

Estrogen-independent Activation of ErbB2 in Neonatally DES-Exposed Mouse Vagina*Shinichi Miyagawa^{1,2,3}, Yoshinao Katsu^{2,3}, Hajime Watanabe^{2,3} and Taisen Iguchi^{1,2,3}**¹School of Life Science, Graduate University of Advanced Studies; ²Center for Integrative Bioscience, Okazaki National Research Institutes; ³CREST, Japan Science and Technology, Japan*

Neonatal treatment of female mice with estrogens, including diethylstilbestrol (DES), induces estrogen-independent persistent proliferation and cornification of vaginal epithelium, resulting in tumor later in life. The molecular mechanisms of these changes, however, have not been elucidated so far. ErbBs, tyrosine kinase receptors and their ligands, epidermal growth factor family, are involved in the development in the reproductive tracts and their aberrant expression frequently occurs in cancer. In order to clarify the correlation between estrogen-independent cell proliferation and erbBs signaling, we examined the expression profile of erbBs and their ligands in neonatally DES-exposed mouse vagina. Female mice were injected (s.c.) with 3 µg /day DES or oil vehicle alone for 5 days beginning on the day of birth (day 0) and ovariectomized on day 46 and sacrificed on day 60. We found that some EGF family ligands were highly expressed and erbB2 protein was activated in neonatally DES-exposed mouse vagina, showing estrogen-independent persistent proliferation and cornification.