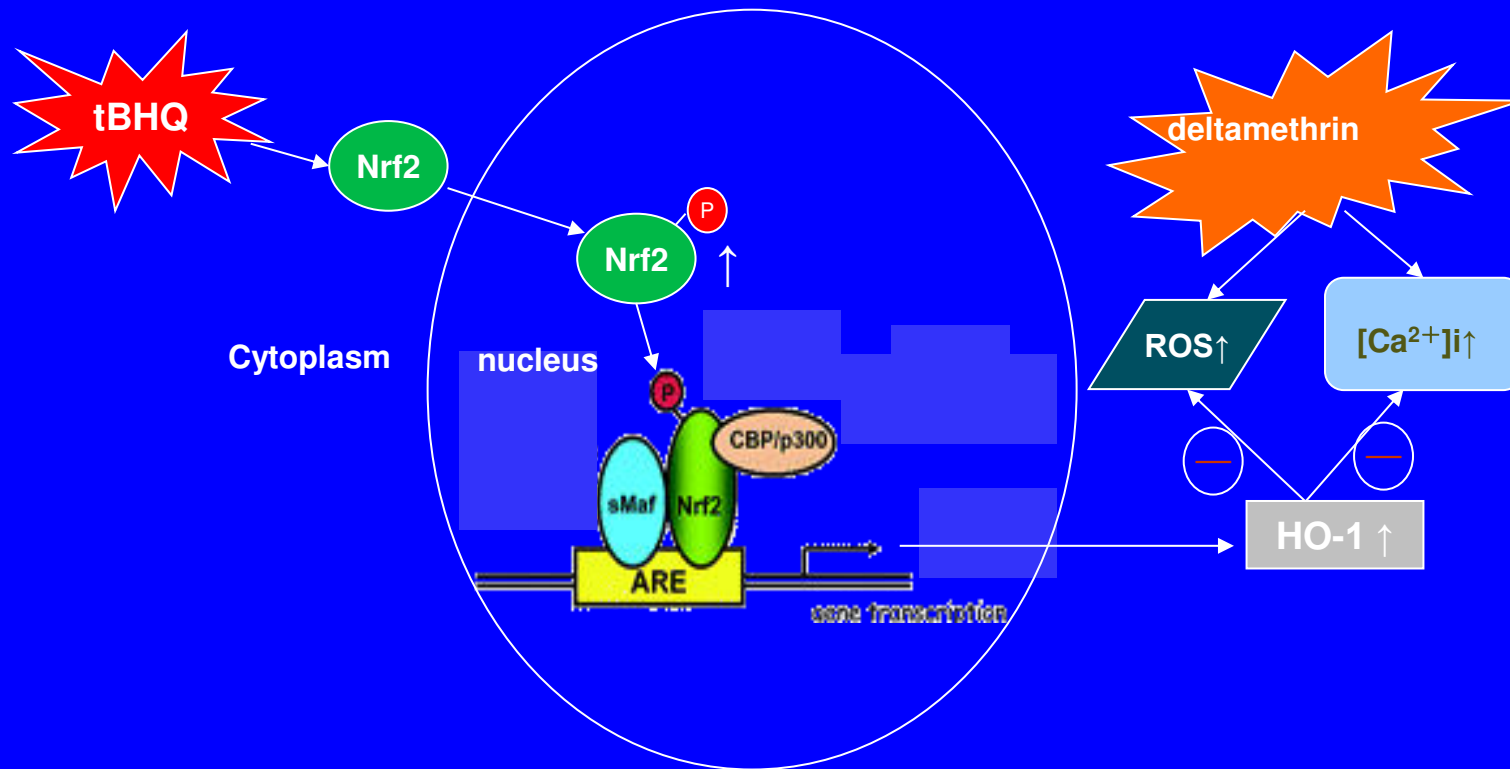
*Toxicology Letters*, 2007, 171(1-2):87-98.

