Mitomed services for DNA testing for IBMPFD (the VCP gene)

VCP Inheritance and Genetics

Mutations in the Valosin Containing Protein (VCP) gene cause an autosomal dominant disorder called Inclusion Body Myopathy associated with Paget's Disease of Bone +/- Frontotemporal Dementia (IBMPFD). It is estimated that 80% of symptomatic people also have a parent with symptoms, 20% of IBMPFD occurs because of a new mutation or without recognized family history. Penetrance is almost complete (approximately 90%), but age of onset of symptoms varies significantly between individuals. Symptoms will typically be recognized by doctors in the 40s or 50s although subtle symptoms may be recognized by the patients as early as their 20s or 30s. Individuals in the same family may have different symptoms and different ages of onset even if they have the same VCP mutation.

VCP, or p97, is the only gene known to cause IBMPFD, but other genes may be found in the future. VCP mutations will be found for approximately 70% of people who meet clinical criteria for IBMPFD. VCP is located at 9p13 - p12, and there is evidence that it is involved in a number of cellular activities including cell cycle control, membrane fusion, and the ubiquitin-proteasome mediated endoplasmic reticulum-associated degradation pathway.

Ordering the VCP test

There are a number of options to order genetic testing of VCP. Physicians can order full sequencing of the gene, or targeted sequencing of exons where mutations are most often found. Turnaround time is within 3 weeks for each tier of testing ordered. Blood samples are most often used for nuclear gene testing, but muscle or other tissue samples will be accepted if necessary.

Tiered Testing Options

5006	VCP whole gene sequencing	Sequencing of all 17 exons of VCP
5007	VCP exon 5 sequencing	63% of identified mutations have been found in exon 5
5008	VCP exons 3, 5, 6, 7, 10 sequencing	All 10 unique mutations identified to date are located in exons 3, 5, 6, 7, and 10 of the VCP gene

Pricing

Test Number	Test Name	Turnaround	Blood Sample	Solid Tissue Sample	CPT codes

Test Number	Test Name	Turnaround	Blood Sample	Solid Tissue Sample	CPT codes
5006	VCP full gene Sequencing	3 weeks	$1,719.00	$1,776.30	(please add 83907 if sending solid tissue), 83891, 83898 x17, 83894, 83904x34, 83912
	VCP sequencing if 5007 ordered previously	3 weeks	$1,547.10	$1,604.40	
	VCP sequencing if 5008 ordered previously	3 weeks	$1,317.90	$1,375.20	
5007	VCP exon 5 sequencing	3 weeks	$343.80	$401.10	(please add 83907 if sending solid tissue), 83891, 83898, 83894, 83904x2, 83912
5008	VCP exon 3,5,6,7,10 Sequencing	3 weeks	$802.20	$859.50	(please add 83907 if sending solid tissue), 83891, 83898 x5, 83894, 83904x10, 83912

Clinical Features

People with IBMPFD may have one or a combination of the three main features. Symptoms may include:

- **Myopathy**: Muscle disease is adult onset, progressive, and the proximal muscles are usually affected before the distal muscles in the legs and arms. It may clinically resemble limb-girdle (LG) or facio-scapulo-humeral (FSH) muscular dystrophy. Family studies have found myopathy in 87 - 92% of people with IBMPFD.
- **Paget's disease of bone** (PDB): Paget's disease is caused by problems with bone turnover, meaning that there are irregularities in the way bone breaks itself down and replaces itself. Symptoms of PDB include bone pain, localized bone enlargement, deformation of the long bones, and deafness from eighth-nerve compression. Family studies have found PDB in 51-57% of people with IBMPFD, usually with an earlier onset

(mean age of 42) than is seen with isolated PDB (mean age of 59 years in those without family history).

- **Frontotemporal dementia** (FTD) that preserves memory but affects reasoning, personality, and language. In family studies approximately 30% of people with IBMPFD have FTD.

Approximately 12% of people with IBMPFD are affected with all three features listed above. 50% of affected people have two of the features, 30% have apparently isolated myopathy, and 8% have apparently isolated PDB or FTD.