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polyomavirus JC small regulatory agnoprotein forms highly stable homodimers and oligomers: Implications for its role during the viral replication cycle

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C virus (JCV) is the etiologic agent of the human brain disease known as progressive multifocal encephalopathy (PML). It encodes a small basic phosphoprotein(71 amino acid long) from its late coding region called agnoprotein, which has been shown to play important regulatory roles in viral replication cycle. In this study, bacterially-produced fusion protein of agno was unexpectedly found to induce multiple high molecular weight protein complexes of unknown identity and function in vitro. We further characterized the nature of these agnoproteinassociated complexes by biochemical approaches in vitro, and investigated the functional consequences of the deletion of the agnoprotein region responsible for the complex formation in vivo. Antibody detection and mass spectrometry studies clearly confirmed that the high molecular weight complexes form due to dimer/oligomer formation property of agnoprotein. Exposure of these complexes to strong denaturing agents, including urea, high concentration of SDS and prolonged heat treatment, had little effect on the integrity of these complexes, demonstrating that agnoprotein forms highly-stable dimers/oligomers. Deletion analysis studies mapped the dimer/oligomer formation domain of agnoprotein to amino acids from 18 to 42. Surprisingly, this domain of agnoprotein was found to assume an alpha-helical structure by computer modeling predictions. Subsequent removal of the alpha-helical region from the viral background severely affected the efficiency of the JCV replication cycle. Collectively, all these findings suggest that agnoprotein may form functionally active homodimer/oligomer complexes in vivo and such structures could be important for its function during the viral propagation cycle and therefore for the progression of JCV-caused disease, PML.

## Biography

MahmutSafak has received his Ph.D. from Thomas Jefferson University Medical School in 1988 and completed his postdoctoral studies at MCP-Hahnemann University at Dr. KamelKhalili's lab in 2000. He is currently a faculty member at the Department of Neuroscience, Temple University School of Medicine. He has published more than 20 papers in reputed journals and wrote several book chapters.