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**DISSERTATION TITLE:** *Neural effects of future CO<sub>2</sub> level on fish*

The continuous increase of carbon dioxide (CO<sub>2</sub>) in the atmosphere is affecting the ocean chemistry in a process commonly referred as ocean acidification. A growing base of scientific evidences have shown that the elevated CO<sub>2</sub> levels can affect fish behaviour and sensory processing, like curiosity, boldness, activity and odour preferences with a resultant threat to marine ecosystem.

In her Ph.D. thesis, Floriana Lai argues that the main link responsible for disturbed behaviour and neural responses in fish is an altered function of a neurotransmitter receptor in fish brain: the GABA<sub>A</sub> receptor. Indeed, the acid-base regulatory mechanisms used by fish to avoid blood and tissue acidosis when exposed to higher CO<sub>2</sub> environment could switch the activity of this important neurotransmitter receptor, from inhibitory to excitatory. This would cause wide spread over-activity in nerve cells, since this receptor is expressed throughout the central nervous system. Its role has been linked to important processes such as brain development, neural migration and excitability, network interaction in the cerebral cortex, memory, learning, cognition, vigilance and behaviour.

The model species used in this Ph.D. thesis is the three-spined stickleback (*Gasterosteus aculeatus*), a fish known to be able to tolerate a wide range of environmental conditions. However, Lai showed that exposure to the high-CO<sub>2</sub> level expected to occur in the future can interfere with the species brain lateralization, which is the hemisphere specialization that confer to animals the ability to carry out parallel processing and simultaneous responses. A prime evidence for an involvement of the GABA<sub>A</sub> receptor in the behavioral CO<sub>2</sub> effects is that a drug, gabazine, that suppresses the activity of the GABA<sub>A</sub> receptor was found to restore the lost behavioural lateralization in a high-CO<sub>2</sub> environment. Subsequently, Lai investigated the mRNA expression level of a wide range of genes that are linked with the GABA<sub>A</sub> receptor, revealing significant changes in the mRNA levels of the  $\alpha$  family subunits that make up the receptor. This could suggest some subunits rearrangements of GABA<sub>A</sub> receptors and possible changes in the receptor functions. Moreover, Lai expanded the field by showing that also brain plasticity may be influenced by exposure to elevated CO<sub>2</sub>, by finding an increased expression of two genes, NeuroD and DCX, regulating the growth and specialization of nerve cells.