

Role of an Ancestral Protein
in the
Mechanism of Restorative Sleep

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Risk to Patients from Surgery: *post-operative sleep disturbance*

PATIENTS, who are hospitalized for surgery:

- Most show impaired REM and SWS during first week
- ~25% show sleep disturbance lasting more than two weeks

Causes:

post-operative sleep disturbance

- Invasiveness of the surgery (pain, cytokine release *etc.*)
- Environmental factors (noise, lighting *etc.*)
- Psychological factors (anxiety, stress *etc.*)
- Care-related issues (vitals, diagnostic procedures *etc.*)
- Agents (opioids, inhalational anesthetics *etc.*)

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post-operative sleep disturbance

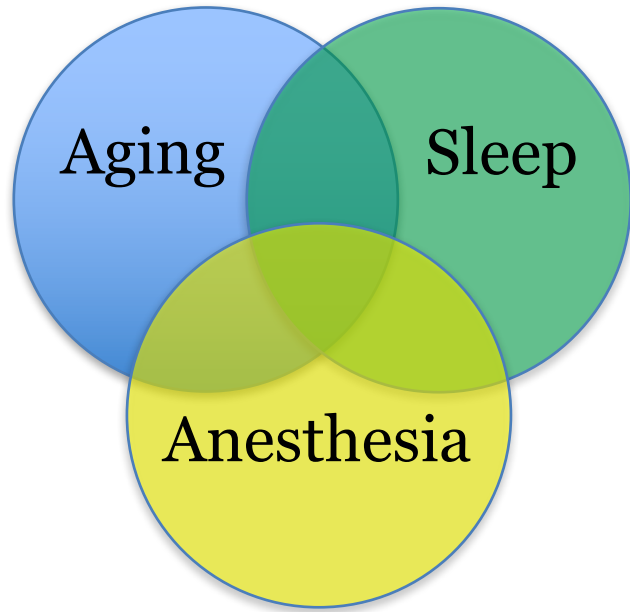
- Invasiveness of the surgery (pain, cytokine release *etc.*)
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- Care-related issues (vitals, diagnostic procedures *etc.*)
- Agents (opioids, **inhalational anesthetics** *etc.*)

Isoflurane to **healthy** volunteers: *brief* impairment of sleep architecture

Risk to Elderly Patients from Surgery: *post-operative cognitive dysfunction*

PATIENTS over age 60, who are hospitalized for surgery:

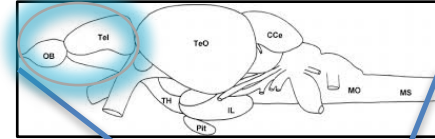
- ~40% show cognitive dysfunction on discharge
- ~12% have cognitive issues 3mo post-op



What is the underlying mechanism of restorative sleep?

