The characterization of toll-like receptor repertoire in Pinna nobilis after mass mortality events suggests adaptive introgression.

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Abstract

The fan mussel *Pinna nobilis* is currently on the brink of extinction due to a multifactorial disease mainly caused to the highly pathogenic parasite *Haplosporidium pinnae*, meaning that the selection pressure outweighs the adaptive potential of the species. Hopefully, rare individuals have been observed somehow resistant to the parasite, stretching the need to identify the traits underlying this better fitness. Among the candidate to explore at first intention are fast evolving immune genes, of which Toll-like receptor (TLR). In this study, we examined the genetic diversity at 14 TLR loci across *Pinna nobilis*, *Pinna rudis* and *Pinna nobilis* x *Pinna rudis* hybrid genomes, collected at four physically distant regions, that were found to be either resistant or sensitive to the parasite *H. pinnae*. We report a high genetic diversity, mainly observed at cell surface TLRs compared to that of endosomal TLRs. However, the endosomal TLR-7 exhibited unexpected level of diversity and haplotype phylogeny. The lack of population structure, associated with a high genetic diversity and elevated dN/dS ratio were interpreted as balancing selection, though both directional and purifying selection were detected. Interestingly, roughly 40% of the *P. nobilis* identified as resistant to *H. pinnae* were introgressed with *P. rudis* TLR. Specifically, they all carried a TLR-7 of *P. rudis* origin, whereas sensitive *P. nobilis* were not introgressed, at least at TLR loci. Small contributions of TLR-6 and TLR-4 single nucleotide

polymorphisms to the clustering of resistant and susceptible individuals could be detected, but their specific role in resistance remains highly speculative. This study provides new information on the diversity of TLR genes within the *P. nobilis* species after MME and additional insights into adaptation to *H. pinnae* that should contribute to the conservation of this Mediterranean endemic species.