Title of the article: Role of the Nijmegen breakage syndrome 1 gene in familial and sporadic prostate cancer.

Abstract: The Nijmegen breakage syndrome 1 (NBS1) gene, which participates in DNA double strand break repair, has been postulated to be a susceptibility factor for a number of cancers, including prostate cancer. Numerous mutations have been identified in NBS1, including the founder mutation 657del5. In this study, a number of analyses were done to determine whether mutations in NBS1 are associated with an increased risk for prostate cancer. The frequency of the 657del5 mutation in both familial prostate cancer cases (1,819 affected men among 909 families) and sporadic prostate cancer cases (1,218 affected men) collected from five centers participating in the International Consortium for Prostate Cancer Genetics were compared with that found in 697 normal controls. Seven individuals were identified to carry the mutation among the 3,037 cases screened: four in the familial group (three from one family and one from another) and three in the sporadic cases. The carrier frequency was 0.22% (2 of 909) for the probands and 0.25% (3 of 1,218) for the sporadic cases of prostate cancer. The 657del5 mutation was not detected in either the 293 unaffected members of the prostate cancer families or in the 697 control samples.
tested. The entire NBS1 gene was also sequenced in 20 of the youngest affected individuals from the Finnish group of familial cases to identify the presence of possible mutations in this high-risk group. One rare (D95N) and one common (E185Q) missense alteration was identified. More detailed analyses of the E185Q polymorphism, along with a third rare variant (R215W), failed to show an association with prostate cancer. Because the 657del5 mutation was absent from the control population, we are unable to determine if this alteration predisposes to prostate cancer. However, our data does suggest that mutations within NBS1, and in particular, 657del5, do not significantly contribute to the overall prostate cancer burden within our patient samples.