Where in the world is PON1? Ancient gene loss may have dire consequences for modern marine mammals

Have you ever lost something? Perhaps you have misplaced your keys or left an umbrella on the bus. Generally speaking, losing things has negative consequences. Without your keys, you are locked out of your house or car, and without your umbrella, you might get stuck in the rain. Believe it or not, genes can also get lost. Our genes typically work by coding for proteins that perform some functions in our body, from keeping our hearts beating to helping us digest food to protecting us from toxins in the environment. When genes mutate in such a way that they can no longer be translated into proteins, and therefore cannot perform their proper functions, we say that they are lost, or, more precisely, have undergone loss of function. Unlike losing other types of things, gene loss can have positive, negative, or neutral effects on an organism’s health and survival. When gene loss has positive or neutral consequences, the loss can spread throughout an entire species over evolutionary time so that the gene no longer functions in that species. In the case of a fixed loss of function, we call the residual, nonfunctional gene remnants pseudogenes.

Although gene loss across a species normally does not have negative consequences when the gene is initially lost, it may have negative consequences later. For example, a species that lives in a consistently cool climate may lose genes necessary for lowering body temperature. If the climate in that species’ habitat increases after the gene is lost, the species will be at a disadvantage. Additionally, just like other commonplace losses, it is easy to lose a gene and difficult to recover it – just imagine how difficult it is to retrieve an umbrella you left on a public bus – so species who suffer current negative consequences of ancient gene loss are unlikely to recover those genes.

A striking example of the negative modern-day consequences of ancient gene loss is the Paraoxonase 1 (PON1) gene in marine mammals. My lab, led by Dr. Wynn Meyer, discovered PON1’s loss of function after developing a method to identify pseudogenes in the mammalian genome. We looked for genes that were lost in ocean-dwelling mammals but not terrestrial mammals, and PON1 stuck out like a sore thumb. Not only does PON1 appear to be non-functional in all the marine mammals tested, but it also appears to remain functional in all terrestrial species. Such consistent loss across a broad range of species suggests that PON1 may have been lost due to the mammalian transition from land back to the water, perhaps in response to a marine diet or the necessity for long, deep diving, although we don’t know for sure yet why PON1 was lost.

Regardless of the reason for PON1’s initial loss of function, its absence may have serious consequences for modern marine mammals. The PON1 gene codes for a protective enzyme – it helps prevent plaque formation in the bloodstream by protecting fat molecules from damage, and, perhaps more importantly to our ocean-dwelling friends, it breaks down organophospate products. Organophosphates are found in agricultural pesticide by-products such as chlorpyrifos oxon and diazoxon, and these pesticides can be found in marine environments near farms due to agricultural run-off. Without functional PON1, marine mammals that live near coastlines may have no way to defend themselves against the negative effects of organophosphate exposure.

To test the ability of marine mammals to break down toxic organophospate products, our collaborators procured marine and terrestrial mammal blood samples and tested their ability to break down chlorpyrifos oxonase and diazoxonase. Marine mammal blood showed little to no activity, which indicates that marine species’ loss of PON1 has left those species unable to break down organophosphates. These findings are particularly alarming in light of the fact that chlorpyrifos has been found in waters off the Florida coastline and organophosphate pesticides have been found along the coast of Australia, waters frequented by at-risk manatees and dugongs, respectively.

Our findings show a striking pattern of ancient PON1 gene loss in marine mammals with potentially severe modern-day consequences – and unlike your misplaced keys, we won’t find PON1 by looking in the dish by the sink. Marine mammals’ unique genetics puts them at particular risk of harm from manmade products, and if we want them to continue to survive and thrive, we must consider their specialized needs when protecting their habitats. And who knows – if we keep them around, we may find even more lost genes.