



# Laurentian SETAC

Laurentian Chapter of the Society of  
Environmental Toxicology and Chemistry

## Ontario Virtual Pub Night

# Transgenerational hypocortisolism and behavioural disruption induced by the antidepressant fluoxetine in male zebrafish *Danio rerio*

**Dr. Marilyn Vera-Chang,**  
Postdoctoral Fellow, Canadian Nuclear Laboratories &  
Ottawa Hospital Research Institute

When: Wednesday October 28 from 6:00 – 7:30 PM

Zoom meeting: Please complete the [RSVP form](#) to  
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# Transgenerational hypocortisolism and behavioural disruption induced by the antidepressant fluoxetine in male zebrafish *Danio rerio*

**Dr. Marilyn Vera-Chang\***,  
Postdoctoral Fellow, Canadian Nuclear  
Laboratories & Ottawa Hospital Research Institute

## Abstract:

The childbearing period is accompanied by an increase in vulnerability to depression and anxiety. Due to the associated risks that these psychiatric disorders may pose to the mother and baby, the selective serotonin reuptake inhibitor fluoxetine (FLX) is often the first line of treatment. Given that FLX crosses the placenta and it is also excreted in breast milk, a developing baby may be susceptible to the disruptive effects of FLX during this highly plastic stage of development. FLX has been prescribed since the late 1980s, which represents nearly 2 human generations of therapeutic use. Although risks to babies and potentially to their descendants are beginning to be assessed in humans, this transgenerational study will require many decades of analysis. Small bodied, with a short generation time, the zebrafish (*Danio rerio*) is an excellent model system for transgenerational toxicology. Here, we demonstrate that a 6-day FLX exposure to a fetus-relevant concentration at a critical developmental stage suppresses cortisol levels in the adult zebrafish ( $F_0$ ). This effect persists for three consecutive generations in the unexposed descendants ( $F_1$  to  $F_3$ ) without diminution and is more pronounced in males. We also show that the in vivo cortisol response of the interrenal (fish “adrenal”) to an i.p. injection of adrenocorticotrophic hormone was also reduced in the males from the  $F_0$  and  $F_3$  FLX lineages. Transcriptomic profiling of the whole kidney containing the interrenal cells revealed that early FLX exposure significantly modified numerous pathways closely associated with cortisol synthesis in the male adults from the  $F_0$  and  $F_3$  generations. We also show that the low cortisol levels are linked to significantly reduced exploratory behaviours in adult males from the  $F_0$  to  $F_2$  FLX lineages. The consequences of experiencing persistent low cortisol levels have recently been linked to behavioural problems in children and chronic fatigue and burnout in adults. This may be a cause for concern given the high prescription rates of FLX to pregnant women and the potential long-term negative impacts on humans exposed to these therapeutic drugs.

\*Co-authors: Antony St-Jacques, Rémi Gagné, Chris Martyniuk, Carole Yauk, Thomas Moon, and Vance Trudeau



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## Biography:

Dr. Vera-Chang was born in Peru. When she was sixteen years old, she moved with her family to Canada. She received a B.Sc. degree in Biochemistry from the University of Ottawa, where she became intrigued about learning the mechanisms by which toxins affect the body. To further pursue this interest, Dr. Vera-Chang completed a Ph.D. degree in Biology with Specialization in Chemical and Environmental Toxicology under the co-mentoring of Professor Vance Trudeau and Emeritus Professor Thomas Moon, where she investigated the transgenerational effects of the highly prescribed antidepressant fluoxetine on the stress axis using zebrafish as a model. Currently, she is a postdoctoral fellow at the Canadian Nuclear Laboratories (CNL) in Dr. Richard Richardson's lab, although she performs her lab work at the Ottawa Hospital Research Institute (OHRI) in Dr. Marjorie Brand's lab, where she is working on "The Canadian Radon & Alpha Particle Induced Disease Biomarker Project" to identify epigenetic biomarkers in the blood cells of Canadian residents induced by radon gas exposure; a carcinogenic gas responsible for ~3,000 lung cancer deaths each year in Canada.