*Toxicol Ind Health*, 2011, 27(7):579-590.



A schematic diagram to show that the pesticide deltamethrin increases free radical production and promotes nuclear translocation of Nrf2 in rat brain.

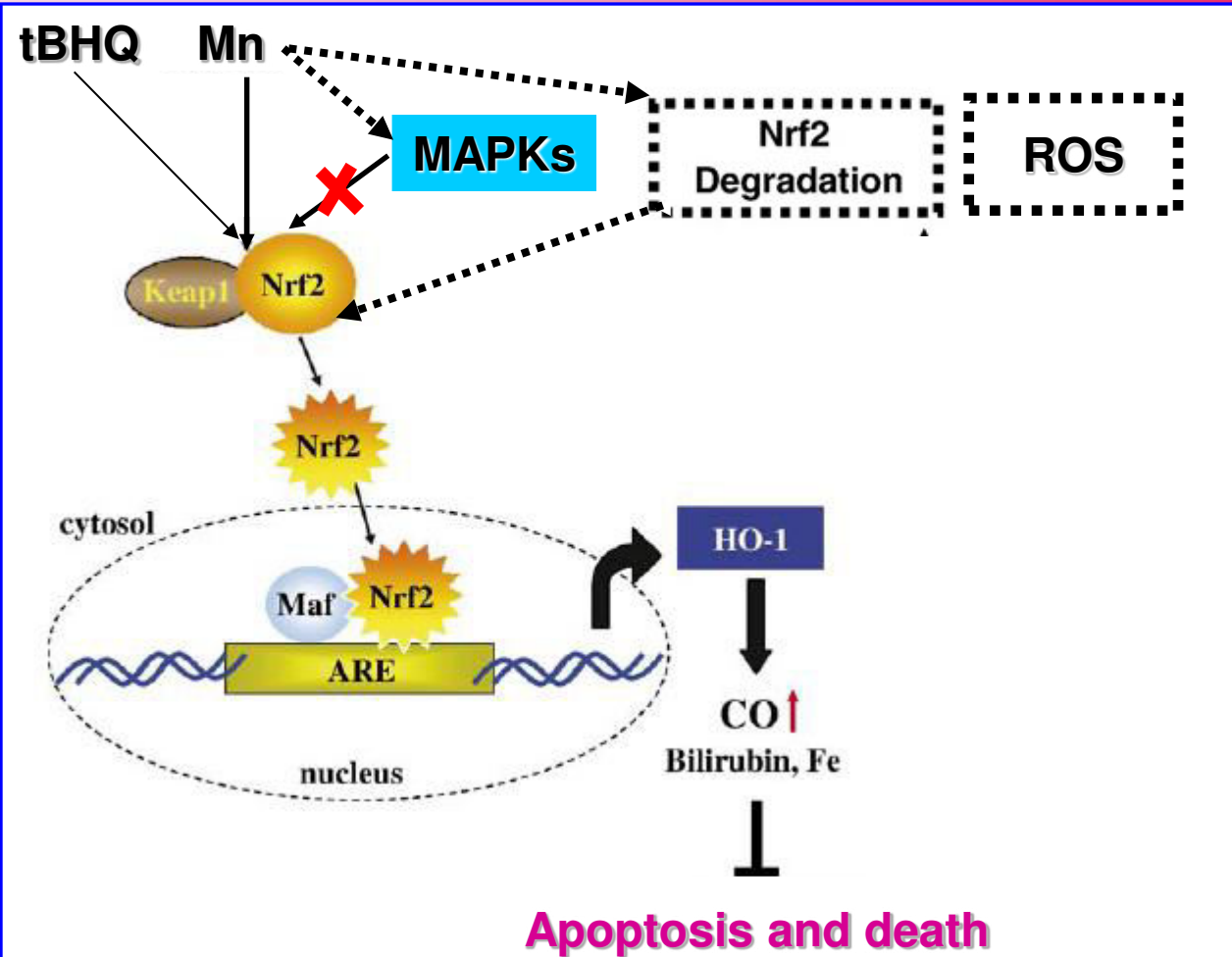
# Finding 2



Nrf2 activation and HO-1 induction by tBHQ protect against deltamethrin mediated oxidative stress

*Chemical Research in Toxicology*, 2007, 20 (9):1242–1251.

