Lactate sensing by carotid body glomus cells

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The carotid body (CB) is a multimodal chemoreceptor organ in which glomus cells sense changes in blood O2, hypoglycemia, CO2, and pH. Recently, it has been suggested that CB glomus cells can also detect an increase in blood lactate, although the underlying mechanisms are unknown. We have investigated the effects of lactate on dispersed single glomus cells and in CB slices. Extracellular L-lactate (2-10 mM, sodium salt) increased glomus cell secretion rate, evaluated by amperometry, without occluding the secretory response to hypoxia and both stimuli (hypoxia and lactate) had additive effects. In accord with the amperometric data, isolated glomus cells responded to both, lactate and hypoxia, with an external Ca2+-dependent increase in cytosolic [Ca2+], as well as accumulation of NADH and reactive oxygen species (ROS). However, the kinetics of NADH increase induced by lactate were faster than those elicited by hypoxia. These data suggest that hypoxia and lactate increase NADH levels and activate glomus cells through separate signal transduction pathways. Increase in extracellular lactate seems to produce accumulation of lactate in the cytosol, which gives rise to NADH generated during the conversion of lactate to pyruvate. In contrast, hypoxia accumulates NADH primarily in the mitochondria, due to slow down of NADH/quinone oxidoreductase activity, which indirectly changes NAD(P)H levels in the cytosol (Fernández-Agüera et al., Cell Metab 2015). Activation of glomus cells by lactate may play an important role in CB-mediated regulation of respiration during exercise and in pathological conditions presenting lactacidemia.