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Utilizing the multicellular model organism C. elegans for investigations of genomic integrity

Merle M Nicolai[1,2,3]*, Ann-Kathrin Weishaupt[2,3], Marcello Pirritano[4], Andrea Hartwig[5], Martin Simon[4], Tanja Schwerdtle[2,6,7], Aswin Mangerich[1] and Julia Bornhorst[2,3]

[1]Department of Nutritional Toxicology, Institute of Nutritional Science, University of Potsdam, Nuthetal, Germany
[2]TraceAge – DFG Research Unit on Interactions of Essential Trace Elements in Healthy and Diseased Elderly (FOR 2558), Berlin-Potsdam-Jena-Wuppertal, Germany
[3]Food Chemistry, Faculty of Mathematics and Natural Sciences, University of Wuppertal, Wuppertal, Germany
[4]Molecular Cell Biology and Microbiology, Faculty of Mathematics and Natural Sciences, University of Wuppertal, Wuppertal, Germany
[5]Karlsruhe Institute of Technology (KIT), Institute of Applied Biosciences, Department of Food Chemistry and Toxicology, Karlsruhe, Germany
[6]Department of Food Chemistry, Institute of Nutritional Science, University of Potsdam, Nuthetal, Germany
[7]German Federal Institute for Risk Assessment (BfR), Berlin, Germany
**merle.nicolai@uni-potsdam.de*

Caenorhabditis elegans (C. elegans) is a well-established multicellular model organism in DNA repair research as most DNA repair pathways found in bacteria, yeast, mammals, and humans are highly conserved in the nematode and next to many other advantages, genetic manipulations are fairly easy to conduct in the worm. In contrast to this, methods for specifically detecting DNA damage are scarce. Classical genotoxicity testing still relies mainly on expensive and time-consuming animal experiments or less transferrable cell culture systems, while meaningful multicellular model organisms in the niche between in vitro and *in vivo* are not yet routinely used.

Transcriptome analysis can be a powerful tool for initial pathway identification for (geno)toxicity. By developing and utilizing novel methods for assessing DNA damage (alkaline unwinding assay, 8oxo-guanine quantification) in C. elegans we provide reliable endpoints for investigating specifically the genomic integrity in a multicellular organism. In combination with investigations of the DNA damage response (poly(ADP) ribosylation quantification), DNA repair (gene expression studies, sensitivity of DNA repair deletion mutants), and endpoints of possible underlying mechanisms for genotoxicity (oxidative stress), we are able to assemble a complete model system for genotoxicity testing from (oxidative) stress, activation of the DNA damage response/ DNA repair to measuring the DNA damage itself - thus creating a modern approach for genotoxicity testing.

Keywords:
C. elegans, 3R, alkaline unwinding, PARylation, DNA repair.