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Abstract: Alzheimer's disease (AD) is histopathologically characterized by neurodegeneration, the formation of intracellular neurofibrillary tangles and extracellular A? deposits that derive from proteolytic processing of the amyloid precursor protein (APP). As rodents do not normally develop A? pathology, various transgenic animal models of AD were designed to overexpress human APP with mutations favouring its amyloidogenic processing. However, these mouse models display tremendous differences in the spatial and temporal appearance of A? deposits, synaptic dysfunction, neurodegeneration and the manifestation of learning deficits which may be caused by age-related and brain region-specific differences in APP transgene levels. Consequently, a comparative temporal and regional analysis of the pathological effects of A? in mouse brains is difficult complicating the validation of therapeutic AD treatment strategies in different mouse models. To date, no antibodies are available that properly discriminate endogenous rodent and transgenic human APP in brains of APP-transgenic animals. Here, we developed and characterized rat monoclonal antibodies by
immunohistochemistry and Western blot that detect human but not murine APP in brains of three APP-transgenic mouse and one APP-transgenic rat model. We observed remarkable differences in expression levels and brain region-specific expression of human APP among the investigated transgenic mouse lines. This may explain the differences between APP-transgenic models mentioned above. Furthermore, we provide compelling evidence that our new antibodies specifically detect endogenous human APP in immunocytochemistry, FACS and immunoprecipitation. Hence, we propose these antibodies as standard tool for monitoring expression of endogenous or transfected APP in human cells and APP expression in transgenic animals.