COBRE
Investigators

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Title of project: Expression of the Novel, Membrane-Bound EstrogenRreceptor (ER), GPR30 in Visual and Auditory Circuits in the Brain of the Goldfish, *Carassius auratus*.

Summary:

While it has long been known that the classic estrogen 17*β*-estradiol (E2) impacts the function of neuroendocrine structures, recent evidence has also shown that E2 impacts structures not associated with neuroendocrine function. In particular, recent work in systems ranging from humans to lower vertebrates has demonstrated that auditory circuits contain both E2 producing and E2 receptive components indicating conservation of function in the vertebrate lineage. Specifically, studies in two classic neuroethological model systems, the songbird and the midshipman fish, have demonstrated E2 plays a complex role in regulation of neuronal function ranging from 1) enhancement of E2 synthesis in response to sensory (auditory) stimulation in a seasonally-dependent manner vs. 2) rapid effects of E2 resultikng in enhanced frequency discrimination and auditory tuning. Classically, the cellular mechanisms underlying E2 actions were thought to occur via nuclear receptors ultimately resulting in transcriptional modifications; however, since Kelly et al. (1977) demonstrated that E2 can alter membrane properties of hippocampal neurons within minutes, it has also been known the E2 can alter neuronal functional rapidly, on a time course which cannot be accounted for by genomic mechanisms.

Against this background, the recent characterization of a non-nuclear, membrane-bound ER, G protein-coupled receptor 30 (GPR30), in 2006 resulted in a dramatic increase in interest and capability to study both the function of membrane bound ERs as well as their role in transducing rapid effects of E2 in the brain. However, there is still ***little known about both 1) the cellular mechanisms underlying the rapid actions of E2 or 2) the function of membrane-bound ERs.*** The goal of this proposal is to study both aspects of this question, and to achieve this I will utilize a classic neuroethological model circuit, the rapid escape response of the goldfish, *Carassius auratus*. The rapid "C-start" escape is triggered by a giant reticulospinal neuron in the brainstem, the Mauthner (M-) cell, which receives massive input from the auditory branch of the VIIIth cranial nerve. For more than 50 years, the M-cell and its circuit have been thoroughly described anatomically, physiologically and behaviorally. Given the identifiably of the few cells involved in the circuit, it provides an ideal model for studying evolutionarily conserved cellular and circuit interactions in the intact vertebrate

central nervous system and auditory regions in particular, as it permits correlation of a well-defined behavior with underlying physiological, anatomical and biochemical processes.