**Abstract**

Enterohemorrhagic *Escherichia coli* (EHEC), a foodborne pathogen, causes severe diarrhea and hemorrhagic colitis in humans. Our previous study has demonstrated that EHEC infects and kills *Caenorhabditis elegans*. Also, *C. elegans* activates the p38 MAPK innate immune pathway to defend EHEC infection. However, the *C. elegans* pattern recognition receptors (PRRs) for EHEC detection and innate immunity regulation remain understudied. PRRs are receptors for host to recognize pathogen- or microbe-associated molecular patterns (PAMPs/MAMPs) or damage-associated molecular patterns (DAMPs) and to activate innate immune response. Here, we aimed to identify potential CePRR for immunity against EHEC. PRRs identified in other metazoans contain several conserved domains, including the leucine-rich repeat (LRR). We therefore constructed a focused RNAi library to screen for *C. elegans* genes with these PRR domains. From the screening, we identified the *iglr-2* gene as a potential PRR candidate. IGLR-2 contains immunoglobulin-like (Ig-like) and LRR domains and is homologous to the *E. coli* (horse) Toll-like receptor 2. We generated *iglr-2* deletion mutants by CRISPR-Cas9 technology and found that *iglr-2* mutants are more susceptible to EHEC infection compared to the parental wild-type N2 strain. Moreover, overexpression of *iglr-2* in *C. elegans* resistance to EHEC. Besides, we found that the *iglr-2* transcript level is significantly up-regulated after EHEC infection. In order to identify the site of action of the *iglr-2* gene, we also created *iglr-2* transcriptional reporter strains and found that *iglr-2* is expressed in neuronal and intestinal cells. Previous study demonstrated that *iglr-2* expression pattern was co-localized with some neurons such as PVD, OLL, AFD and AWB. From our results, *C. elegans* lost the ability to avoid pathogens when it lost the *iglr-2* function specifically in neurons. The *iglr-2* overexpression strain, which was more resistant to EHEC infection originally, showed more susceptibility to EHEC infection upon knockdown of the p38 MAPK cascade, but no difference upon knockdown of other immune signaling pathways. Taken all together, our data suggested that *iglr-2*, a potential PRR, plays an important role in *C. elegans* to defend against EHEC infection by activating the pathogen-avoidance behavior and immune responses via, at least in part, p38 MAPK pathway or other unidentified immune cascades.

**Results**

**A.** RNAi screening identified *iglr-2* as a potential pattern recognition receptor (PRR) candidates in *C. elegans*

**B.** *iglr-2* null mutants created by CRISPR-Cas9 genome editing are hypersusceptible to EHEC

**C.** Overexpression of *iglr-2* confers *C. elegans* resistant to EHEC.

**D.** *iglr-2* is expressed in neuron and anterior/posterior intestine and may act in these tissues defense EHEC

**E.** *iglr-2* involves in EHEC avoidance behavior

**F.** p38 MAPK pathway acts as downstream of *iglr-2*

**Conclusions**

1. We identified a membrane protein, IGLR-2, containing Immunoglobulin-like and leucine rich repeat domains could be a potential pattern recognition receptor (PRR) in *C. elegans* by RNAi screening.
2. The mechanism of *iglr-2* to defense against EHEC is a combination of pathogen-avoidance behavior and immune responses via, at least in part, activated p38 MAPK pathway or other unidentified immune pathway.
3. We believe that by understanding the function of host factors could shed light on aspects of immunity in EHEC infection.

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