

is recruited to DNA double strand breaks and is required for ATM activation. - In response to doxorubicin, ATM activation is dependent on ING3 but not on TIP60, whose recruitment to DNA breaks also depends on ING3. - These events lead to ATM-mediated phosphorylation of NBS1 and of major mediators of the DNA damage response. - Upon genotoxic stress, DNA repair by Non Homologous End Joining (NHEJ) or Homologous Recombination (HR) were impaired in absence of ING3. - Immunoglobulin Class Switch Recombination (CSR), a physiological mechanism requiring NHEJ repair, was impaired in the absence of ING3. Conclusions: Since deregulation of DNA double strand break repair is associated with genomic instability, we propose a novel function of ING3 as a caretaker tumor suppressor involved in the DNA damage signaling and repair.

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Computer modeling of phase separation at PML nuclear bodies

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The biophysical mechanism of liquid-liquid phase separation (LLPS) has emerged as an

attractive idea to explain the formation and function of membrane-less organelles, such as nuclear bodies. Our aim is to simulate the genesis of promyelocytic leukemia nuclear bodies (PML-NBs) at the molecular level using computer models in order to gain insight on LLPS within PML-NBs. To this end, we have generated a computer model of PML-NB assembly which uncovers molecular details of their genesis and a spatial map of its LLPS-driving elements. Model predictions can be exploited to test new hypotheses of PML-NB structure in the wet lab in an iterative process. The established computer model may be expanded to other membrane-less organelles to reveal their structural details.

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Interplay of DNA replication, repair and chromatin

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Half a century ago the elucidation of the DNA double helix structure was quickly followed by the visualization of replicons in DNA fibers. To connect 1D DNA replication/repair information with whole cell 3D data in mammalian cells, we combined super resolution microscopy and time-lapse analysis of S-phase dynamics with genome size and DNA replication fiber analysis. We found that the subnuclear replication structures can be optically resolved down to single replicons during all S-phase stages. This sets aside the conventional inter-