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### THE CARBOXYTERMINAL-TRUNCATED EXTRACELLULAR CALCIUM-SENSING RECEPTOR IN TELEOSTS POSSESSES ESSENTIAL FUNCTIONAL DOMAINS

The extracellular Ca<sup>2+</sup>-sensing receptor (CaR) is a member of the seven-transmembrane domain, G protein-coupled receptor superfamily. The teleost fish CaR shares structural features with mammalian CaRs, including substantial overall amino acid (aa) sequence identity in the N-terminal extracellular, transmembrane, and C-terminal intracellular (ICD) domains, and identity in specific amino acids critical to receptor trafficking, dimerization and ligand binding. Our studies of the tilapia (*Oreochromis mossambicus*) CaR (tCaR) demonstrated effective functional coupling of the receptor to both phospholipase C (PLC) and MAPK signaling cascades in response to elevated extracellular Ca<sup>2+</sup> (Loretz *et al.*, *J. Biol. Chem.* 279:53288-53297, 2004). The 90-aa ICD of teleost CaRs is one-half in length that of mammalian CaRs due to both deletion and truncation. Studies to localize functional coupling in mammalian CaRs point to a juxtamembrane  $\alpha$ -helical segment (G protein-mediated PLC and MAPK cascade activation) and to a more distal  $\beta$ -strand segment (high affinity filamin A interaction stabilizing CaR) positioned midway along the ICD, with intervening (“tether”) and C-terminal disordered coil segments (*cf.* Zhang and Breitwieser, *J. Biol. Chem.* 280:11140-11146, 2005). Remarkably, secondary structure prediction modeling of the tCaR ICD reveals corresponding  $\alpha$ -helical and  $\beta$ -strand segments, but only abbreviated coil segments. Despite truncation and deletion to shorten the disordered coil tether compared with mammalian CaRs, teleost CaRs possess the apparent essential functional domains for intracellular signaling. Future discovery of non-mammalian tetrapod CaR structures and activities will help to refine our knowledge of these functional domains and reveal a more complete evolutionary history.