



Title of Research:

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Development of a short-term *in vivo* assay for thyroid hormone disrupting activity in maternal rats and their fetus/pups as prescreening for potential of developmental neurotoxicity.

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Summary of Research:

As thyroid hormones (THs) are essential for brain development, concern has been raised that mild THs disrupting chemicals may have potential to interfere with the developing brain. Since guideline studies to evaluate developmental neurotoxicity require significant resources, a simple screening assay would be valuable. The Comparative Thyroid Assay (CTA) is a candidate screening test, but it requires several animals and advanced techniques of sampling and THs measurements. We are currently attempting to develop a downsized CTA that reduces the animal number, while adding extra parameters in offspring (brain THs levels and histology). We had shown that 6-propylthiouracil (PTU, 10 ppm) induced severe (> 50%) reduction of THs and offspring brain abnormalities (heterotopia), while phenobarbital (PB, 1000 ppm) induced mild (approx. 30%) reduction of THs but did not induce brain abnormalities. Recently, the previous findings at PB 1000 ppm were reproduced, and detection of heterotopia was improved by step section. These findings suggest that the modified CTA is feasible and reliable and mild suppression of THs may have little impact on offspring brain development. Further studies should be investigated.

Timeline:

March 1, 2021 – February 28, 2022.

Topics:

Oral presentation at JCIA LRI Annual Workshop 2021 “Development of a short-term *in vivo* assay for thyroid hormone disrupting activity in maternal rats and their fetuses/pups as prescreening for potential of developmental neurotoxicity.” (On-line, August 20th, 2021)

Publications:

OHidenori Suto¹, Akira Sato², Keiko Ogata¹, Kenta Minami¹, Tadashi Kosaka², Hitoshi Hojo², Naofumi Takahashi², Naruto Tomiyama², Katsumasa Iwashita¹, Hiroaki Aoyama², Tomoya Yamada¹ (¹ Sumitomo Chemical Company, Ltd. ² The Institute of Environmental Toxicology)
“Development of a short-term *in vivo* assay for thyroid hormone disrupting activity in maternal rats and their fetuses/pups as prescreening for potential developmental neurotoxicity: Propylthiouracil and phenobarbital examples. I. Findings in maternal rats and their fetuses”. The 48th Annual Meeting of the Japanese Society of Toxicology, Kobe, Japan, July 9th, 2021.

OAkira Sato¹, Hidenori Suto², Keiko Ogata², Kenta Minami², Tadashi Kosaka¹, Hitoshi Hojo¹, Naofumi Takahashi¹, Naruto Tomiyama¹, Katsumasa Iwashita², Hiroaki Aoyama¹, Tomoya Yamada² (¹ The Institute of Environmental Toxicology ² Sumitomo Chemical Company, Ltd.)
“Development of a short-term *in vivo* assay for thyroid hormone disrupting activity in maternal rats



and their fetuses/pups as prescreening for potential developmental neurotoxicity: Propylthiouracil and phenobarbital examples. II. Findings in maternal rats and their pups". The 48th Annual Meeting of the Japanese Society of Toxicology, Kobe, Japan, July 9th, 2021.

Tomoya Yamada (Sumitomo Chemical Company, Ltd.)

"A short-term *in vivo* assay for thyroid hormone disrupting activity in maternal rats and their fetuses/pups as prescreening for potential developmental neurotoxicity". The 61st Annual Meeting of the Japanese Society Teratology, On-line, August 8th, 2021.

Tomoya Yamada (Sumitomo Chemical Company, Ltd.)

"Comparative Thyroid Assay: Current situation of a short-term *in vivo* assay for thyroid hormone disrupting activity in maternal rats and their offspring as prescreening for potential developmental neurotoxicity". The 49th Annual Meeting of the Japanese Society of Toxicology, Sapporo, Japan, July 2022.

Kenta Minami¹, O Hidenori Suto¹, Akira Sato², Keiko Ogata¹, Kenta Minami¹, Tadashi Kosaka², Hitoshi Hojo², Naofumi Takahashi², Naruto Tomiyama², Hiroaki Aoyama², Tomoya Yamada¹ (¹ Sumitomo Chemical Company, Ltd. ² The Institute of Environmental Toxicology)

"Feasibility and reliability of a downsized comparative thyroid assay for evaluating thyroid hormone disrupting activity in maternal rats and their offspring: reproducibility study with sodium phenobarbital". The 49th Annual Meeting of the Japanese Society of Toxicology, Sapporo, Japan, July 2022.