

Heat shock system helps bug come back to life after drying up

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Heat shock factor, which exists in a single form in invertebrates but multiple forms in vertebrates, is an essential part of the ability of living cells to survive stressful conditions such as heat, cold, radiation, and, it turns out, desiccation.

The larva of the sleeping chironomid Polypedilum vanderplanki, a mosquito-like insect that inhabits semi-arid areas of Africa, is well known for being able to revive after nearly complete desiccation, losing up to 97 percent of its body's water content. However, researchers have previously been unable to determine the genetic mechanisms the insects use to achieve this feat, or the identity of the master gene that induces desiccation tolerance. Now, researchers from an international collaboration including Oleg Gusev of the RIKEN Innovation Center and collaborators from NARO, Kazan Federal University (Russia) and Skoltech University (Russia) have discovered that a gene called heat shock factor, which is present in some form in nearly all living organisms on Earth, has been co-opted by the species to survive desiccation.

Heat shock factor is an essential part of the ability of living cells to survive stressful conditions such as heat, cold, radiation, and, it turns out, desiccation. In desert insects, the researchers found, the gene is able to upregulate itself in certain conditions, and this upregulation leads to a number of downstream processes, including the synthesis of heat shock proteins that are able to protect proteins in the cell from misfolding.



To perform the research, published in the *Proceedings of the National Academy of Sciences*, the researchers compared data on RNA expression in the sleeping chironomid with a closely related species, Polypedilum nubifer, which is not capable of surviving desiccation. They found that in the sleeping chironomid, hundreds of genes, including genes known to be involved in forming a "molecular shield" against damage due to dehydration, were already expressed during the early stages of desiccation. They discovered that a certain DNA motif, TCTAGAA, which is the binding site for HSF, was strongly enriched around the transcription start site of the genes activated by desiccation in the sleeping chironomid, but not the other species. Intriguingly, they found that only in the desiccation-tolerant species, genes responsible for the synthesis of trehalose, a sugar that can stabilize cells in a dry state, contained the TCTAGAA motif.

To shed further light on the role of trehalose, they treated a cultured cell line from the sleeping chironomid with the sugar, and found that many of the genes activated by desiccation were also activated, and further, that the trehalose treatment led to the activation of the HSF gene. This effect of trehalose was prevented by knocking down the HSF gene, showing the HSF was clearly involved in the response.

According to Oleg Gusev, who led the group, "The discovery that heat shock factor is an important regulator of gene expression in response to desiccation was very interesting for us. It seems that these extremophilic insects in the process of evolution have coopted a very conservative transcription factor and its action for their own needs to survive without water by evolving a special gene structure and adjusting their genome sequence for these needs. Our data suggests the following story: HSF is activated during dehydration, and then HSF actually self-activates by binding to the upstream region of its own gene. This leads to the activation of the downstream genes that allow the insects to survive desiccation. What was very surprising to us was the finding that trehalose



itself can activate HSF."

Looking to the future, he continues, "One potential application of this finding will be in preserving cells outside the body in a dry state, if we can active the HSF gene. We now have a good understanding of how it works in this insect, so we will want to investigate if this is true for other organisms as well."

More information: Pavel V. Mazin et al. Cooption of heat shock regulatory system for anhydrobiosis in the sleeping chironomid Polypedilum vanderplanki, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1719493115

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