The NMR solution structure and dynamics of K7: "A poxvirus protein that adopts a Bcl-2 fold"

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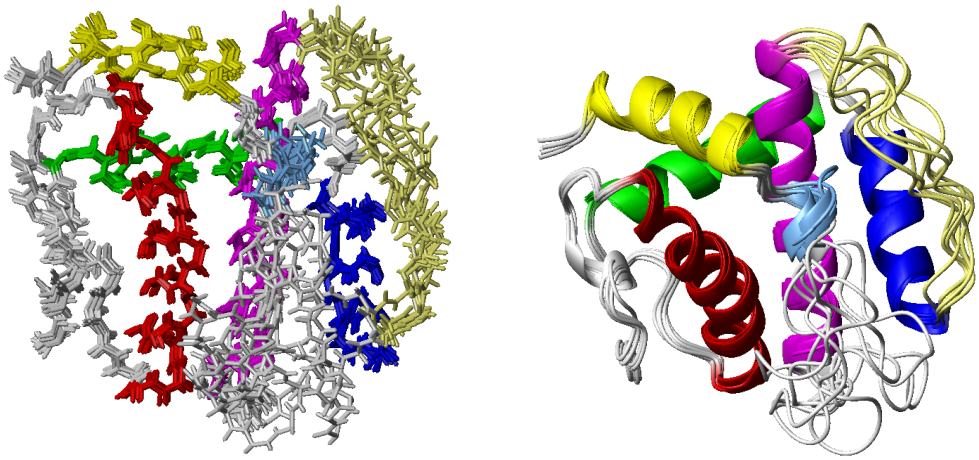

Poxviruses have evolved numerous strategies to evade host innate immunity. Vaccinia virus (VACV) proteins A46 and A52 were previously shown to antagonize Toll-like receptor (TLR) dependent signaling pathways. Vaccinia virus K7 is a 149-residue protein with previously unknown structure that is highly conserved in the orthopoxvirus family. K7 bears sequence and functional similarities to A52, which interacts with several cellular partners to suppress NF-κB anti-viral pathways and stimulate the secretion of the anti-inflammatory cytokine IL-10.

We determined the NMR solution structure of K7 using a novel protocol combining the Marvin/PASD approach of XPLOR-NIH for initial structure calculation with refinement via ARIA 2.2. This protocol did not require manual assignment of nOe spectra. The structure of K7 reveals an α-helical fold belonging to the Bcl-2 family despite having an unrelated primary sequence. ^{1}H-^{15}N dynamics measurements show fast dynamics and conformational exchange to be present in two disordered meander regions in the structure which are present as α̃ helices in the Bcl-2 family of structures. The high sequence homology of these regions in K7 and A52 suggests that they contain an interaction site which is common to the binding partners of both these proteins.

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