ZEBRAFISH,
as the animal model

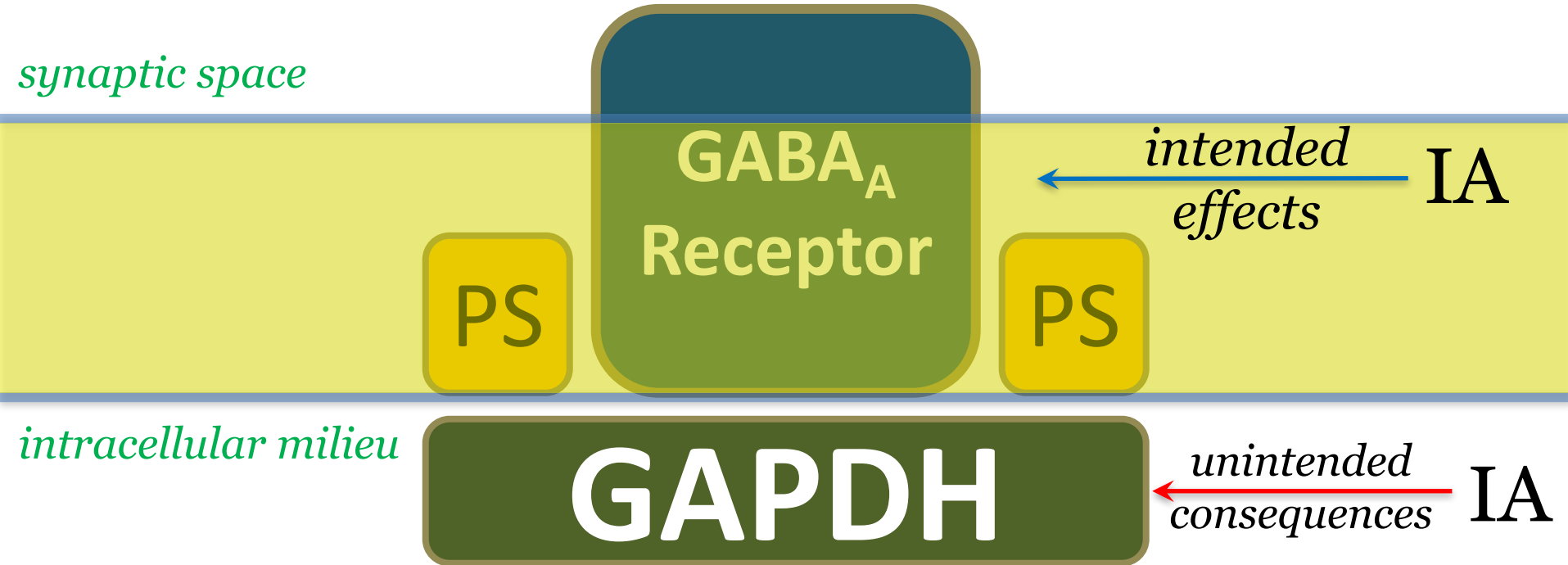
telencephalon:
FOREBRAIN



TFE →

