Conflicts and compromises: TMAO as an osmolyte and chemical chaperone in dogfish red blood cells experiencing environmental stress

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The spiny dogfish shark (*Squalus acanthias*) like most elasmobranchs, uses the organic osmolytes urea and TMAO to osmoconform to their environment. TMAO is also a chemical chaperone, stabilizing proteins and preventing denaturation. Using dogfish red blood cells as our model, we hypothesized that cells experiencing acute heat or osmotic heat stress would be protected from protein damage by TMAO, and would therefore not induce the highly conserved molecular chaperone HSP70. HSP70 was not induced following an acute 1 h heat shock (from 13 – 24°C) in red blood cells incubated with physiological concentrations of TMAO. Despite a lack of HSP induction, these cells showed no indication of apoptosis, membrane damage, excess protein oxidation or ubiquitination. In contrast, a hypo-osmotic stress (50% NaCl) resulted in a significant increase in HSP70 and protein oxidative damage, but only in cells with TMAO. Regardless of the stressor or the presence of TMAO, haemoglobin-oxygen affinity remained constant. Thus, TMAO appears to sufficiently protect dogfish cells from the potentially damaging effects of heat stress without the need for inducible HSPs, but this osmolyte may provoke cellular stress in hypo-osmotic conditions.