# ABSTRACT

The maintenance of protein homeostasis (proteostasis) is crucial for any organism to survive and reproduce in an ever changing surrounding. This includes the ability to sense and respond to environmental cues. In this context, degradation of dispensable proteins is a prerequisite for a rapid and appropriate adaptation. Despite the identification of a multitude of factors involved in these processes, the role of microRNAs in the context-dependent regulation of proteostasis and longevity has been understudied so far.

In order to elucidate the role of microRNAs within proteostasis mechanisms, their influence on ubiquitin-dependent degradation pathways and proteotoxic stress sensitivity was analyzed in *Caenorhabditis elegans*. This led to the identification of the microRNA *mir-71* as an indispensable regulator of proteome stability. In this regard, *mir-71* is required in a specific subset of olfactory neurons, so called amphid wing C (AWC) cells. Exclusive expression of *mir-71* in AWC neurons was sufficient to rescue proteostasis defects in the intestine and support lifespan. Moreover, *mir-71* targets the conserved toll and interleukin 1 receptor domain protein TIR-1 in AWC neurons. Remarkably, abrogation of *mir-71* binding sites in the 3' untranslated region of *tir-1* entirely phenocopied loss of *mir-71*, which proved that a single target mRNA facilitates *mir-71*- dependent deficiencies. In line with its importance in AWC olfactory neurons, *mir-71* was also necessary to coordinate proteostasis adjustments to different food sources and thus, link olfactory perception with the regulation of proteome stability.

In summary, this study revealed a yet uncharacterized cell-nonautonomous signaling pathway between olfactory neurons and the intestine in *C. elegans*. The depicted results further broaden the understanding of inter-tissue signaling and additionally link olfactory experience with organismal adjustments under the control of a microRNA.