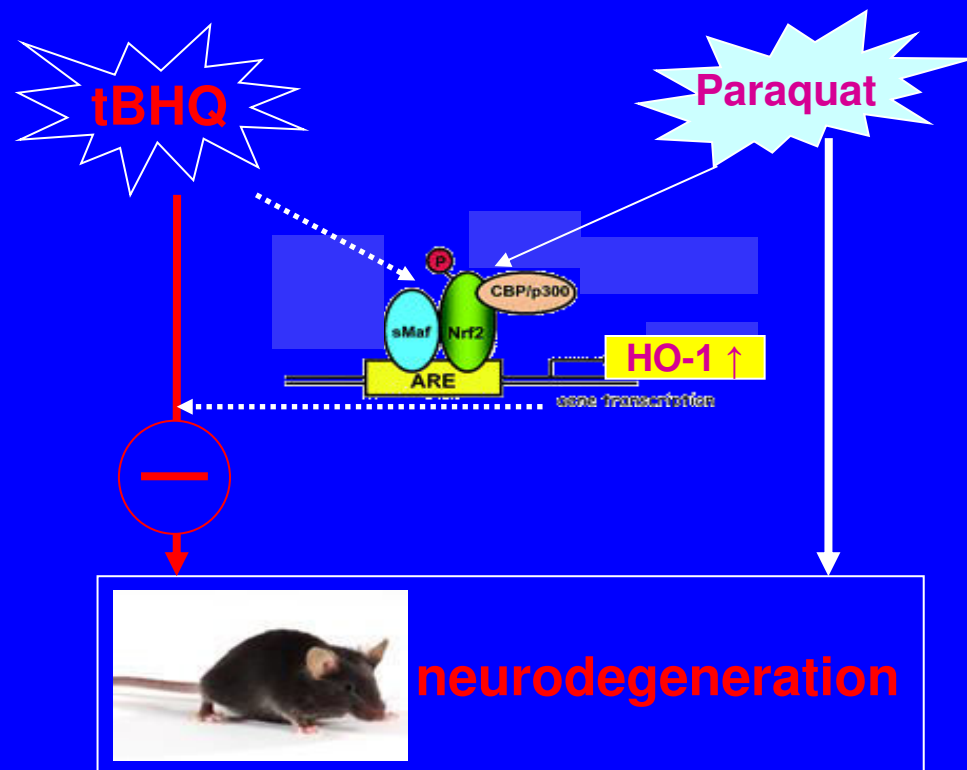
# Finding 3



*Archives of Toxicology*, 2011, 85:901-910

*Journal of Applied Toxicology*, 2011, 31:690-697.

