

## **GENERATION AND ANALYSIS OF A TRANSGENIC ANIMAL EXPRESSING A DOMINANT-NEGATIVE THYROID HORMONE RECEPTOR IN THE CEREBELLAR PURKINJE CELL.**

<sup>1,2</sup>Noriyuki Koibuchi, <sup>2</sup>Misae Ohta, <sup>1</sup>Hisaka Jingu

<sup>1</sup>Department of Physiology, Gunma University School of Medicine, Maebashi, Japan, <sup>2</sup>CREST, Japan Science and Technology Cooperation.

Thyroid hormone (TH) is essential for normal brain development. Since molecular structures of several endocrine disrupters are similar to that of TH, these substances may exert their effect, at least in part, by competitively binding nuclear TH-receptor (TR). However, molecular mechanisms of TH action in developing brain is not fully understood. To study the brain-specific TH action, we have generated a transgenic animal expressing a dominant-negative TR in the cerebellar Purkinje cell. Postnatal body weight increase is completely identical to that of normal mouse, indicating that this mouse is generally euthyroid. Morphologically, disappearance of external granule cell layer is retarded, and Purkinje cell dendrite arborization is decreased, events typically seen in hypothyroid animals. Furthermore, these mice showed a mild cerebellar ataxia. These results indicate that thyroid hormone, at least in part, acts directly to Purkinje cell to induce cerebellar development.