

P007 A genetic approach to study the function of latrophilin in *C.elegans*

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Black widow spider venom (BWSV) is known to cause neurotransmitter release from nerve terminals due to its content of high molecular weight proteins, the latrotoxins (LTX), that are known to bind with high affinity to three neural proteins in mammals. We have established *C.elegans* as a model organism to study the function of the binding protein, latrophilin (a member of the class B family of G-protein coupled receptors), and its role in regulating neurotransmitter release by latrotoxins, by showing that latrophilin is required for lethality of BWSV by RNAi experiments. However, a latrophilin-knockout worm is required for determining the function of the latrophilin gene. The *lat-1(ok1465)* allele has a deletion of the *lat-1* gene, and we know that ~97% of *lat-1(ok1465)* homozygous worms arrest or die before adulthood, with only 3 adult offspring per animal; moreover, there is strong interaction between the *lat-1* allele and various G-protein mutants. However, it is unclear if this lethality is due to the deletion in the *lat-1* gene, or to adventitious mutations introduced during the process of mutagenesis to create this allele. When transgenic worms were created with the B0457 cosmid (containing the full sequence of the *lat-1* gene), they rescued the lethality of *lat-1(ok1465)* worms, whilst concurrent injections with the *unc-54::C* marker plasmid yielded six surviving adults from >80 transgenic embryos, showing that the rescue was not due to the *unc-54::C*. Our results show that the *lat-1(ok1465)* allele causes developmental lethality and also an increase in defecation cycle timing, and that the B0457 cosmid can rescue both these defects. This is strong evidence that the *lat-1* gene is responsible for these defects. Current work aims to rescue the *lat-1(ok1465)* defects with a *lat-1* cDNA construct, and to determine the role of this gene in mediating the toxicity of Black Widow Spider venom.