# Finding 4



*Archives of Toxicology, 2013, 86(11):1729-1740.*

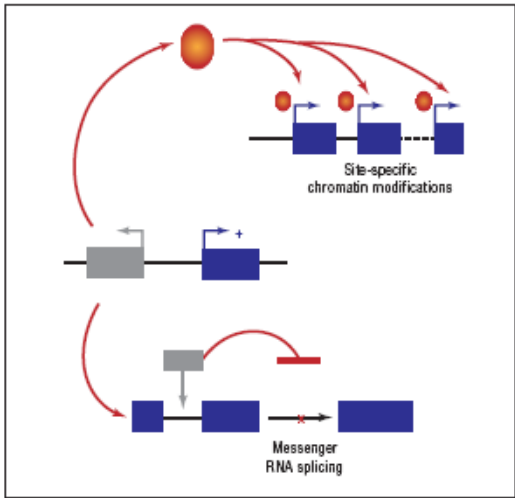
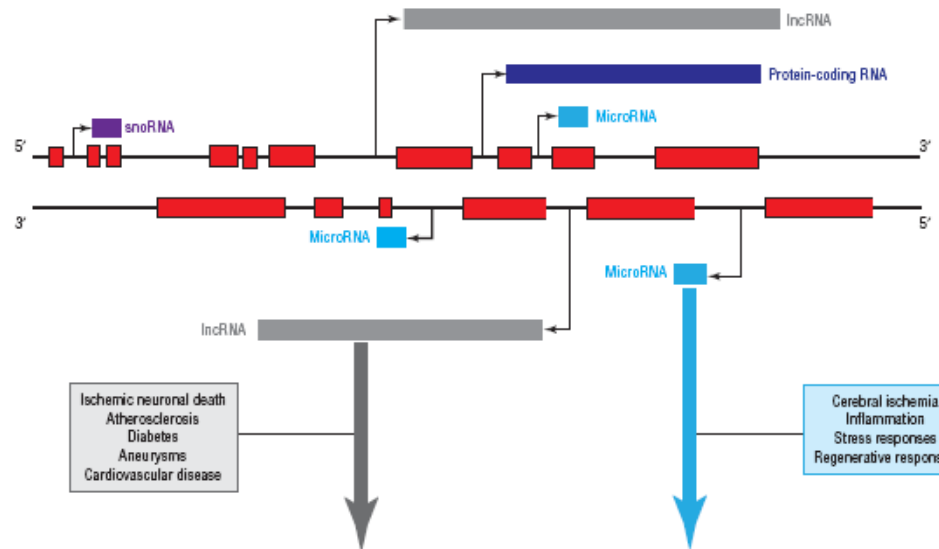
# Conclusion

- Nrf2 protects from neurotoxicity in cell models and laboratory models.
- The Nrf2/ARE pathway as a potential therapeutic target in neurotoxicity resulted from environmental chemical.

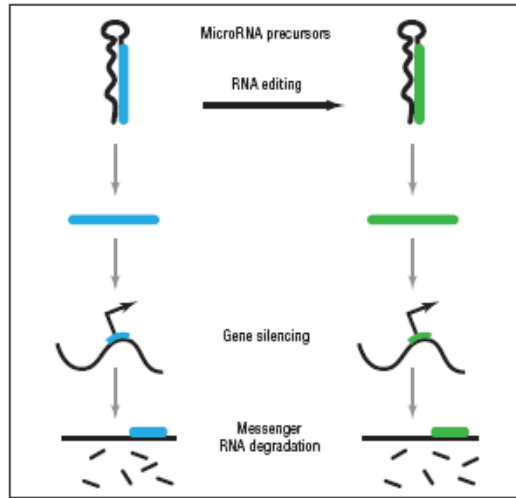
## **Part III.**

**The role of non-coding RNA (ncRNA)  
in the neurotoxicity induced by PQ.**





lncRNA regulation



MicroRNA regulation

# Finding 5

- **In vitro, PQ can increase the rate of apoptosis of cells and change miRNA expression profiling, which maybe one of the mechanism of neurotoxicity induced by PQ.**
- **In vitro, MPTP can also change miRNA expression profiling. It is different from but related to that of PQ.**

