Salt management and evolution

Philip B. Bell

We are familiar with the iconic images that attempt to portray the fish-to-tetrapod transition that typically is believed to have occurred some 385 million years ago. But what evolutionary changes would have been required to enable dedicated marine organisms to conquer terrestrial habitats? Most obviously, fins would need to strengthen markedly, developing weight-bearing elbows and bendable wrists. The incipient forelimbs and hindlimbs would need to develop digits. And, of course, these putative limbs would require the acquisition of associated complex musculature as well as their secure attachment to the developing pectoral and pelvic girdles respectively. The foregoing aspects of 'redesign' are fairly obvious ones, but numerous *physiological* 'problems' also had to be solved for the alleged conquest of land to have taken place during the mid-Devonian.

Keeping salt in or out?

A formidable challenge faced by any would-be fish-a-pod is what to do about salt. A failure to control the salt content of the body fluids (0.9% in humans) plays havoc with blood pressure. Marine animals live in an aqueous medium in which the salinity is about 3.5%; actually 34–37 parts per thousand. This is principally due to Na^+ and Cl^- ions—but Mg^{2+}, Ca^{2+}, K^+, and SO_4^{2-} also contribute—these six constituents together constituting about 99% of this salt.[1] Marine fish face the challenge of keeping salt *out* since the salinity of their blood is a lot lower than the sea water. Without the constant excretion of salt, regulated via the kidneys and the gills, they would lose too much water from their body tissues by osmosis.[2] In stark contrast, the supposed transition of ocean-going animals up onto land (whether into fresh water or subaerial habitats) faces a formidable problem: how to hold on to salt. Research published in *Proceedings of the National Academy of Sciences* is claimed to have shed light on this evolutionary dilemma.[3]

The kidneys are key organs of osmoregulation in vertebrates such as humans. It is well known, for instance, that hypertension (high blood pressure) has potentially deadly consequences. It is now understood that the proper functioning of mineralocorticoid (aldosterone) receptors (MRs) is vital.[4] Indeed, any impairment or interruption of these receptors is strongly linked to kidney pathology.[5] Since renal MRs are found throughout terrestrial vertebrates, evolutionary scientists consider that they have been conserved over hundreds of millions of years. However, in marine fish the MRs help eliminate excess Na^+ ions; conversely, in humans and other terrestrial animals the MRs operate in reverse to retain salt. Moreover, the hormone ligands that turn MRs *on* in fish (progesterone and spironolactone) turn them *off* in humans.[3] The PNAS paper's lead author, Prof. Peter Fuller (*Hudson Institute of Medical Research*, Australia) believes that a better understanding of these MRs would help solve the salty problem faced by our 'Devonian ancestors'. He and his team created a chimera MR (a hybrid of human and zebrafish MRs) and compared its action with that of zebrafish and human MRs.

Where the zebrafish MR has the amino acid leucine in helix 8 of its ligand-binding domain—and this is true for other fish species too—humans and most other terrestrial vertebrates have threonine (rodents have serine). When the researchers substituted leucine for threonine (in the hybrid) the MR's response to ligand-binding changed from agonistic (*on*) to antagonistic *(off)*.[3] Understandably, Prof. Fuller and his team are encouraged by this neat result: "We may be able to design drugs that target previously unrecognized interactions within the receptor, rather than just blocking it."[6]

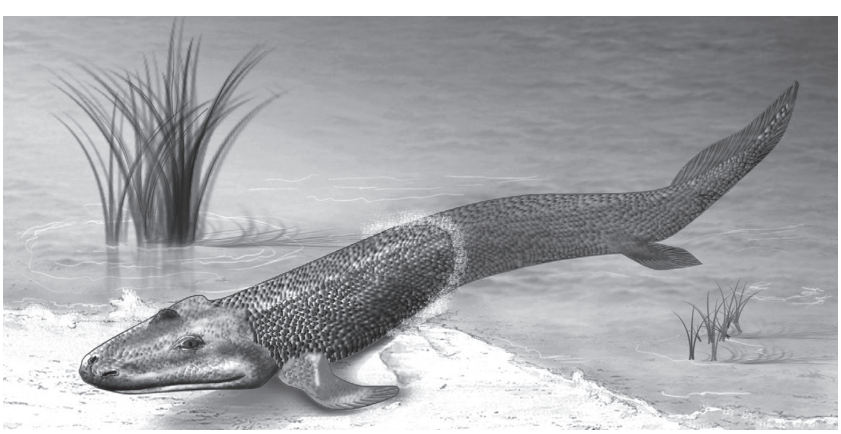

Figure 1. The possibility that osmoregulative function in fish might be altered via mutation of MR genes provides no support for the supposed evolutionary conquest of terrestrial environments.

Nice research, wrong conclusions

However, these findings are a far cry from demonstrating how the claimed evolutionary transition from sea to land or freshwater took place (see figure 1). A whole suite of physiological changes would need to occur simultaneously for such a fundamental alteration to osmoregulative function to be adaptive rather than lethal. Assuming that some fish species *could* undergo such a radical switch in renal MR function—perhaps enabling marine species to survive in brackish or even fresh water (e.g. by swimming up estuaries or by being stranded in low-saline lakes following large-scale flooding of continental margins)—the physiological plasticity of the body overall would actually bespeak superlative, front-loaded design, as many body subsystems adjust, *within* the limits and parameters already encoded within the genome.

A number of extant fish species are known to transition very successfully between marine and fresh water (e.g. eels and salmon, famously) and it would be interesting to explore the outcome of tinkering with their renal MRs. However, fascinating though these experiments on fish-human hybrid MRs are, it is wishful thinking to claim, as did one headline, that they "reveal how animals left the oceans".[6] Rather, this research could yet throw light on how some fish and other aquatic vertebrates may have survived the Flood of Genesis 6–8.[7]

References

1. There are also trace amounts of other ions, e.g. fluoride, see: Mackenzie, F.T., Duxbury, A.C., and Byrne, R.H., Seawater, *Encyclopædia Britannica* online, last updated 14 August 2018; accessed 2 December 2019.
2. The opposite problem is faced by freshwater fish whose osmoregulation is thus entirely different from that of marine fish.
3. Fuller, P.J., Yao, Y.-Z., Jin, R., He, S., Martín-Fernández, B., Young, M.J., and Smith, B.J., Molecular evolution of the switch for progesterone and spironolactone from mineralocorticoid receptor agonist to antagonist, *PNAS* **116**(37):18578–18583, 22 August 2019 | doi:10.1073/pnas.1903172116.
4. Shibata, S. and Fujita, T., The kidneys and aldosterone/mineralocorticoid receptor system in salt-sensitive hypertension, *Curr. Hypertens. Rep*. **13**(2):109–115, April 2011 | doi:10.1007/s11906-010-0175-6.
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6. Luntz, S., Fish-human hybrid hormone receptors reveal how animals left the oceans, iflscience.com, 28 August 2019; accessed 2 December 2019.
7. Batten, D. and Sarfati, J., How did fish and plants survive the Genesis Flood? creation.com/fish-plants-survive-flood, 24 February 2006.