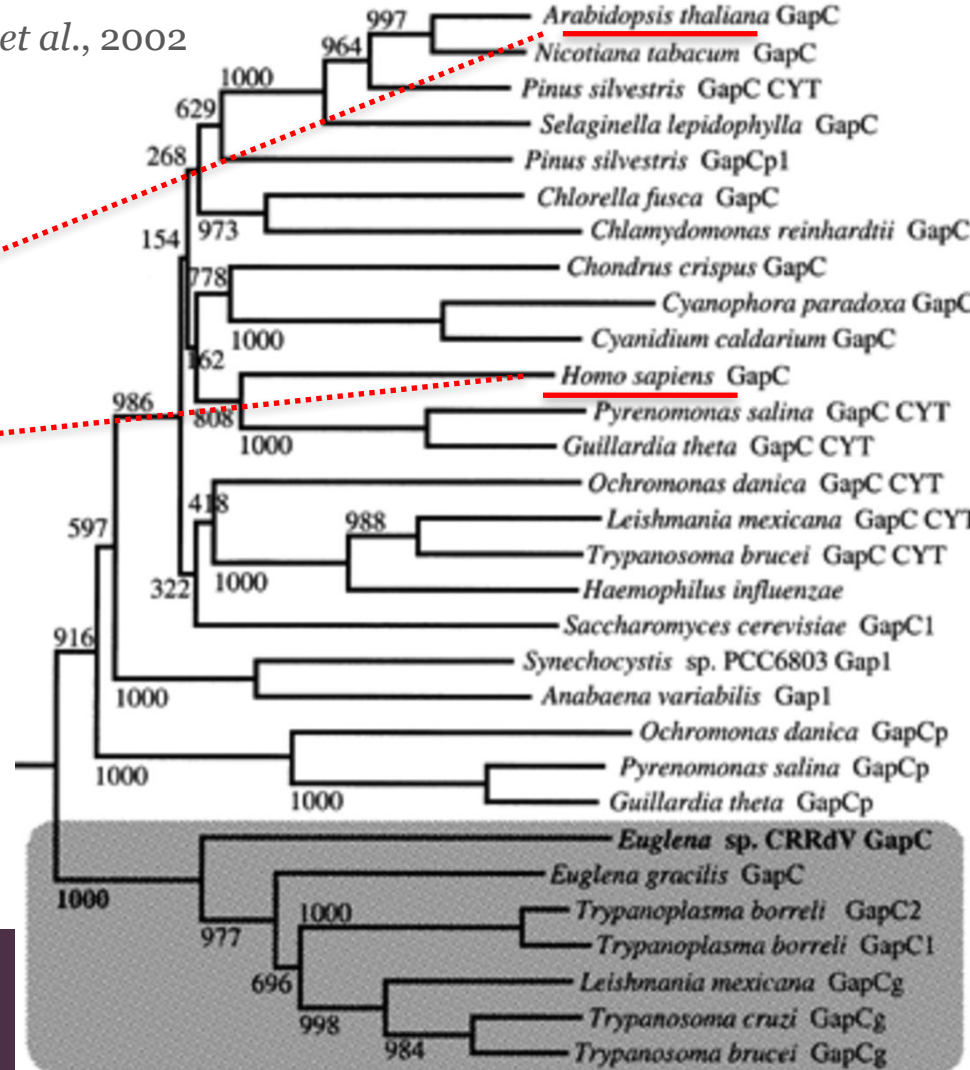


Target Neuronal Macromolecular Complex

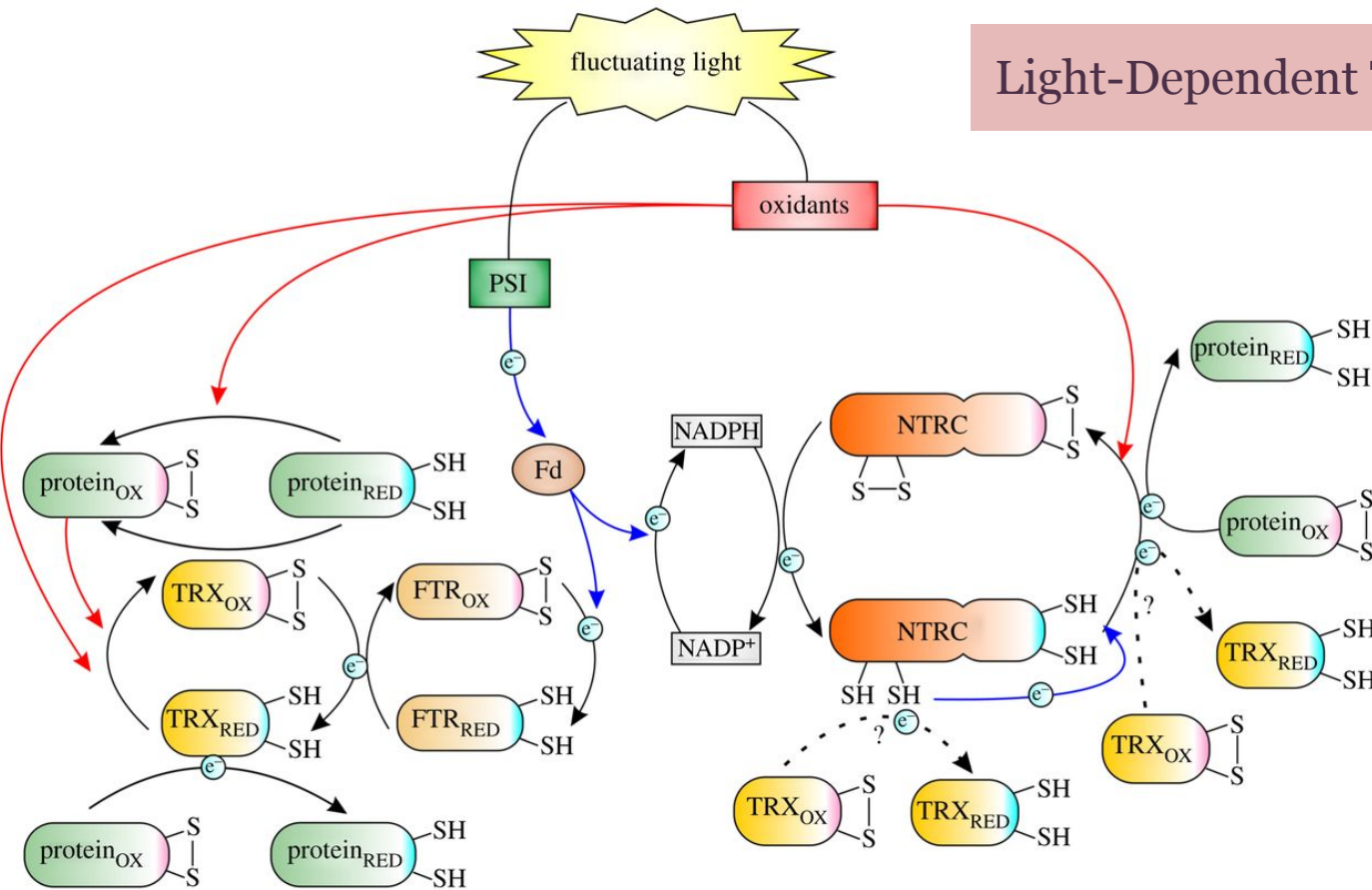