*Unpublished data*

# Finding 6

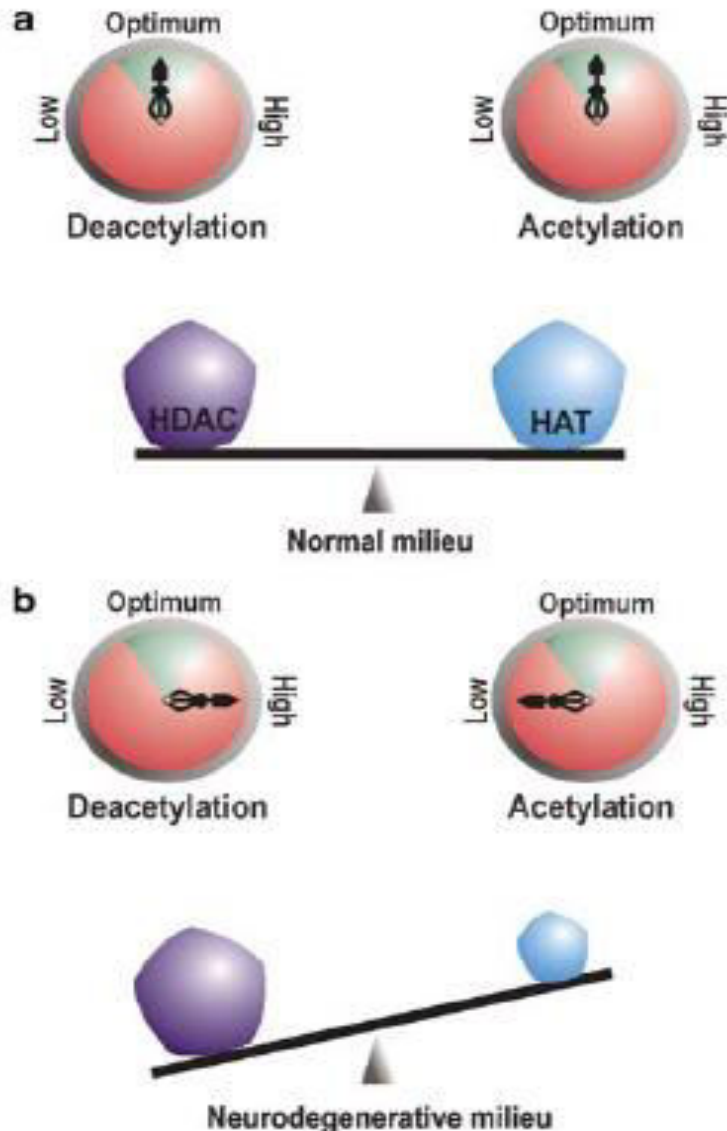
- **In vivo, PQ can change miRNA/lncRNA expression profiling, which maybe one of the mechanism of neurotoxicity induced by PQ.**
- **In vivo, MPTP can also change miRNA/lncRNA expression profiling. It is different from but related to that of PQ.**
- **There are some specific miRNAs/lncRNA related to the transcription factor Nrf2, interaction of miRNA/lncRNA and Nrf2 may involve in neurotoxicity induced by PQ or MPTP.**

