

Title of Research:

15_PT01-01

Development of new *in vivo* screening method to validate the low-dose effects induced by estrogenic chemicals using estrogen reporter mice

Principal Investigator:

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Summary of Research:

So far we have been developing a new short-term *in vivo* screening test method for xenoestrogens by using our transgenic mice carrying estrogen-responsive reporter gene (E-Rep mice) and systemic *in vivo* imaging analysis as an end point. This method has been shown the possibility of a high-superiority test method that can solve several problems of the uterotrophic bioassay which is the only *in vivo* screening test method standardized as an OECD test guideline No.440. In the current period, using our established test method, we evaluated estrogenic/anti-estrogenic potential of Bisphenol A (BPA) which is a typical xenoestrogens.

As a result, in the state of estrogen depletion, BPA showed estrogenic effect at high doses, of which action was not nonlinearity. On the other hand, in the state of maintaining the physiological estrogen level in the test animal, BPA showed anti-estrogenic effect.

These results indicate that it has been confirmed that BPA acts as a xenoestrogen in our new method. In addition, our results suggest that our new test method using systemic *in vivo* imaging analysis should perform the test in both the state of maintaining the physiological estrogen level and of estrogen depletion.

Timeline:

April 1, 2018 – March 31, 2019

Topics:

None

Publications:

- 1) Törner K, Nakanishi T, Matsuura T, Kato Y, Watanabe H, Genomic integration and ligand-dependent activation of the human estrogen receptor α in the crustacean *Daphnia magna*, ***PLoS One***, 13:e0198023 (2018)