GS03-6 **Mechanism and novel therapeutics of anxiety-like behavior in rats induced by doxorubicin and cyclophosphamide combination treatment**

○ Yusuke SUMIYOSHI[1], Nanami NAITO[1], Yuka NAKAMURA[1], Shiho KAN[1], Soichiro USHIO[2], Ikuko MIYAZAKI[3], Masato ASANUMA[3], Yoshihisa KITAMURA[1,2], Toshiaki SENDO[2]

[1]Dept. Clin. Pharmacy, Okayama Univ. Grad. Sch., [2]Dept. Pharmacy, Okayama Univ. Hosp., [3]Dep. Med. Neurobiol. Okayama Univ. Grad. Sch.

We examined whether combination treatment with doxorubicin and cyclophosphamide, a traditional chemotherapy for breast cancer, induced anxiety-like behavior in rats. Furthermore, we evaluated the role of the serotonin $(5\text{-HT})_{2A}$ receptor subtype in the anxiety-like behavior induced by such chemotherapy. Rats were intraperitoneally injected with doxorubicin and cyclophosphamide once a week for 2 weeks. This caused the rats to display anxiety-like behavior during the light-dark test. This anxiety-like behavior was significantly inhibited by mirtazapine, a 5-HT_{2A} receptor antagonist/5-HT_{1A} receptor agonist, and tandospirone, a partial 5-HT_{1A} receptor agonist. The anxiety-like behavior induced by doxorubicin and cyclophosphamide combination treatment is mediated by hyperfunctioning of the 5-HT_{2A} receptor. On the other hand, N-acetylcysteine (NAC) is a glutathione precursor with potent antioxidant properties. NAC treatment ameliorated the anxiety-like behavior induced by combination treatment with doxorubicin and cyclophosphamide. Thus, 5-HT_{2A} receptor antagonists, 5-HT_{1A} receptor agonists or antioxidant might be useful for treating chemotherapy-induced anxiety disorders.