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Closely related parasites targeting the same host can show extensive venom variation: the case of *Leptopilina* parasitoids of *Drosophila*

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The knowledge of the molecular bases of variation in parasite virulence is essential for understanding the way hosts and parasites coevolve. However, little is known of the mechanisms of virulence variation and their impact on the extent of diversity in closely related eukaryotic parasites, except for some mammalian parasites that use antigenic variation. One of the best model to address this issue in immune suppressive parasites is the interaction between *Leptopilina* parasitic wasps and their *Drosophila* hosts, in which virulence polymorphism has been largely documented and characterization of two major immune suppressive factors has been performed. Here, we provide evidence to support the quantitative regulation of transcription of venom

proteins as a major mechanism for inter- and intraspecific variation of virulence in parasitoids. A large-scale combined transcriptomic and proteomic approach first allowed us to identify most of the proteins secreted in the venom of *Leptopilina heterotoma* and two strains of *L. boulardi*. Abundance comparisons then revealed extensive quantitative variation in venom proteins between the two closely related *Leptopilina* species, reflecting the dissimilarities in virulence strategies used by these parasitoids to escape immune response of the host. At the intraspecific level, quantitative variation was observed as well, although at a lesser extent, between both *L. boulardi* strains that differ in their virulence properties, although qualitative variation was suggested to also occur. Interestingly, an aspartylglucosaminidase, one of the major protein of the *L. heterotoma* venom, although not found in *L. boulardi*, is the most abundant venom component in *Asobara tabida*, another parasitoid of *Drosophila*, thus shedding light on a convergent recruitment mechanism of venom proteins between phylogenetically unrelated parasitic wasps. Overall, our work suggests a fast evolution of the venom of parasitoids, widely used in biological control, likely through quick and reversible changes in gene regulation.