PTPN11 Testing in Noonan Syndrome

*Clinical features:*

Individuals with Noonan syndrome have distinct facial features that include eyes that appear to be widely spaced apart and slanting downwards, light colored iris, and abnormally shaped or positioned ears. Heart defects, particularly thickening of the pulmonary valve or heart muscle, are present in most patients with Noonan syndrome. Other features include short stature, skeletal abnormalities, webbed neck and prolonged bleeding. Approximately one-quarter of affected individuals have mental retardation.

*Inheritance:*

Noonan syndrome is a genetic disorder that has autosomal dominant inheritance, meaning that the risk to children born to an affected parent is 50%. Like most autosomal dominant disorders, a significant percentage of persons with Noonan syndrome are the first ones in their family to have it. This is due to new DNA changes that occurred during the generation of the egg or sperm from which that individual developed.

*Reasons for referral:*

1. Confirmation of a clinical diagnosis
2. Genetic counseling
3. Prenatal diagnosis

*Test-methods:*

DNA is obtained from the cells to be tested. Next, the DNA sequence of the coding regions of the Noonan syndrome disease gene, called *PTPN11*, is read. The sequence obtained is compared to the known sequence of the gene to see if a mutation is present.

*Test sensitivity:*

Like several genetic disorders, Noonan syndrome can be caused by mutations in more than one gene. The *PTPN11* gene is the most common Noonan syndrome disease gene. It accounts for about 50% of cases of Noonan syndrome. Therefore, this test will be negative one-half the time but that does not mean that the diagnosis of Noonan syndrome is wrong.

If a *PTPN11* mutation has been identified in a person with Noonan syndrome, this test can determine whether or not a family member or his/her fetus has the disorder with nearly 100% accuracy.

The ability of this test to find a *PTPN11* mutation is very high. The overall ability of this test to find a *PTPN11* mutation, if there is one, is ~98%.