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Agnoprotein and its coding sequences play regulatory roles in JC virus gene transcription and replication in glial cells

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It has been suspected that human neurotropic virus, JC virus (JCV), late agnoprotein may play regulatory roles in JCV gene transcription and replication. Here, we investigated the importance of this protein and its coding sequences in such processes by using point (Pt) and deletion (Del) mutants of the virus. Results from transcription studies showed that expression of viral early and late genes was substantially decreased in cells transfected with agnoprotein Pt mutant and completely abolished in cells transfected with agnoprotein deletion mutant compared to wild type (WT). These observations suggest a possibility that agnoprotein coding region, in addition to agnoprotein itself, may be involved in regulation of JCV gene expression. DNAse I footprinting analysis of agnoprotein coding region in this respect revealed several protected areas supporting the idea that an unidentified transcription factor(s) perhaps interacting with specific regulatory elements present within the coding region of agnoprotein may participate in viral gene regulation. We extended our studies to analyze the effect of both mutants on viral DNA replication and showed that compared to WT DNA replication, the level of viral DNA replication was significantly decreased in cells transfected with agnoprotein Pt mutant, and completely abrogated in cells transfected with agnoprotein Del mutant, corroborating with the observations obtained from transcription studies. These results collectively suggest that agnoprotein and its coding sequences may play important roles in regulation of JCV transcription and DNA replication and, thereby, in successful completion of the viral lytic cycle.

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