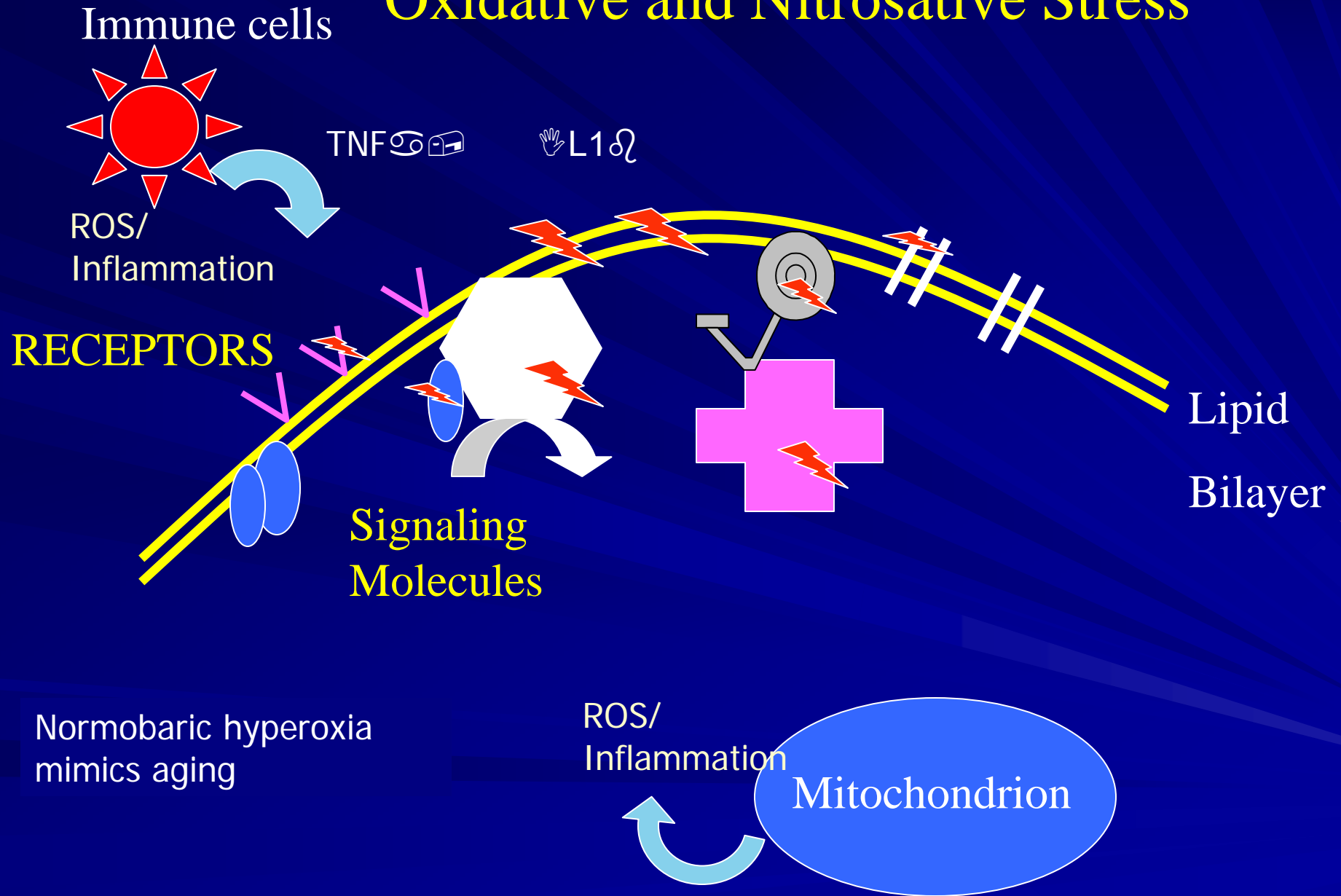


# Inflammation and Oxidative Stress in Aging and Cognition: Nutritional Interventions

Paula C. Bickford, PhD



# Oxidative and Nitrosative Stress



Therapeutic approaches to altered cognition in aging:

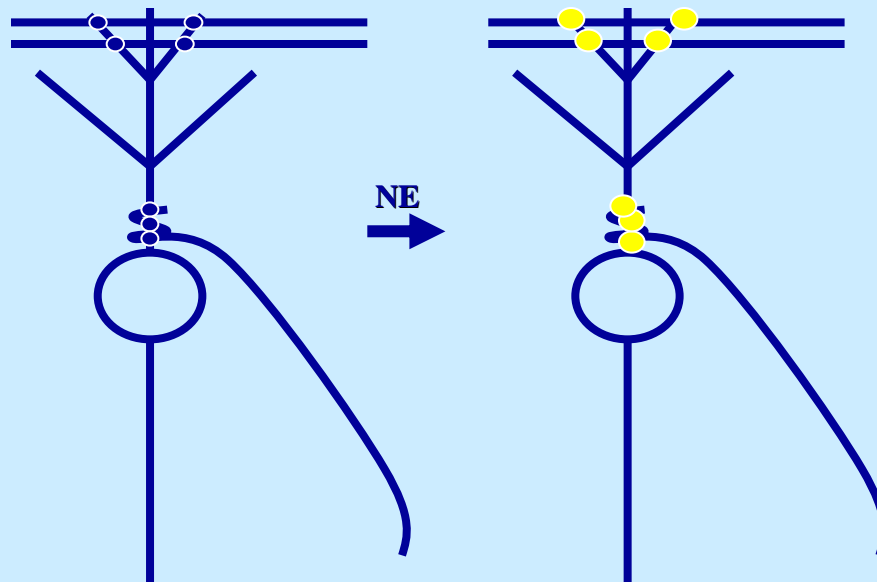
**GOAL:** Improve **functional** life span and reduce health care expenditures by prevention of disease and other aspects of unhealthy aging .

- Target receptor systems
- Target signal transduction systems
- Target underlying causes of dysfunction such as inflammation, oxidative stress

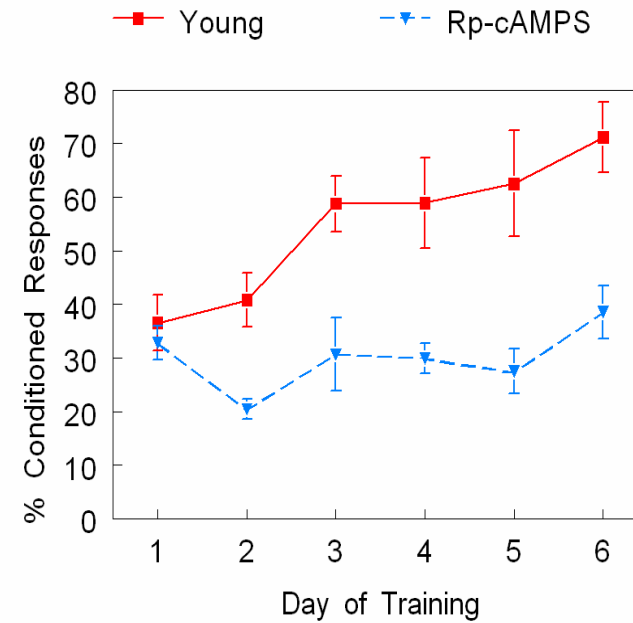
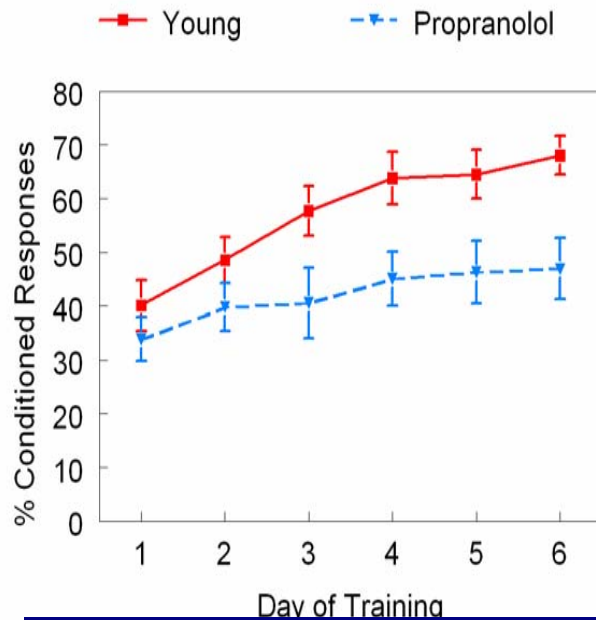
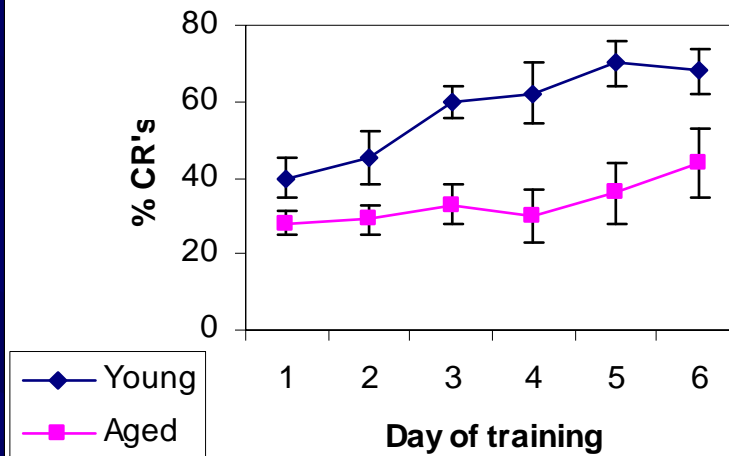


