



## Fetal Hemoglobin Quantitative Trait Locus 1

### Alternative Names

HBFQTL1  
Hemoglobin F, Hereditary Persistence of,  
Pancellular  
Hereditary Persistence of Fetal Hemoglobin,  
Pancellular  
HPFH  
Delta-Beta Thalassemia

### Record Category

Disease phenotype

### WHO-ICD

Diseases of the blood and blood-forming organs  
and certain disorders involving the immune  
mechanism > Haemolytic anaemias

### Incidence per 100,000 Live Births

Unknown

### OMIM Number

141749

### Mode of Inheritance

Autosomal dominant

### Gene Map Locus

11p15.5, 11p15.5

### Description

During development, the globin genes, responsible for producing hemoglobin, are activated in a sequence. In fetal life, a specific form of hemoglobin, called the fetal hemoglobin (HbF) is produced. The fetal hemoglobin consists of two chains of alpha globin and two gamma globin chains. Around the time of birth, gamma globin production decreases significantly, while beta globin synthesis increases. Most adults have only trace amounts of HbF. Hereditary Persistence of Fetal Hemoglobin (HPFH) is a condition where significant fetal hemoglobin production continues after birth and well into adulthood. Affected subjects do not usually show hypochromia or microcytosis. The fetal hemoglobin, meanwhile, is distributed in a pancellular fashion among all the

red cells. These cells resemble normal adult cells with respect to the non-hemoglobin proteins as well as the oxygen dissociation curve. Individuals with HPFH are usually healthy, or present with very mild clinical conditions. Although they do not produce any delta or beta globin chains, the HbF makes up for this loss.

### Molecular Genetics

HPFH is caused by mutations that inhibit the synthesis of hemoglobin A and A2. Essentially, this stems from the absence of production of the beta and delta globin chains. HbF is produced as a compensatory mechanism for the loss of HbA. Various studies have identified several mutations causing HPFH. These include both deletional and non-deletional types of mutations. Most of the deletions have been found in the gamma-delta intergenic region, and are hypothesized to deregulate the normal developmental pattern of gamma-globin gene expression by juxtaposing normally distant cis-acting factors into the vicinity of the gamma genes. The deletional types of mutations are mostly point mutations that have been seen to occur in the promoter region of either of the two highly similar gamma-globin genes; HBG1 and HBG2.

### Epidemiology in the Arab World

#### Algeria

In a case of a non-deletion form of Sicilian beta-0 hereditary persistence of fetal hemoglobin, Ragusa et al. (1989) found three nucleotide variations (haplotype III) in the putative enhancer 3-prime to the A-gamma gene (T-C at +2285, C-A at +2476, and A-G at +2676), identical to those observed in a case of Seattle HPFH. They concluded, however, that these variations are not responsible for the increased fetal hemoglobin expression since they were found in a severe case beta-0-thalassemia from Algeria (mutation in IVS1 nt1 position) with homozygosity for haplotype III and inefficient fetal hemoglobin production.

#### Kuwait



In a study, Adekile et al. (2007) investigated the HbF levels in 149 patients with sickle cell disease, ranging from 3-months to 60-years in age. All except four patients were homozygous for the SAI (Saudi Arabia/India) haplotype; the four exceptions being heterozygous SAI/Benin. As expected, SCD patients in this study showed elevated HbF levels. These levels, however, were highest in those in the age group < 5 years of age. In fact, in patients < 2 years of age, the mean HbF level was elevated as much as 30%. Adekile et al. conjectured that this elevation of HbF levels in SCD patients with the SAI haplotype could be responsible for the observation of Kuwaiti SCD patients not developing the early vasculopathy or bacterial infections that are characteristic of the disease.

#### **Qatar**

Fawzi et al. (2003) undertook a hospital-based study, in which they studied 1,702 Qatari nationals (905 females and 797 males) referred for investigation on suspicion of a hemoglobinopathy. All patients were subjected to analysis through hemoglobin electrophoresis and full blood count, sickling, and other screening studies. Of these, 16% showed a normal electrophoresis pattern, while in another 8.6%, the pattern was considered inconclusive, either due to the presence of iron deficiency anemia or due to a recent blood transfusion. Among these patients, 0.53% were diagnosed with Hereditary Persistence of Fetal Hemoglobin, based on the observation of high HbF level in the presence of microcytosis and absence of anemia.

#### **References**

- Adekile A, Al-Kandari M, Haider M, Rajaa M, D'Souza M, Sukumaran J. Hemoglobin F concentration as a function of age in Kuwaiti sickle cell disease patients. *Med Princ Pract.* 2007; 16(4):286-90. PMID: 17541294 [FT]
- Fawzi ZO, Al-Hilali A, Fakhroo N, Al-Bin-Ali A, Al-Mansour S. Distribution of hemoglobinopathies and thalassemias in Qatari nationals seen at Hamad hospital in Qatar. *Qatar Med J.* 2003; 12(1):20-4.
- Ragusa A, Lombardo M, Bouhassira E, Beldjord C, Lombardo T, Nagel RL, Labie D, Krishnamoorthy R. Nucleotide variations in the 3' A gamma enhancer region are linked to beta-gene cluster haplotypes and are unrelated to fetal hemoglobin expression. *Am J Hum Genet.* 1989; 45(1):106-11. PMID: 2472742

#### **Related CTGA Records**

Hemoglobin - Beta Locus

Hemoglobin, Gamma G

**Sickle Cell Disease**

#### **External Links**

<http://www.enerca.org/PublicPages/Anaemiascovered/HereditarypersistenceoffoetalhaemoglobinHPFH/tabid/177/Default.aspx>

<http://www.genecards.org/cgi-bin/carddisp.pl?gene=HPFH>

#### **Contributors**

**Pratibha Nair: 12.1.2012**

Ghazi O. Tadmouri: 1.6.2009

Pratibha Nair: 26.5.2009

