Title: Noonan Syndrome *GeneReview* — Spatial distribution of the common *PTPN11* variant c.922A>G in testes

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Note: The following information is provided by the authors listed above and has not been reviewed by *GeneReviews* staff.

Yoon et al [2013] examined the spatial distribution of the common *PTPN11* variant c.922A>G in testes from 15 unaffected men and found that the pathogenic variants were not uniformly distributed across each testis as would be expected for a mutational hot spot but were highly clustered and showed an age-dependent germline mosaicism. It is suspected that mutated spermatogonial stem cells gain an advantage that allows them to increase in frequency. SHP-2 interacts with the transcriptional activator STAT3. Given STAT3's function in mouse spermatogonial stem cells, this interaction might explain the mutant's selective advantage by means of repression of stem cell differentiation signals.

References

Yoon SR, Choi SK, Eboreime J, Gelb BD, Calabrese P, Arnheim N. Age-dependent germline mosaicism of the most common noonan syndrome mutation shows the signature of germline selection. Am J Hum Genet. 2013;92:917-26.