ANALYSIS OF INTERACTIONS BETWEEN THE GERMLINE RNA HELICASES (GLHs) AND THEIR REGULATORS KGB-1 AND CSN-5 IN *CAENORHABDITIS ELEGANS*

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ACADEMIC ABSTRACT

The *Caenorhabditis elegans* germline RNA helicases (GLHs) are constitutive components of P granules, non-membranous aggregates of protein and RNA that segregate with the nematode germline. The GLHs are critical for fertility. The novel MAP kinase, KGB-1, interacts with the GLH proteins, and the null *kgb-1(um3)* strain results in sterile worms at high temperatures; the germlines of these worms contain endomitotic replicating oocytes (EMO). We find that in *kgb-1(um3)* adults, while GLH-4 levels are similar to wild type, levels of GLH-1 are increased up to seven fold and the morphology of P granules is grossly affected. Binding of KGB-1 to GLH-1 requires a MAP kinase docking site. KGB-1 can phosphorylate GLH-1 using *in vitro* kinase assays, and GLH-1 is degraded by the proteasome in a KGB-1-dependent manner. In addition, KGB-1 physically associates with CSN-5 (COP9 signalosome subunit 5), another GLH binding partner. RNA interference (RNAi) of *csn-5* results in sterile worms with under-proliferated germlines, mirroring the combined *glh-1* and *glh-4* RNAi phenotype. In contrast, elimination of *csn-5* in the *kgb-1(um3)* background

results in significantly more fertile worms than in non-injected *kgb-1* worms. Based on these biochemical and genetic interactions, we propose KGB-1 and CSN-5 may oppositely regulate GLH-1, with KGB-1 degrading and CSN-5 protecting GLH-1. This cooperative system could maintain proper GLH-1 levels during normal germline development, as well as prevent excess GLH accumulation during the stressful conditions of high temperature and aging.