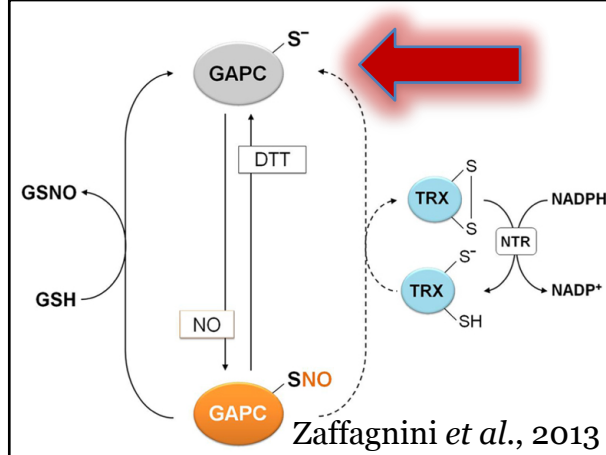
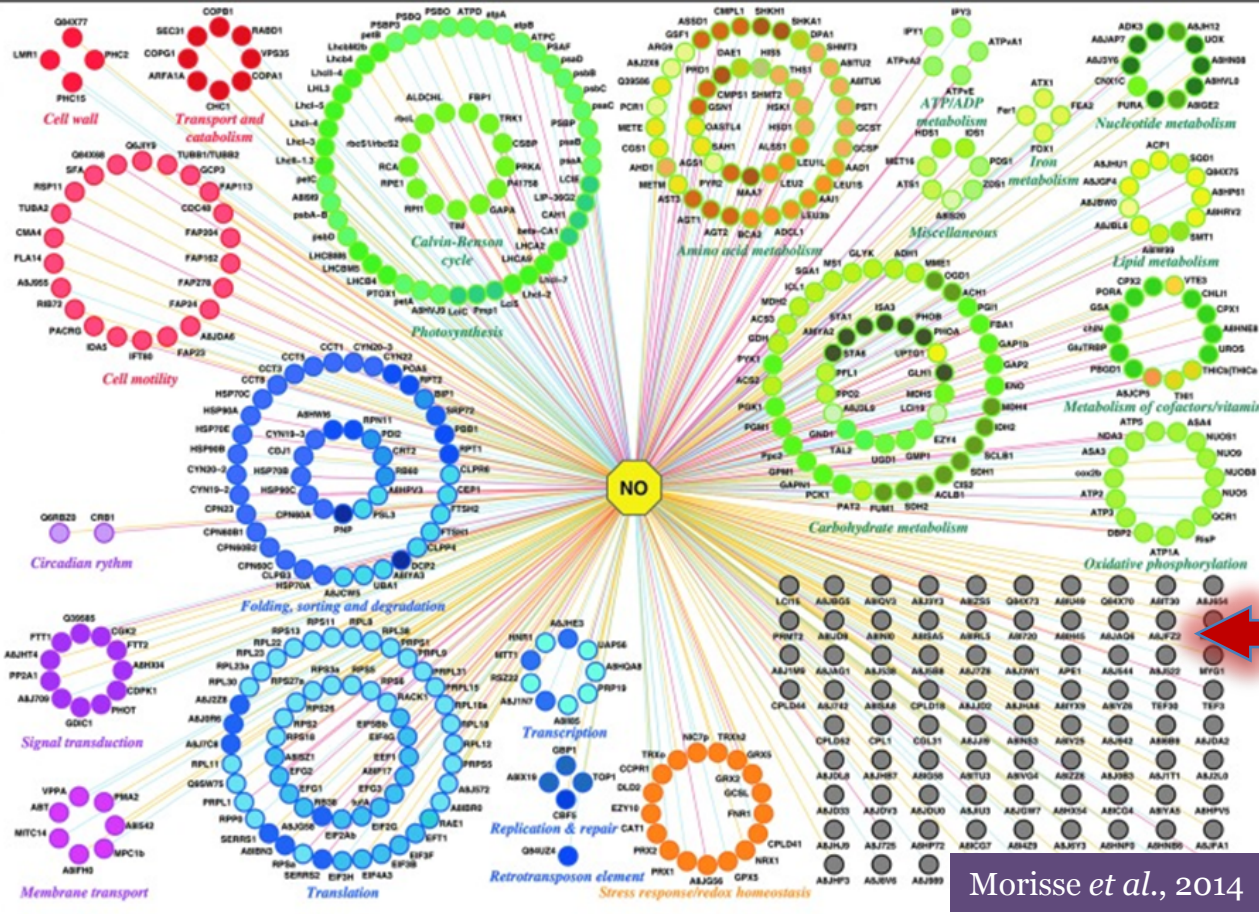
ANCESTRAL *Protein*: GAPDH

