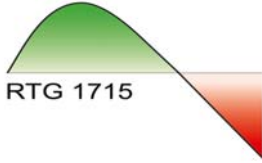


STRESS & AGING

Specific Subject of RTG 1715: Molecular Signatures of Adaptive Stress Responses



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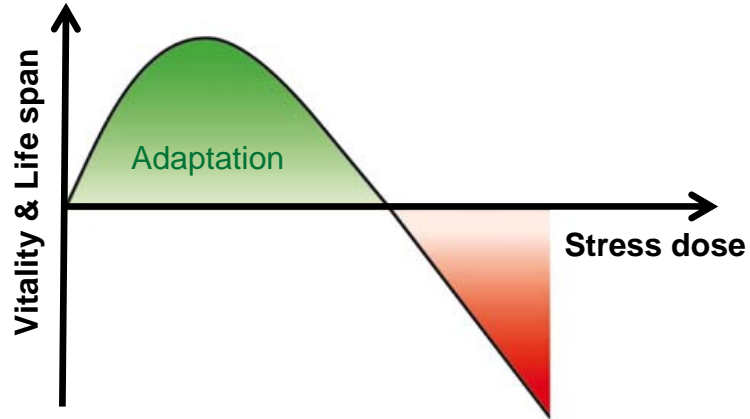


Introduction

Organisms are perpetually facing noxious insults but exhibit surprising diverse reaction patterns. Depending on the strength, frequency and quality of these stress stimuli biological systems may react with increased vitality and increased life span or with injury and degeneration. Whereas a multitude of such specific stress responses has been observed in diverse biological systems the underlying molecular mechanisms are mainly unknown.

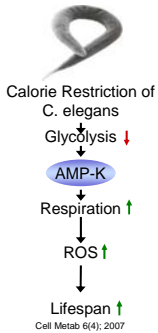
Our Research Training Group (RTG) aims to explore specific signaling reactions controlling these ambivalent reaction patterns of cells and organisms to noxious effects. The adaptive responses of signaling networks to defined stress stimuli will be investigated in a time- and dose-resolved manner using cellular and organismic models. The anticipated results are expected to significantly advance the understanding of the molecular signatures of stress responses and may also promote ongoing efforts for the effective use of the organism's preventive and regenerative potentials in modern medicine.

Working Hypothesis



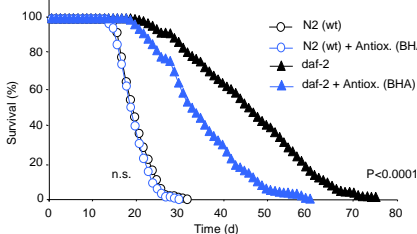
Exemplary Projects

**Mitochondrial ROS signaling
Mediates increased life expectancy**
Michael Ristow, Dept. of Human Nutrition, University Jena



Experimental setup and first results

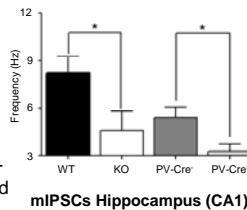
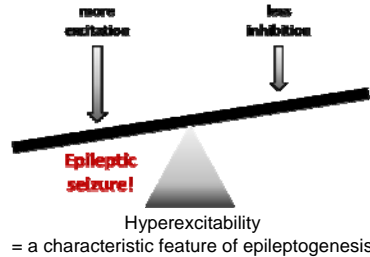
ROS formation induces lifespan extension
C. elegans lifespan



Impaired Insulin/IGF1 signaling promotes a mitochondria-derived, transient ROS signal that culminates in increased stress defense and increased longevity.

Role of NHE1 in the control of pH_i and synaptic transmission in the brain
Christian A. Hübner, Inst. of Human Genetics, Univ. Hospital Jena

NHE1-deficient mice show a complex phenotype including impaired growth, neurological symptoms including epilepsy and an early mortality (Cox et al. 1997).

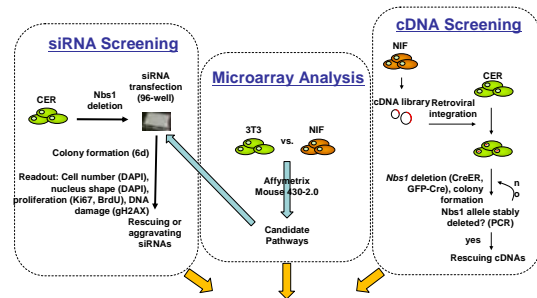


The frequency of mIPSCs is reduced implicating less spontaneous release of GABA in brain slices from NHE1 constitutive and parvalbuminergic (PV) conditional KO mice.

Identification of novel cell death pathways controlled by DNA damage response
Zhao-Qi Wang, Fritz-Lipman-Institute Jena

Experimental setup

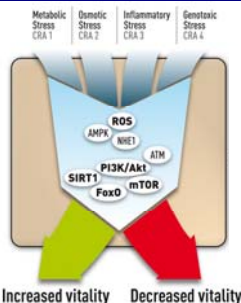
Microarray, cDNA library and siRNA screening approaches will be used to identify factors that regulate cell death in NIF cells using a cellular model of inducible deletion of Nbs1 in MEFs.



Functional Assays in cellular and mouse models

The project is aimed to screen for pathways connecting DNA damage response and survival signaling and to characterize these pathways in cellular and mouse models.

Joint Aim



In four Core Research Areas (CRA)
RTG 1715 seeks to investigate:

How do signaling networks mediate adaptive stress responses?

Synopsis

- Most of the stress responses affect cellular death and survival and aging processes in the organisms under investigation.
- First experimental results of the RTG disclose novel signaling reactions mediating adaptive stress responses of cells and organisms.
- The advanced understanding of the molecular signatures of stress responses may promote ongoing efforts for the effective use of the organism's preventive and regenerative potentials in modern medicine.