High-altitude adaptation in Andean frog hemoglobin-O_2 binding. Enthalpic consequence of reduced chloride sensitivity

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Consequent to the intrinsic exothermic nature of heme oxygenation, haemoglobin-O_2 affinity decreases with rising temperature. This negative oxygenation enthalpy ($\Delta H'$) increases O_2 unloading from blood in warm tissues as O_2 demand increases. However, the temperature sensitivity may become maladaptive, and is often reduced, in regionally-heterothermic animals, where it potentially hinders O_2 unloading (in cold extremities of cold-tolerant mammals) or causes excessive unloading (in warm muscles and eyes of fast-swimming fish). As exemplified by the 'additional' chloride-binding site found in Hbs of cold-tolerant ruminants, such reductions are frequently due to increases in endothermic, oxygenation-linked dissociation of allosteric effectors (chloride, protons and organic phosphates like ATP and 2,3-diphosphoglycerate) that decrease Hb-O_2 affinity *in vivo*.

Does the lack of specific chloride binding sites correspondingly increase temperature sensitivity? The major isoHb of the water-breathing Andean frog *Telmatobius peruvianus* is an ideal study-model: unlike Hb of African lowland *Xenopus laevis*, it lacks α-chain chloride-binding sites and its O_2 affinity is virtually insensitive to chloride. In contrast to drastic effects in *Xenopus*, physiological chloride concentrations only marginally reduce the temperature sensitivity of *Telmatobius* Hb. Maintenance of pronounced temperature sensitivity in the presence of chloride predictably enhances cutaneous O_2 uptake in cold and hypoxic Andean ponds.