81% homologous

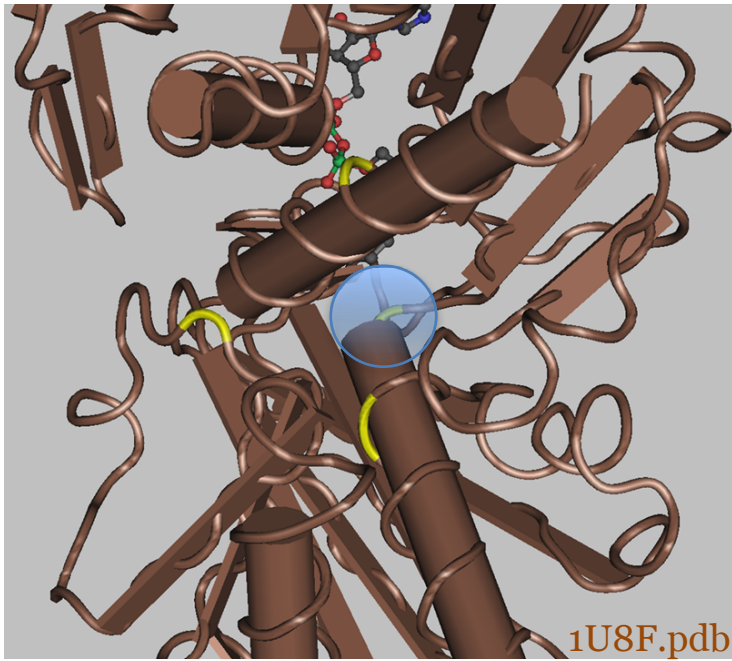


Light-Dependent Thioredoxin Pathways

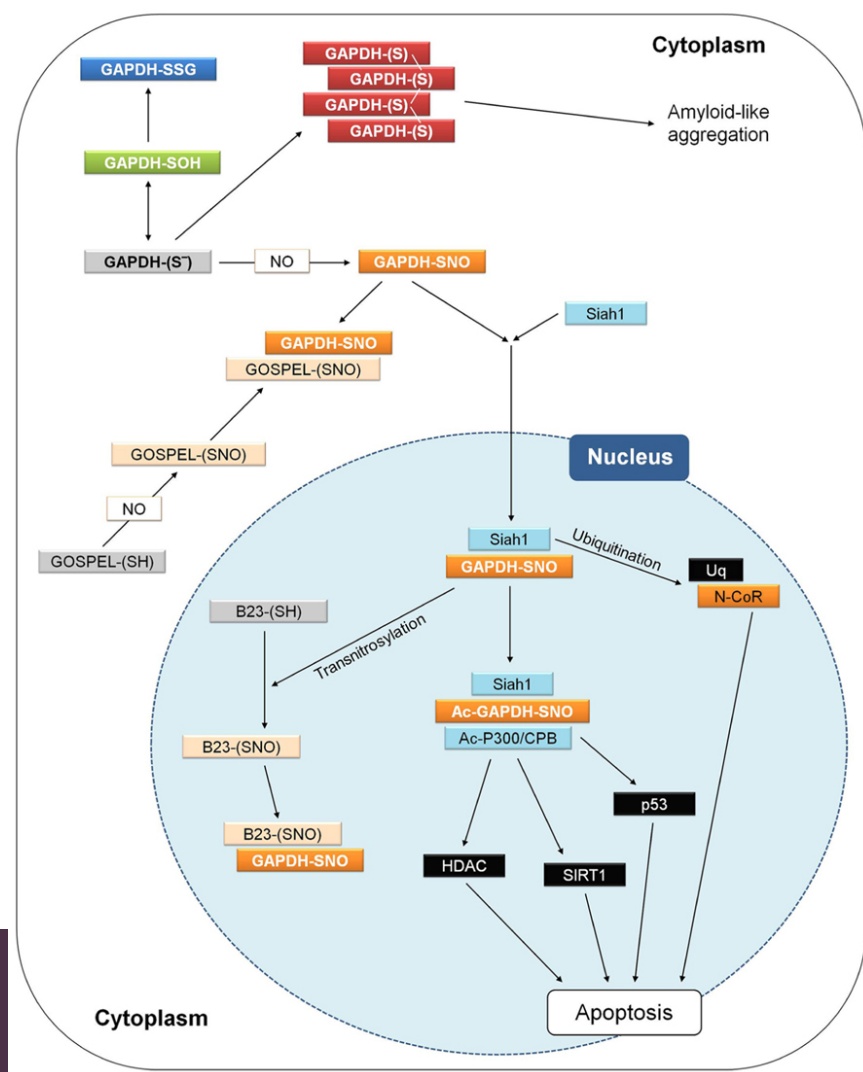




