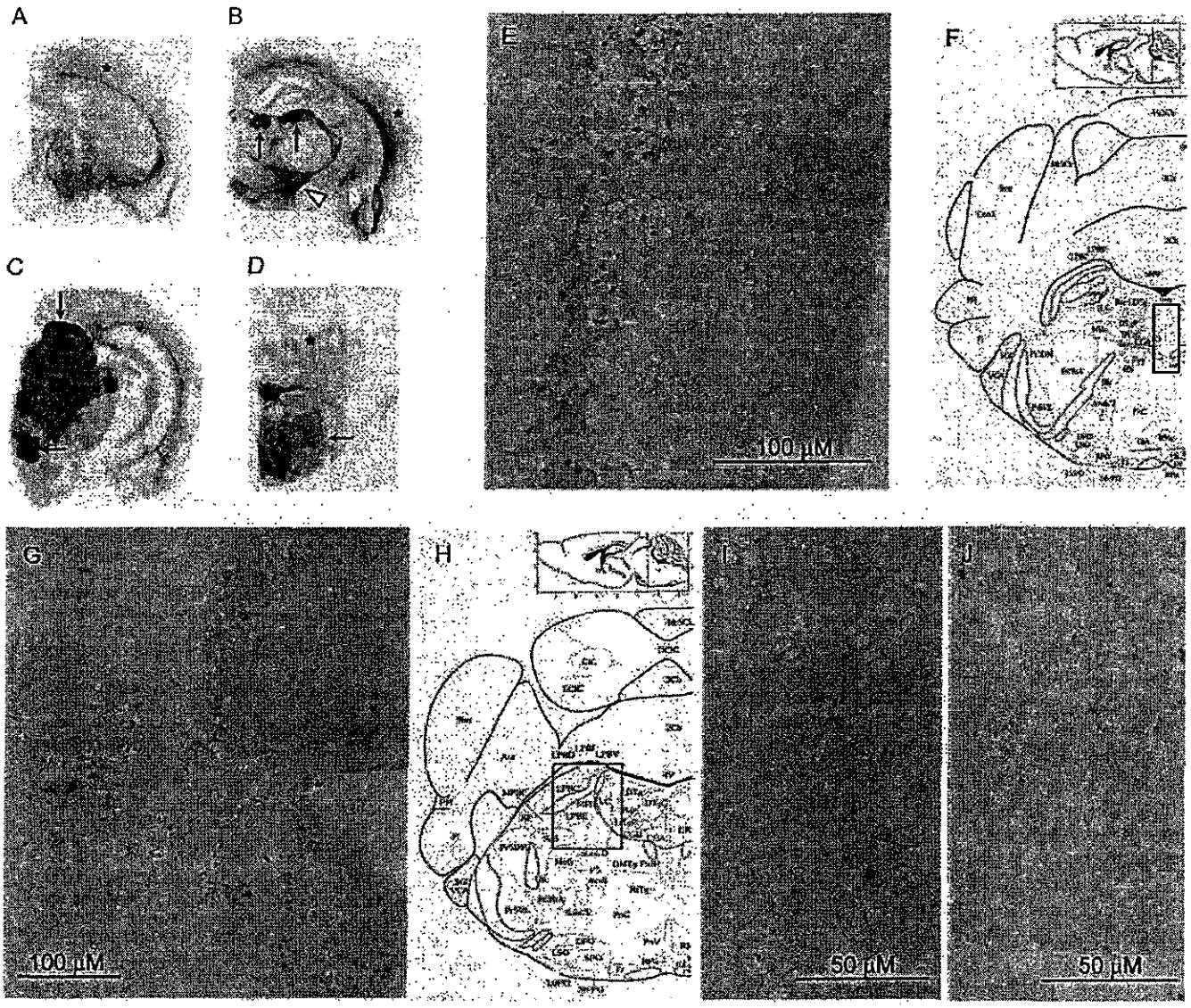

FIG. 3. Histoblot analysis and immunohistochemistry of BASE strain-infected and sCJDMM1-infected Tg(HuPrP) mice. (A to D) The histoblot analysis revealed preferential immunostaining of the PrP^{Sc} in the dorsal thalamic nuclei (arrows in panel B), along with hypothalamic nuclei (arrowhead) and brain stem nuclei (arrows in panels C and D), while PrP^{Sc} in the cerebral and cerebellar cortices (stars in panels A, B, and D) was mostly limited to the deep and inferior cortical regions. (E to J) The PrP immunostaining (E and G) of the intensely PrP-reactive brain stem nuclei in histoblot analysis (boxed regions in panels F and H) revealed coarse PrP granules, while the PrP immunostain in the cerebral cortex (I) was minimal and characterized mostly by a plaque-like pattern. In contrast, widespread fine-granular PrP immunostaining was observed in the cerebral cortex of symptomatic Tg40 mice following inoculation of sCJDMM1 brain homogenates (J). Monoclonal antibody 3F4 was used for all the staining.

ized Tg mice with PrP-129M and possibly for humans with PrP-129MM. The BASE strain also appears to be more virulent than BSE-C in bovinized Tg mice, since the incubation time for the BASE strain is 185 ± 12 days, whereas that for BSE-C is 230 ± 7 days (7). Nevertheless, compared with the 100% attack rate and incubation times of ~9 months for sCJDMM1 and sCJDMM2 in the Tg40 line (Table 1), the 60% attack rate and unusually long incubation times (20 to 22 months) for the BASE strain in the same Tg line suggest that the transmission barrier from the BASE strain to humans with PrP-129MM is still quite significant.

PK-resistant PrP^{Sc} was also detected in the spleen in 4 out of 18 BASE strain-infected Tg40 mice. In contrast, no spleen involvement could be demonstrated for the Tg40 mice following i.c. inoculation with human PrP^{Sc} from sCJDMM1. This is the first report of the presence of PrP^{Sc} in the spleens of humanized Tg mice after i.c. inoculation with a BSE strain, suggesting that the BASE strain, like BSE-C, where at least in vCJD-infected subjects PrP^{Sc} and prion infectivity have been detected in spleens and tonsils (6, 11), is intrinsically lymphotropic. Therefore, lymphoid tissues of BASE strain-infected individuals might also carry prion infectivity.

The gel mobility of the PK-resistant PrP^{Sc} recovered from the BASE strain-inoculated Tg40 mice was consistently slightly faster than the mobility of BSE-C, as originally reported for the BASE strain (8). The computed difference in gel mobilities