Role of the 207-218 peptide region of Moloney murine leukemia virus integrase in enzyme catalysis

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X-ray diffraction data on a few retroviral integrases show a flexible loop near the active site. By sequence alignment, the peptide region 207-218 of Mo-MLV IN appears to correspond to this flexible loop. In this study, residues H208, Y211, R212, Q214, S215 and S216 of Mo-MLV IN were mutated to determine their role on enzyme activity. We found that Y211A, R212A, R212K and Q214A decreased integration activity, while disintegration and 3?-processing were not significantly affected. By contrast H208A was completely inactive in all the assays. The core domain of Mo-MLV integrase was modeled and the flexibility of the region 207-216 was analyzed. Substitutions with low integration activity showed a lower flexibility than wild type integrase. We propose that the peptide region 207-216 is a flexible loop and that H208, Y211, R212 and Q214 of this loop are involved in the correct assembly of the DNA-integrase complex during integration.