A Novel Function of NBS1 in Neural Development

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Neurogenesis is controlled by proliferation and differentiation of neuroprogenitors as well as by maturation of newly generated neurons. The DNA damage response (DDR) plays an important role in neural development through its classical function in the activation of the cell cycle checkpoint and of the apoptosis program in neural stem cells and neuroprogenitors. However, whether and how the DDR molecules function in postmitotic neurons and thereby regulate the brain development are largely unknown. It is well established that NBS1 (mutated in Nijmegen Breakage Syndrome, NBS) is a key DDR molecule in the MRN complex (MRE11/RAD50/NBS1) and functions primarily to activate ATM in response to DNA double strand breaks (DSBs) in cycling cells, by arresting cell proliferation and causing apoptosis. Interestingly, NBS1 expresses highly in developed neurons, suggesting a potential role in postmitotic cells. However, we find that NBS1 is dispensable in survival of postmitotic neurons. Of note, the deletion of NBS1 affects the arborization and migration of newly born neurons. Disruption of NBS1 results in a high level of Notch1. The migration defect of NBS1-deficient cells can be rescued by suppressing the Notch pathway. We thus identify a novel function of NBS1 in postmitotic neurons and this function may explain the progressive mental retardation in the NBS patient.