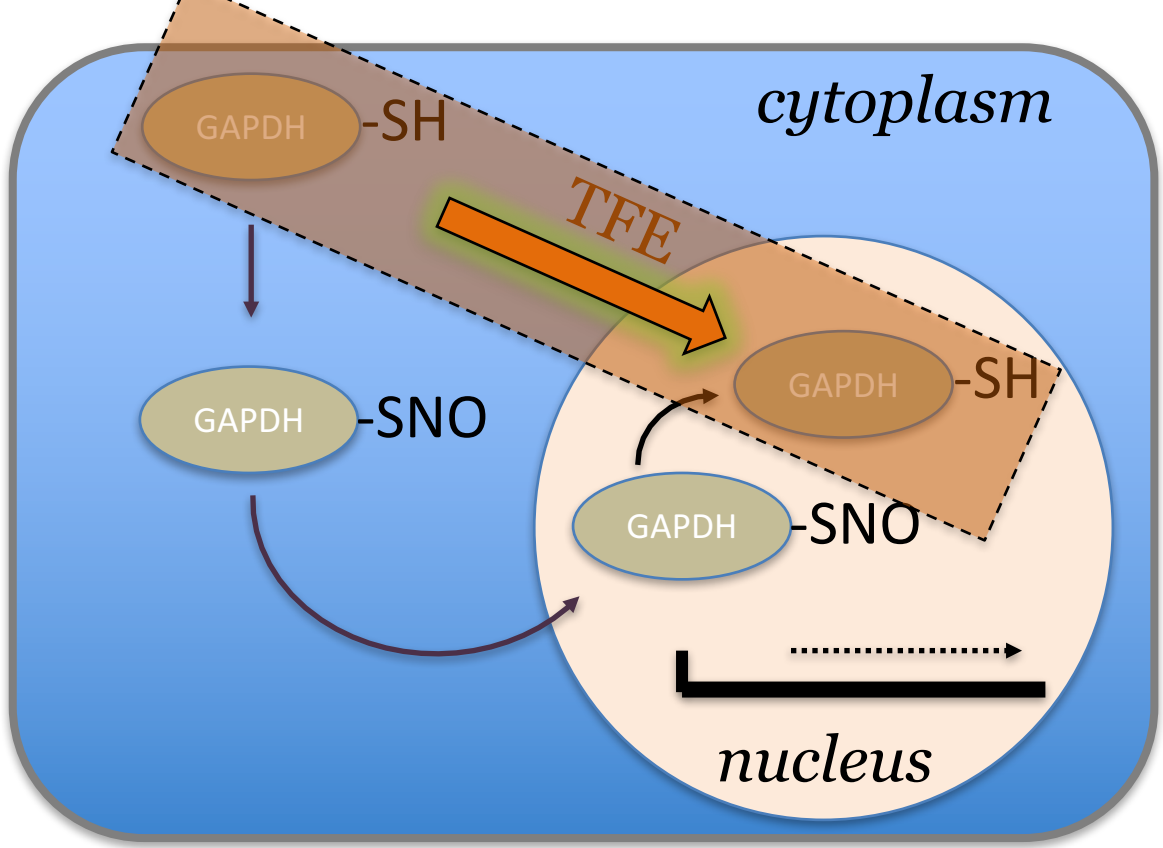
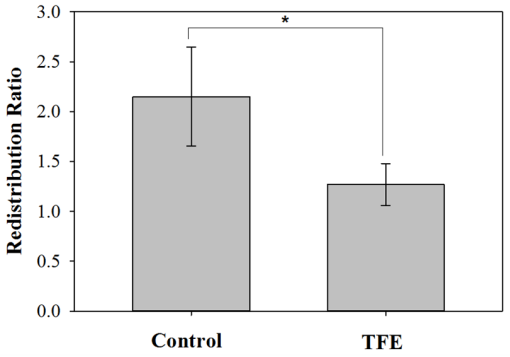
Functional annotation of S-nitrosylated proteins in *Chlamydomonas*