*Unpublished data*

## **Part IV.**

**The role of Histone acetylation in the neurotoxicity induced by manganese.**

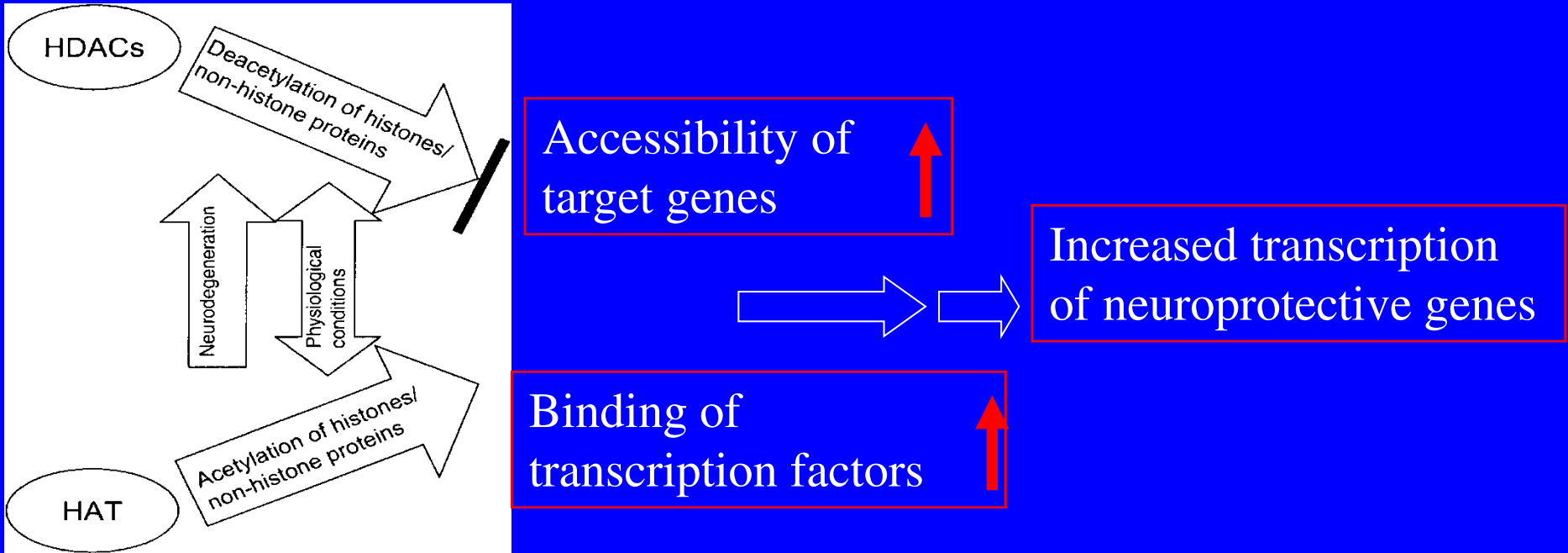
# Neuronal acetylation homeostasis



Pentagons on the balance beam represent the protein level (dose) of HATs and HDACs, while compasses represent their activity. Enzymatic activity within the green arc of the compass is physiologically optimum.

(a) In neurons under normal conditions, the dose and activity of HATs and HDACs are poised in a fine balance where they counteract each other to ensure physiological homeostasis.

(b) During neurodegeneration, critical loss of HAT protein level ensue a rebated HAT dose and activity. This reclines the acetylation balance towards excessive deacetylation of target moieties



**Fig. (1).** Differential effects of histone deacetylases (HDAC's) and histone acetyl transferases (HAT) on the transcription of neuroprotective genes. In acute and chronic neurodegeneration, the acetylation/ deacetylation homeostasis is shifted towards decreased acetylation of histones and non-histone proteins. *Modified after [19].*



- **Shi Nian**
- **Wu Siying**
- **Lin wei, Wang Zhangjin**
- **You Junyi, Zhou wenhua, Lian Shuangqing,  
Zhang chenzhi, Huang bin**
- **Wang qingqing, Wang lijun, Guo zhenkun**

➤ **National Natural Science Foundation in China**

(Grant NO.81172715 ,30800936, 30371225 )

➤ **Fujian Province Funds for Distinguished Young Scientists**

(2012J06018)

➤ **Natural Science Foundation of Fujian province** (Grant

C0610020)

➤ **Program for New Century Excellent Talents in Fujian**

**Province University** (NCETFJ, JA11103)



# **Journal of Environmental & Analytical Toxicology Related Journals**

- **Journal of Environmental Analytical Chemistry**
- **Journal of Pollution Effects & Control**

# **Journal of Environmental & Analytical Toxicology Related Conferences**

- **International Summit on Past and Present Research Systems of Green Chemistry**
- **International Summit on Toxicology & Applied Pharmacology**



# OMICS International Open Access Membership

**OMICS International Open Access Membership enables academic and research institutions, funders and corporations to actively encourage open access in scholarly communication and the dissemination of research published by their authors.**

**For more details and benefits, click on the link below:**

**<http://omicsonline.org/membership.php>**

