

Publication

Apoptin protein multimers form distinct higher-order nucleoprotein complexes with DNA

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The chicken anaemia virus-derived protein apoptin is a tumour-specific cell-killing agent. It is biologically active as a highly stable, multimeric complex, consisting of 30-40 monomers. In tumour cells, but negligibly in normal cells, apoptin is imported into the nucleus prior to the induction of apoptosis. Immunoelectron microscopic data we report here indicate that apoptin predominantly co-localises with heterochromatin and nucleoli within tumour cells. Apoptin's preference for these DNA-dense nuclear bodies may be explained by our finding that apoptin cooperatively forms distinct superstructures with DNA in vitro. These superstructures do not grow beyond a diameter of similar to 200 nm, containing up to 20 multimeric apoptin complexes and similar to 3 kb of DNA. Furthermore, we show a single apoptin multimer to have eight independent, non-specific DNA-binding sites which preferentially bind strand ends, but which can also collaborate to bind longer stretches of DNA. Apoptin's high affinity for naked, undecorated double- and single-stranded DNA and for DNA fibre ends suggests that it may also capture such DNA in superstructures in vivo. Since these forms of DNA are predominantly found in transcriptionally active, replicating and damaged DNA, apoptin could be triggering apoptosis by interfering with DNA transcription and synthesis.

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