## The Model: NE and Learning

- NE is a neuromodulator that increases signal to noise Freedman R, Hoffer BJ, Woodward DJ, Puro D (1977)
- Gilbert (1975) proposed that NE could influence consolidation based on Marr-Albus.
- NE influences the acquisition of motor learning tasks (Watson and McElligott, 1983) and delay eyelid conditioning (Winsky and Harvey 1992; Gould, 1998; Cartford and Bickford, 2002).
- NE receptors ( $\beta$ -adrenergic) show functional declines with age, that correlate with loss of learning (Bickford, 1993; Gould and Bickford, 1997)

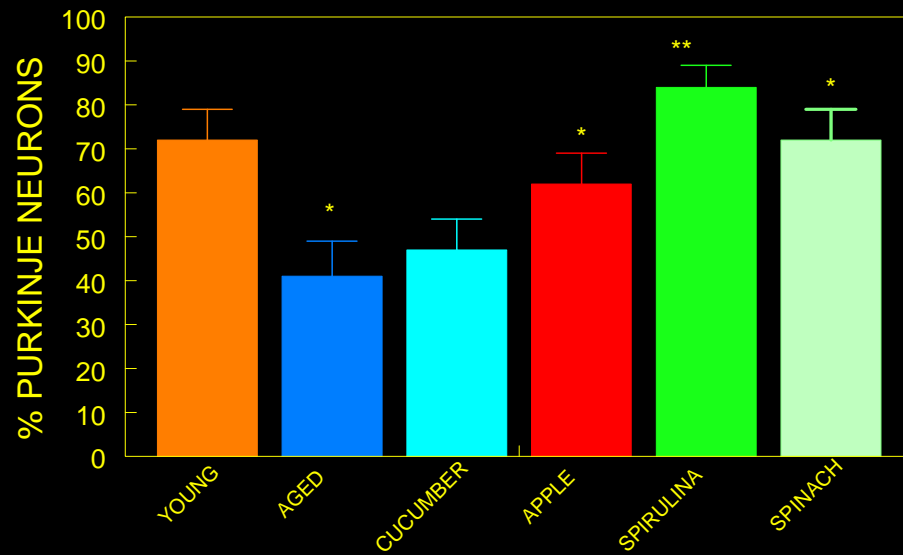


## Delay Conditioning learning - Differences between young and aged rats



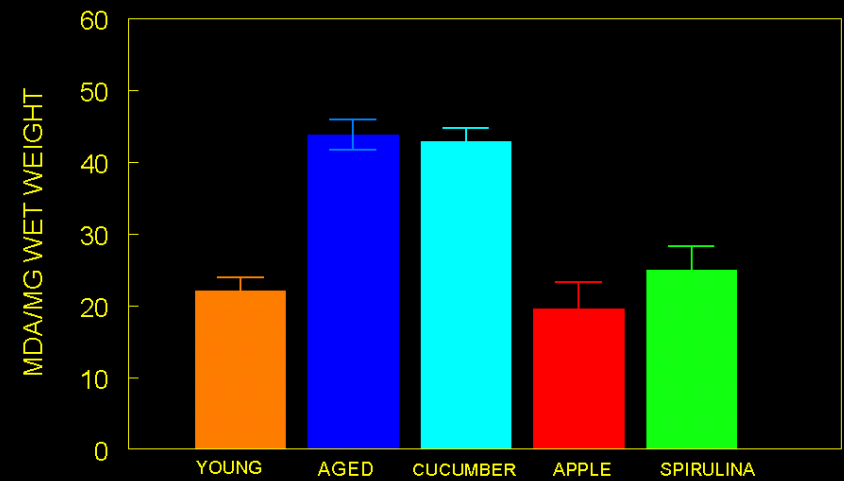
Infusion into cerebellar interpositus nucleus and lobus simplex

