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## Cooperative Sequence Specific Assembly of Human Parvovirus B19 NS1 Nuclease Domain at Promoter and Origin Sequences

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Human Parvovirus B19 (B19V) is a ubiquitous virus known to cause Fifth disease in children, as well as a benign, self-limiting infection in adults. In addition, in a subset of cases, B19V can lead to any one of a number of serious illnesses, including the possible triggering autoimmune disease in genetically susceptible individuals. NS1 is the main replicative protein of B19V, is required for viral replication and viral gene expression, and is also implicated in the inflammation-related pathology of B19V infections, both short and long-term. We purified recombinant NS1 nuclease domain (residues 2-176) and tested its DNA cleavage activity and specificity, as well as its binding to sequences derived from the viral origin of replication and several different promoter sequences including those of the IL-6 and TNFα genes. We find that the NS1 nuclease domain cleaves at its predicted site at the viral origin (the trs), although with limited sequence specificity, and requires that the trs be single stranded. As predicted, it becomes covalently attached to the DNA during cleavage. The NS1 nuclease domain also bound sequence specifically and cooperatively to double stranded DNA containing viral origin and promoter sequences, as well as to the human p21 promoter sequences. Stoichiometric measurements indicate multiple (7-10) tandemly bound copies on the DNA. In contrast, only weak, non-sequence-specific binding was seen to the previously identified regions of the human IL-6 and TNFα promoters. Full length NS1, or cooperation with host proteins, may be required for interaction with those DNA sequences. In addition, we will also present recent and ongoing work on the structure of the NS1 nuclease domain bound to DNA, and the identification of host proteins which interact with full length NS1.

Reference:

Sanchez, J.L., Romero, Z., Quinones, A., Torgesun, K.R. & Horton, N.C. (2016) “DNA Binding and Cleavage by Human Parvovirus B19 NS1 Nuclease Domain”, *Biochemistry*, 55, 6577-6593.