

EXPRESSION PATTERNS OF PROMOTERS FOR NPY Y1 AND Y5 RECEPTORS IN Y5RITTA AND Y1RVENUS BAC TRANSGENIC MICE

Angela Longo, Alessandra Oberto, Elena Acquadro, Thorsten Busb, Rolf Sprengel and Carola Eva

Dipartimento di Anatomia, Farmacologia e Medicina Legale; Sezione di Farmacologia, Università degli studi di Torino

Department of Molecular Neurobiology Max Planck Institute for Medical Research, 69120 Heidelberg, Germany

In the rat brain Y1 and Y5 receptors are co-expressed in various forebrain regions where they mediate several NPY activated functions, including feeding behaviour, anxiety, neuronal excitability and

hormone secretion. We studied the distribution pattern and cellular co-localization of the Y1 and the Y5 receptor gene expression in the mouse brain by using transgenic mice with genomically integrated BAC clones, where the coding regions of the Y1 and Y5 receptor genes were replaced by Venus and the synthetic transcription factor itTA reporter genes, respectively (Tg^{Y5RitTA/Y1RVenus} mice). Analysis of itTA-mediated activation of Cre recombinase and of Venus fluorescence revealed copy number-dependent expression levels, between the lines, but comparable patterns of expression. In three transgenic lines the itTA directed Cre expression was high in the olfactory system, cerebral cortex, hippocampus and basai ganglia. Weaker expression was found in most of the hypothalamic nuclei of line 25, the highest expressing transgenic line. Activation of Cre was itTA-dependent and could be regulated by doxycycline. Venus fluorescence was intense and widely expressed through the brain and it co-localized with Cre immunostaining in neurons of distinct brain regions, including the cerebral cortex, basolateral amygdala, dentate gyrus and paraventricular nucleus. These data provide a detailed and comparative mapping of Y1 and Y5 receptor promoter activity within cells of the mouse brain. The Tg^{Y5RitTA/Y1RVenus} transgenic mice generated here also represent a genetic tool for conditional mutagenesis via the Cre lox system, particularly of genes involved in feeding behavior, neuronal excitability and hormone secretion.