## NOREPINEPHRINE MODULATION

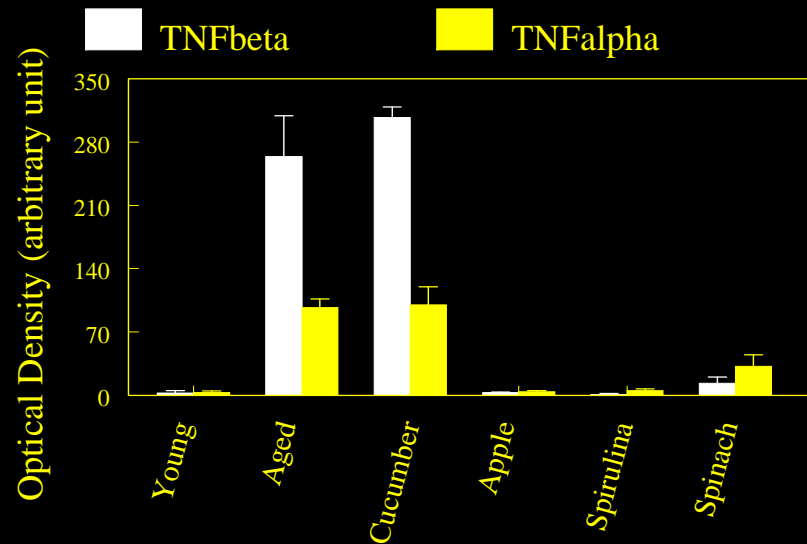


\* p<0.05 vs young \*\* p<0.05 vs aged

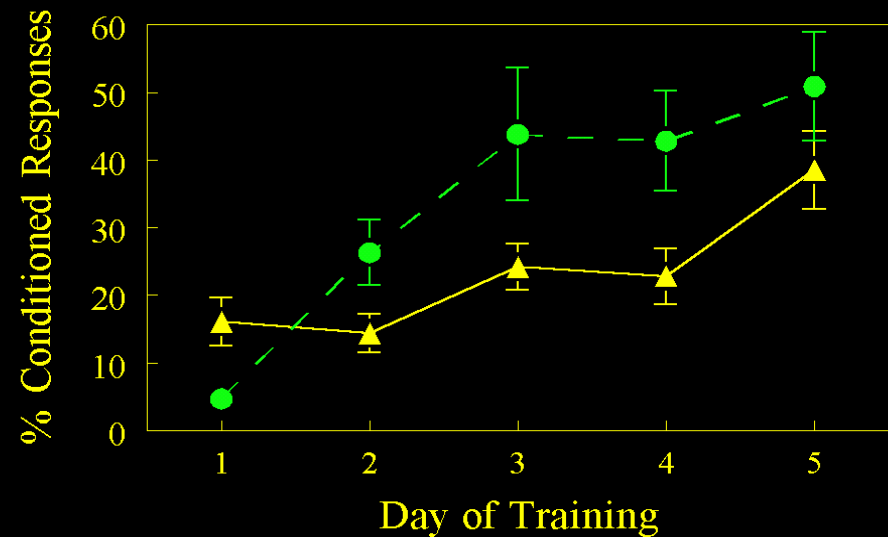
## MALONDIALDEHYDE



## TNFBeta and TNFalpha mRNAs expression



