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:
A blood sample is drawn (about 1 teaspoon) and DNA is obtained from the white blood cells. Next, the DNA sequence of the two portions of the Noonan syndrome disease gene, called PTPN11, is read. These two sections, called exon 3 and exon 8, were selected because 75% of mutations are found there. If no mutation is found in them, the remaining 13 sections of the gene (exons 1,2, 4-7, 9-15) are sequenced for mutations.

Test sensitivity:
Like several genetic disorders, Noonan syndrome can be caused by mutations in more than one gene. The PTPN11 gene has been identified as a 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%. If only the search of exons 3 and 8 is requested, that limited test will find about 75% of PTPN11 mutations.