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and harmful conditions to examine a whole organism. *C. elegans* changes its preference for the smell of pathogenic and the smell of wild-type worms show into aversion. The *odr-1* mutant worms, but in the presence of the odorant, showed a delayed avoidance in both conditions which also evoke stress responses. Connections between cellular and the odorant, benzaldehyde.

Animals with both light- and odor was applied as an indicator for the regulation of the stress response and defends the cell with the mechanism of aversion, we found that in wildtype, *daf-16* and

daf-16 has robust effects on both growth, i.e. concentrated odorant. We found that tissue-damaging conditions and stress responses. The nucleus already after 15 minutes. We found that independent. We found that *jnk-1* mutation did not show a sign of detoxification due to autofluorescent gut-granules observed during ageing. We found attraction to benzaldehyde, absence of the odorant. The *daf-16* translocation is an aversive response.

It is possible that due to tissue-damage resulting in cellular responses may play a role in the perception of cell damage and induction of aversion. In our further experiments we focus on understanding the role of LROs, and kinases like *kbg-1*, *mlk-1* in aversion. Our findings can contribute to understand the neuro-endocrine mechanisms behind the communication between somatic cells and neurons upon stress.

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THE MOLECULAR BACKGROUND OF THE EFFECTIVENESS OF BORTEZOMIB IN COMBINATION WITH ANTIOXIDANTS IN MELANOMA AND MYELOMA CELL LINES

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Bortezomib is a proteasome inhibitor chemotherapeutic agent that is the first-line therapy of multiple myeloma; however, recently studies offer it as a new, promising drug also to treat melanoma. Bortezomib-induced peripheral neuropathy (BIPN) is one of the most common and dose-limiting side-effects of bortezomib. The treatment of BIPN is based on neuroprotective antioxidants, e.g. alpha lipoic acid and thiamine.

The objective of our experiments was: (i) to verify the cytotoxic effects of bortezomib in melanoma and myeloma cell lines; (ii) to test the influence of the alpha lipoic acid and thiamine on the tumor growth inhibitory effect of bortezomib as well as (iii) to study the mechanisms of the effects of bortezomib + antioxidants co-treatments.

The model cells were U266 myeloma, WM35 primary and A2058 metastatic melanoma cell lines. Based on the therapeutic serum levels the tested concentrations were: (i) bortezomib: 20, 100 and 300 ng/mL; (ii) alpha lipoic acid: 10 and 100 µg/mL (iii) thiamine: 150 and 300 nM. Impedimetry (xCELLigence SP) was used to evaluate the cytotoxic effects elicited by bortezomib and the cell viability modulated by the antioxidants. To study the cell cycle profile, Cell-Clock™, a redox dye was applied and evaluated by ImageJ. Apoptotic effects were analyzed by flow cytometry after annexin V assay and phospho-p53 immunostaining.

Our results showed that bortezomib acted as a cytotoxic agent in our model cells and blocked the U266 cell cycle in the G1 phase. Alpha lipoic acid enhanced the cytotoxic effect of bortezomib (20 ng/ml) in U266 cells, while it had a restrictive effect on the antitumor actions of bortezomib in melanoma cells. However, the alpha lipoic acid significantly affected the U266 cell cycle (G1 arrest) by itself, combination of bortezomib + alpha lipoic acid the cell cycle blocking effect was not pronounced. Thiamine was barely cytotoxic and influenced the cell cycle, but in combination with bortezomib the higher concentration (300 nM) was proved to antagonize the effect of bortezomib on the growth and cell cycle of myeloma cells. In all model