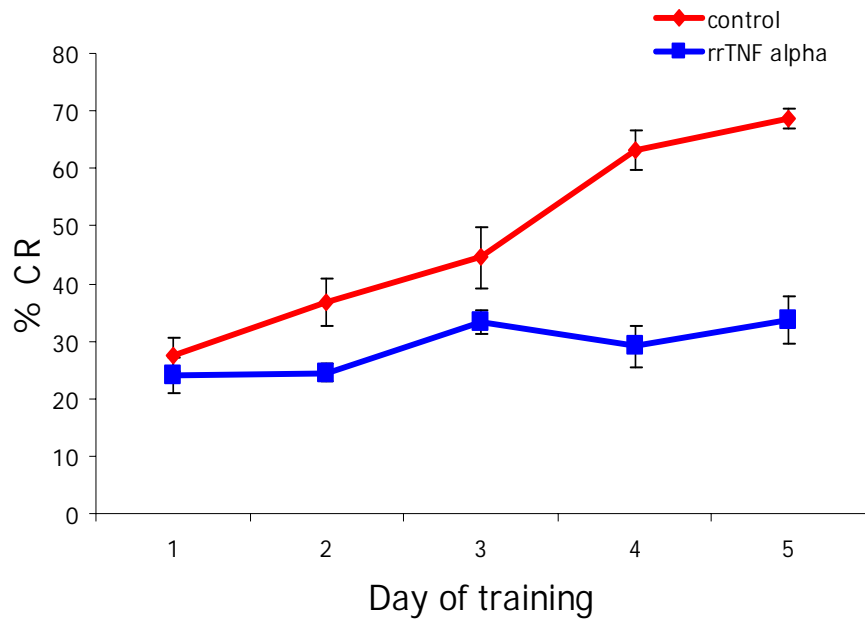
▲ Control ● Spinach



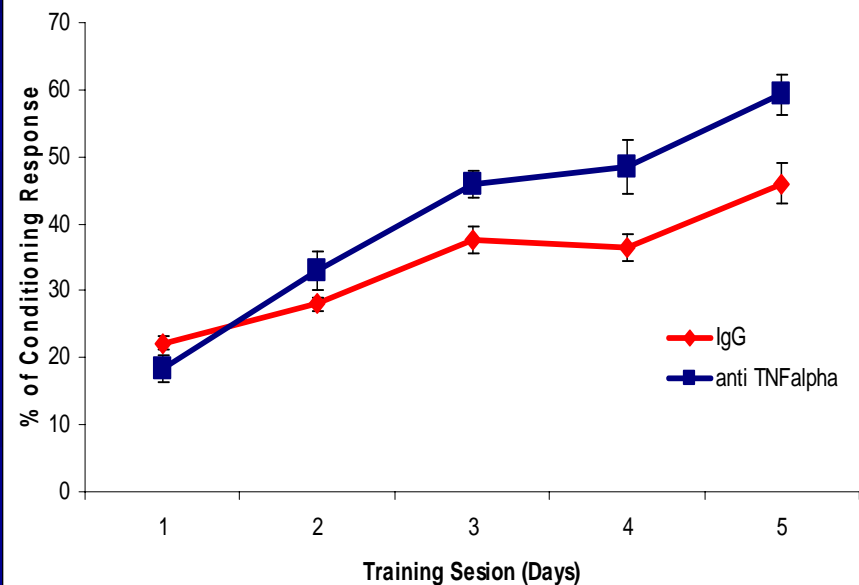
Cucumber and Apple and Spinach incorporated at 2% of diet, Spirulina at 0.1% fed in rat chow for 2 weeks or 8 weeks.

