# *INMAP* Overexpression Inhibits Cell Proliferation, Induces Genomic Instability and Functions through p53/p21 Pathways

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## Abstract

INMAP is a spindle protein that plays essential role for mitosis, by ensuring spindle and centromere integrality. The aim of this study was to investigate the relevant functions of INMAP for genomic stability and its functional pathway. We overexpressed *INMAP* in HeLa cells, resulting in growth inhibition in monolayer cell cultures, anchorage-independent growth in soft agar and xenograft growth in nude mice. In this system caused micronuclei (MNi) formation, chromosome distortion and *γH2AX* expression upregulation, suggesting DNA damage induction and genomic stability impairment. As a tumour biochemical marker, lactate dehydrogenase (LDH) isoenzymes were detected to evaluate cell metabolic activity, the results confirming that total activity of LDH, as well as that of its LDH5 isoform, is significantly decreased in *INMAP*-overexpressing HeLa cells. The levels of p53 and p21 were upregulated, and however, that of PCNA and Bcl-2, downregulated. Indirect immunofluorescence (IIF) and coimmunoprecipitation (CoIP) analyses revealed the interaction between INMAP and p21. These results suggest that INMAP might function through p53/p21 pathways.

**Keywords** INMAP, Cell proliferation, Genomic instability, p53/p21 pathways, Tumorogenesis, Chromosome aberration