GAPDH: nuclear translocation



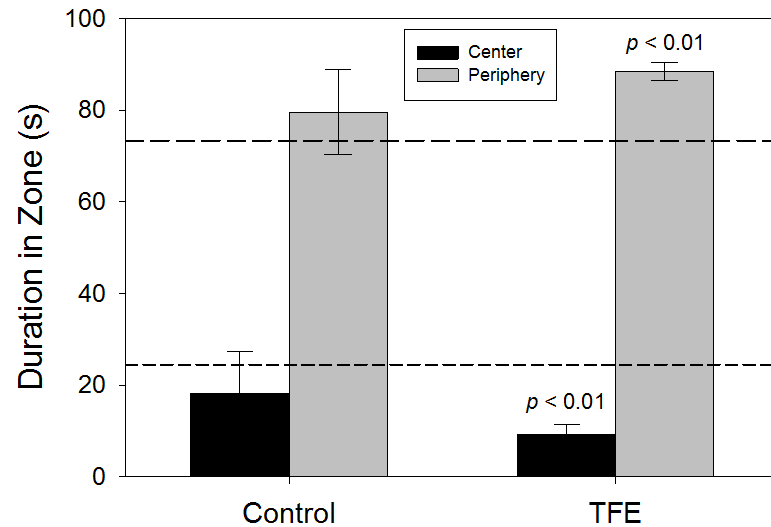
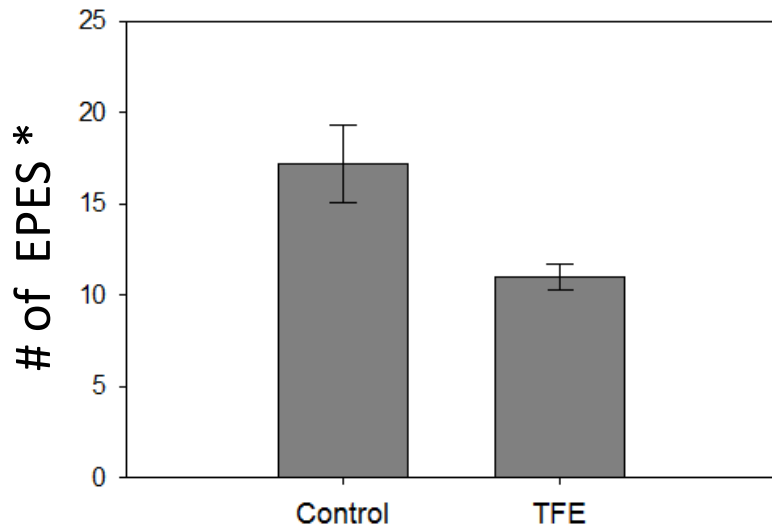
Our Study: *key observation*



additional observations...