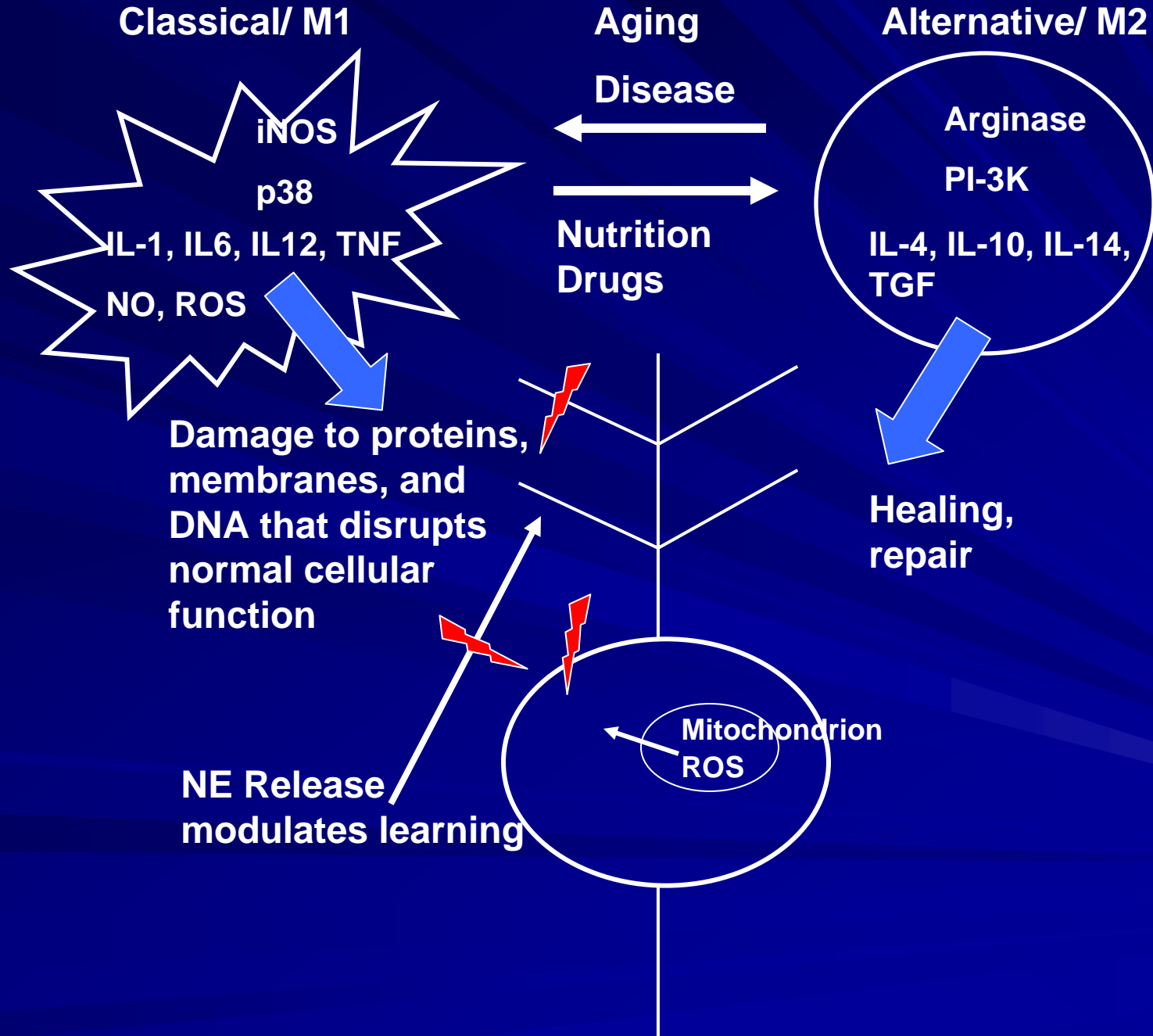
- Aging results in loss of NE signal transduction and declines in learning
- Aging is associated with increases in oxidative damage and inflammation
- Dietary supplementation can improve learning and decrease oxidative stress and inflammation
- Is inflammation directly involved, and can targeting inflammation improve learning?

Eyeblink Conditioning After rrTNF alpha Delivery in Young F344 Rats



Effect of anti-TNF-alfa administration on the conditioning learning in F344 22 months old





# Conclusions

- Aging is associated with increased inflammation and oxidative damage
- Nutritional interventions can decrease markers of aging and inflammation
- Nutritional interventions improve cerebellar dependent motor learning
- Targeting drugs and nutraceuticals that decrease oxidative stress and inflammation may help improve **functional** lifespan