Embargoed for 00:01 GMT WEDNESDAY 01 MARCH 2017

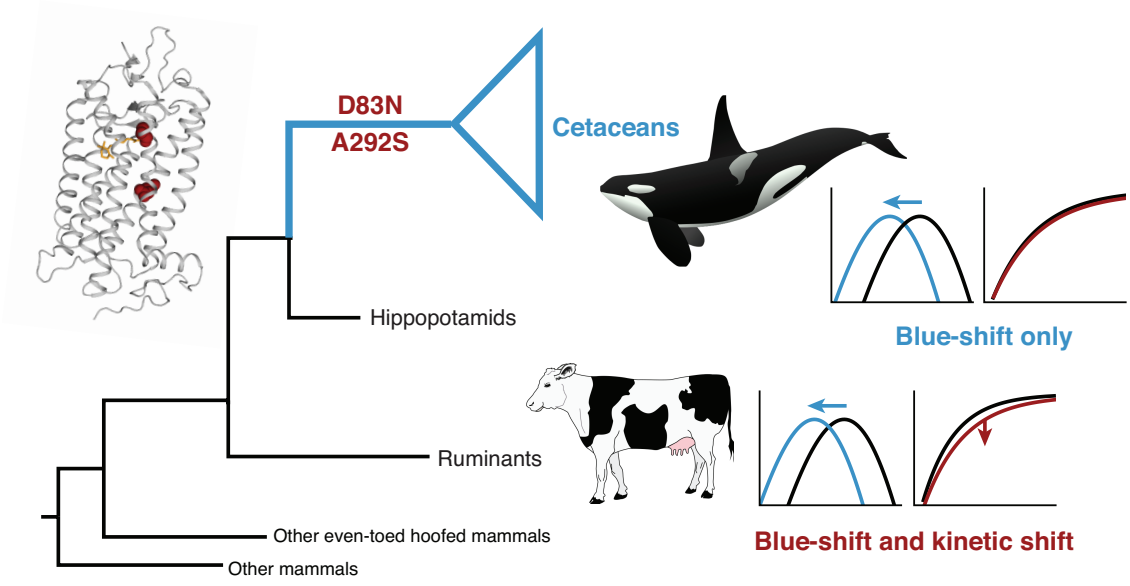
Context matters for evolution at the molecular level

Naturally occurring mutations in a visual protein have different effects in whales than in terrestrial mammals

Does a genetic mutation in one organism have the same effect in another from a different species? How to predict the effects of genetic change is a central question not just in evolutionary biology, but in all life science fields that rely on extending the results of experimental genetics in model organisms to other species.

New research from the Department of Ecology and Evolutionary Biology at the University of Toronto has tackled this question in an intriguing system. PhD candidate, Sarah Dungan, and Dr. Belinda Chang conducted mutation experiments on the visual protein, rhodopsin, from the killer whale (a member of a larger group of aquatic mammals called cetaceans) and compared the results with a commonly used model (bovine rhodopsin). They discovered that naturally occurring mutations in the killer whale rhodopsin inconsistently affect the protein's light-response properties when applied across species.

Published on March 01, 2017 in the scientific journal, *Proceedings of the Royal Society B: Biological Sciences*, the study's results also suggest that ancestral differences in the background genetic context of cetacean rhodopsin influenced the protein's evolution as cetaceans transitioned from their terrestrial ancestors into aquatic environments.



Two naturally occurring mutations (D83N and A292S) in killer whale rhodopsin together cause an adaptive blue-shift in spectral sensitivity without any concurrent changes to kinetic properties. This is not the case when the same mutations are induced in a model organism (bovine rhodopsin), an example of intramolecular epistasis. Figure credit: Sarah Dungan, University of Toronto

It turns out that two key amino acid mutations, D83N and A292S, evolved in cetacean rhodopsin over the terrestrial-aquatic transition. Both of them shift the spectral sensitivity of rhodopsin into the blue part of the light spectrum, an adaptation for underwater vision.

“These two mutations have evolved repeatedly in different lineages of aquatic vertebrates, a situation known as parallel evolution,” explains Dungan, “Their effect on spectral tuning is widely known, but we found that they also change a non-spectral aspect of rhodopsin’s function, the kinetic rates associated with light-activation. What was surprising is that, for this trait, they don’t affect bovine and killer whale rhodopsin the same way.”

For D83N in particular, the result was a pronounced slowing of kinetic rates in bovine rhodopsin, but reversing the mutation in the killer whale resulted in almost no change. This phenomenon, where the same mutation has inconsistent effects across varying genetic backgrounds, is called intramolecular epistasis.

“We would have missed this important finding if we’d only used the model system [bovine rhodopsin] for our experiments. In this case, context matters,” says Dungan.

Dungan’s experiments attributed the D83N inconsistency to an epistatic interaction effect from another site in the killer whale protein, which differs from the bovine model due to an ancestral mutation that occurred before whales diverged from their hippopotamus relatives.

“We’re seeing now that, as a result of ancestral genetic context, parallel genetic mutations don’t necessarily correspond to parallel phenotypic [trait] changes,” elaborates Dr. Chang “Though fascinating, it certainly muddles our ability to predict how traits have evolved based on genetic sequence data alone.”

So what then is the evolutionary relevance of the intramolecular epistasis in cetacean rhodopsin?

Dungan and Dr. Chang hypothesize that the resilience of killer whale rhodopsin kinetic processes to spectral tuning mutations may have a been a boon for whale ancestors transitioning into aquatic environments – they could reap the benefits of spectral blue-shifts that better match their environment without interference in the protein’s reaction rates.

The study’s results, published in *Proceedings of the Royal Society B: Biological Sciences*, show experimental evidence of intramolecular epistasis in killer whale rhodopsin, indicating that the functional roles of natural mutations in the visual evolution of cetaceans, and the nature of the selective pressures behind them, need reassessment.

Funding for the study was provided by the Natural Sciences and Engineering Research Council of Canada (NSERC), and the University of Toronto Vision Science Research Program (VSRP).

Source: http://rspb.royalsocietypublishing.org/content/284/1850/20162743