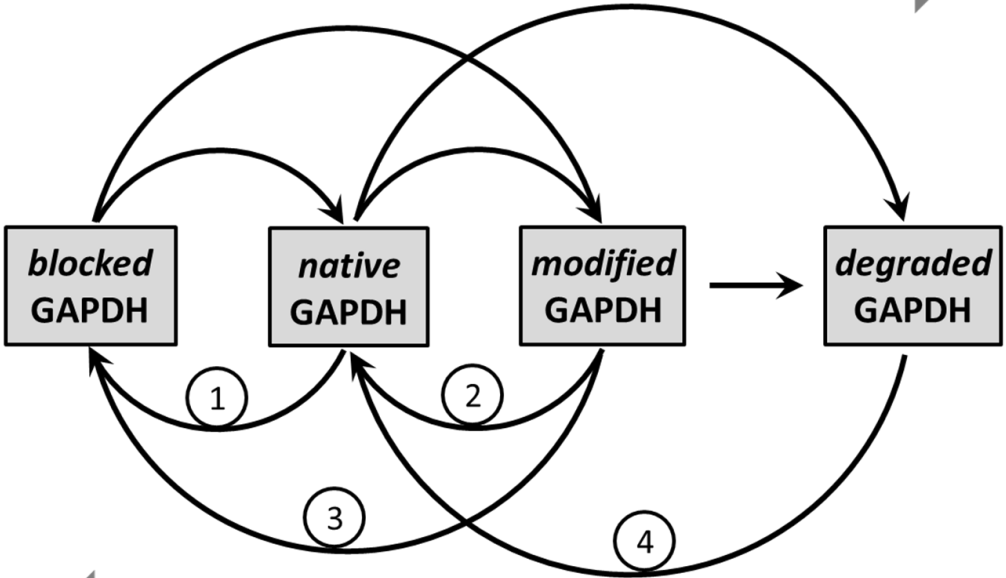
25%

75%



conclusions

WAKEFULNESS



RESTORATIVE SLEEP

Brain Gene Expression:

SLEEP Genes

- NAPDH Synthesis:
 - *Transketolase*
- Glutathione System:
 - *glutathione peroxidase*
 - *glutathione S-transferase*
- Sulfhydryl-Related Proteins:
 - *N-ethylmaleimide sensitive factor*
 - *cysteine-sulfinatase decarboxylase*

WAKEFULNESS Genes

- Glutamatergic Signaling:
 - *Ves1/homer [receptor clustering]*
 - *glutamate/aspartate transporter*
 - *glutamine synthetase*
- Aerobic Energy Metabolism:
 - *pyruvate dehydrogenase phosphatase*
 - *cytochrome b oxidase*
 - *GLUT1 [glucose transporter]*

Brain Gene Expression:

SLEEP Genes

- Glutathione System:
 - *glutathione S-transferase*
- Sulfhydryl-Related Proteins:
 - *N-ethylmaleimide sensitive factor*
 - *GAPDH*

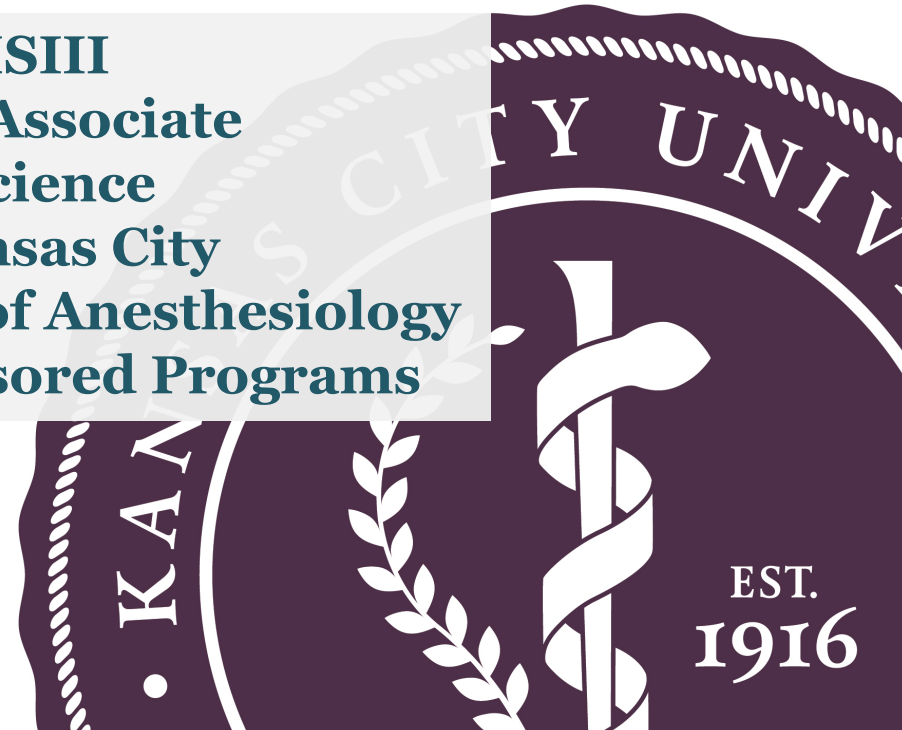
WAKEFULNESS Genes

- Glutamatergic Signaling:
 - *glutamine synthetase*
- Aerobic Energy Metabolism:
 - *pyruvate dehydrogenase E1 alpha*

acknowledgements

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Questions?

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