190 NBS1, the Nijmegen breakage syndrome protein, regulates the localization of DNA repair complex hRAD50/hMRE11/NBS1

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NBS1 (p95), the protein responsible for Nijmegen breakage syndrome (NBS), shows a weak homology to the yeast Xrs2 protein at the N-terminus region, known as the forkhead-associated (FHA) domain and the BRCA1 carboxyl-terminus (BRCT) domain. The protein interacts with hMRE11 to form of a complex with a nuclease activity for initiation of both non-homologous end joining and homologous recombination. We analyzed the functional domain of NBS1 using NBS cells transfected with various mutants of NBS1. The hMRE11-binding domain near amino acids 700 on the C-terminus of NBS1 is essential for both nuclear localization of the complex, and for cellular radiation resistance. On the other hand, the FHA/BRCT domain regulates nuclear foci formation of the multi-protein complex in response to DNA damage, but is not essential for nuclear transportation of the complex and radiation resistance. Since FHA/BRCT domain is widely conserved in eukaryotic nuclear proteins related to the cell cycle, gene regulation, and DNA repair the foci formation could be associated with multi-phenotypes of NBS other than radiation sensitivity.

191 Screening of protein interacting with FANCG by Yeast two-hybrid system

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Fanconi anemia (FA) is an autosomal recessive disorder characterized by skin pigmentation, high incidence of cancer, and a diverse variety of congenital malformations. The cells from FA patients display chromosome instability, abnormal G2 cell cycle check point, and hypersensitivity to DNA cross-linking agents such as mitomycin C. At least 8 complementation groups (FA-A to FA-H) have been described. Among these, *FANCA*, *FANCC*, *FANCE*, *FANCF* and *FANCG* genes have been identified. It has been reported that FANCG is identical with XRCC9, suggesting FA genes might be involved in repair from DNA damage. In addition, FANC protein involved in maintenance of the fidelity of DNA end-joining. These reports suggest that syudy on the FANC genes might help understanding the repair mechanisms of DNA damage.
We identified interacting protain with FANCG,using yeast two-hybrid system. The system is able to analysis protein-protein interaction *in vivo*. This protein contains BRCT domain, which is in volved in DNA repair, cell cycle.

192 The Role of *WRN* Mutation in Werner Syndrome Cells Which Are Hypersensitive to 4-nitroquinoline-1-Oxide

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Werner syndrome (WS) is an autosomal recessive disease whose phenotypes mimic premature aging. WS gene (*WRN*) was mapped on chromosome 8 and recently shown to encode DNA helicase and exonuclease activities. We previously showed that a SV40-transformed WS cell line (WS780) is sensitive to 4-nitroquinoline-1-oxide (4NQO) and UV-irradiation and that these abnormal phenotypes are not corrected by introduction of a chromosome 8. Here, we demonstrate that a whole cell hybrid between a WS780 cell containing an introduced-chromosome 8 and a control cell shows a normal sensitivity to 4NQO, although the cell hybrid is still sensitive to UV-irradiation. This result suggests that a chromosome other than chromosome 8 is responsible for the 4NQO sensitivity in WS780 cells and also that the mechanism of 4NQO sensitivity in WS780 is different from that of UV-irradiation.