# Demonstration of bladder receptor binding selectivity after oral administration of solifenacin by using muscarinic $M_2$ knockout mice

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Anticholinergic agents such as oxybutynin and solifenacin are clinically used to treat overactive bladder. Solifenacin was demonstrated to have relatively more functional selectivity to the bladder tissue over the salivary glands by findings from *in vitro* and *in vivo* studies using animal models. However, the mechanism of such bladder selectivity of solifenacin is not fully understood. In current study to elucidate the mechanism of bladder selectivity of solifenacin, we investigated muscarinic receptor binding characteristics of oral solifenacin to the bladder and submandibular glands of $M_2$ subtype knockout mice, compared with oral oxybutynin.

The muscarinic receptors in each tissue of wild type and $M_2$ subtype knockout mice were measured by radioligand binding assay using [N-methyl-$^3$H]scopolamine after oral administration of oxybutynin and solifenacin. There was little difference between bladder and submandibular gland of $M_2$ knockout mice in *in vitro* muscarinic receptor binding activities of oxybutynin and solifenacin, suggesting equal affinity to the residual (predominantly $M_3$) muscarinic receptors in both tissues. In contrast, compared with that after oral oxybutynin, oral solifenacin exerted significantly greater binding activity to the bladder muscarinic receptors of $M_2$ knockout mice, while oral solifenacin exhibited significantly smaller binding activity to the submandibular gland muscarinic receptors. These data indicate that oral solifenacin, unlike oral oxybutynin, may exert greater binding to bladder $M_3$ muscarinic receptors than submandibular gland under *in vivo* condition. In conclusion, the present study has shown that oral solifenacin might be advantageous for the treatment of overactive bladder, in terms of high selectivity to the bladder.