Cystic Fibrosis (CF)- Carrier screening

ORDER NAME
Cystic Fibrosis Carrier Screen (EPIC Order Code=LAB11121)
- If EPIC is not an option, complete and submit a paper requisition to Genomicslab@upmc.edu
- Paper requisitions can be found on the INFONET. Search for “genetics requisition form.”

BACKGROUND
Cystic fibrosis (CF) is an autosomal recessive disorder affecting the respiratory tract, exocrine pancreas, intestine, male genital tract, hepatobiliary system, and exocrine sweat glands. Pulmonary disease is the major cause of morbidity and mortality, and pancreatic insufficiency with malabsorption occurs in the majority.

The Cystic Fibrosis Carrier Screen detects a subset of disease-causing variants including the ACMG (American College of Medical Genetics) 23. The sensitivity of detection depends on ethnicity (55-95%) and is highest in populations where CF is most common. See pages 2-5 for the CF variant list table.

INDICATIONS FOR TESTING
CF carrier screening is recommended by the American College of Medical Genetics and Genomics and the American College of Obstetricians and Gynecologists and is routinely offered to women who are currently pregnant. Other indications include:

- Preconception carrier screening /sperm and egg donor carrier screening
- Carrier identification for reproductive partner of known CF carrier
- Carrier identification in individuals with a positive family history
- Abnormal fetal ultrasound

Other indications postnatally:
- Supports a diagnosis of pancreatitis

RESULT
Unaffected carriers have a heterozygous variant in the CFTR gene.

METHOD
Mass Spectrometry-Polymerase Chain Reaction (PCR)

LIMITATIONS
It detects the CFTR variants specified in the table. It will not detect other sequence variants, large deletions or duplications, or rearrangements in the CFTR gene.

SPECIMEN REQUIREMENTS
- Whole blood – EDTA tube required, 3-5 ml
- Previously extracted DNA (concentration >25 ng/ul, volume >20 ul, minimum of 1 ug total DNA, 260/280>1.7)
- Saliva provided in Oragene (OGD-500) collection kits

TURNAROUND TIME
14 days

CPT CODE
81220

CFTR Variant List Table

HGVS Nomenclature		
Variant Name (cDNA)	Variant Name (Protein)	Legacy Mutation Name
c.1A>G	p.Met1Val	M1V
c.54-5940_273+10250del21kb	p.?	dele2.3
c.115C>T	p.Gln39Ter	Q39X
c.178G>T	p.Glu60Ter	E60X
c.200C>T	p.Pro67Leu	P67L
c.223C>T	p.Arg75Ter	R75X
c.254G>A	p.Gly85Glu	G85E
c.262_263delTT	p.Leu88IlefsTer22	394delTT
c.273+1G>A	p.?	405plus1
c.274-1G>A	p.?	406min1
c.274G>A	p.Glu92Lys	E92K
c.274G>T	p.Glu92Ter	E92X
c.292C>T	p.Gln98Ter	Q98X
c.325_327delTATinsG	p.Tyr109GlyfsTer4	457TAT>G
c.328G>C	p.Asp110His	D110H
c.349C>T	p.Arg117Cys	R117C
c.350G>A	p.Arg117His	R117H
c.366T>A	p.Try122Ter	Y122X
c.442delA	p.Ile148LeufsTer5	574delA
c.489+1G>T	p.?	621plus1
c.531delT	p.Ile177MetfsTer12	663delT
c.532G>A	p.Gly178Arg	G178R
c.579+1G>T	p.?	711plus1
c.579+3A>G	p.?	711plus3
c.579+5G>A	p.?	711plus5
c.580-1G>T	p.?	712min1
c.595C>T	p.His199Tyr	H199Y
c.613C>T	p.Pro205Ser	P205S
c.617T>G	p.Leu206Trp	L206W
c.658C>T	p.Gln220Ter	Q220X
c.720_741del	p.Gly241GlufsTer13	850del22
c.948delT	p.Phe316LeufsTer12	1078delT
c.988G>T	p.Gly330Ter	G330X
c.1000C>T	p.Arg334Trp	R334W
c.1007T>A	p.Ile336Lys	I336K
c.1013C>T	p.Thr338Ile	T338I
c.1021T>C	p.Ser341Pro	S341P

HGVS Nomenclature		
Variant Name (cDNA)	Variant Name (Protein)	Legacy Mutation Name
c.1021_1022dup	p.Phe342HisfsTer28	1154insTC
c.1040G>A	p.Arg347His	R347H
c.1040G>C	p.Arg347Pro	R347P
c.1055G>A	p.Arg352Gln	R352Q
c.1081delT	p.Trp361GlyfsTer8	1213delT
c.1116+1G>A	p.?	1248plus1
c.1130dup	p.Gln378AlafsTer4	1259insA
c.1202G>A	p.Trp401Ter	W401X>TAG
c.1203G>A	p.Trp401Ter	W401X>TGA
c.1209+1G>A	p.?	1341plus1
c.1327_1330dup	p.Ile444ArgfsTer3	1461ins4
c.1364C>A	p.Ala455Glu	A455E
c.1393-1G>A	p.?	1525min1
c.1397C>A	p.Ser466Ter	S466X>TAA
c.1397C>G	p.Ser466Ter	S466X>TAG
c.1400T>C	p.Leu467Pro	L467P
c.1418delG	p.Gly473GlufsTer54	1548delG
c.1466C>A	p.Ser489Ter	S489X
c.1475C>T	p.Ser492Phe	S492F
c.1477C>T	p.Gln493Ter	Q493X
c.1519_1521delATC	p.Ile507del	I507del
c.1521_1523delCTT	p.Phe508del	F508del
c.1545_1546delTA	p.Tyr515Ter	1677delTA
c.1558G>T	p.Val520Phe	V520F
c.1573C>T	p.Gln525Ter	Q525X
c.1585-1G>A	p.?	1717min1
c.1585-8G>A	p.?	1717min8
c.1624G>T	p.Gly542Ter	G542X
c.1645A>C	p.Ser549Arg	S549R
c.1646G>A	p.Ser549Asn	S549N
c.1647T>G	p.Ser549Arg	S549R>AGG
c.1652G>A	p.Gly551Asp	G551D
c.1654C>T	p.Gln552Ter	Q552X
c.1657C>T	p.Arg553Ter	R553X
c.1675G>A	p.Ala559Thr	A559T
c.1680-886A>G	p.?	1811plus1.6kb
c.1679G>A	p.Arg560Lys	R560K

HGVS Nomenclature		
Variant Name (cDNA)	Variant Name (Protein)	Legacy Mutation Name
c.1679G>C	p.Arg560Thr	R560T
c.1680-1G>A	p.?	1812min1
c.1736A>G	p.Asp579Gly	D579G
c.1753G>T	p.Glu585Ter	E585X
c.1766+1G>A	p.?	1898plus1
c.1766+1G>C	p.?	1898plus1
c.1766+3A>G	p.?	1898plus3
c.1766+5G>A	p.?	1898plus5
c.2012delT	p.Leu671Ter	2143delT
c.2051_2052AA>AA	p.Lys684SerfsTer38	2183AA>G
c.2052dupA	p.Gln685ThrfsTer4	2184insA
c.2052delA	p.Lys684AsnfsTer38	2184delA
c.2125C>T	p.Arg709Ter	R709X
c.2128A>T	p.Lys710Ter	K710X
c.2175dupA	p.Glu726ArgfsTer4	2307insA
c.2195T>G	p.Leu732Ter	L732X
c.2215delG	p.Val739TyrfsTer16	2347delG
c.2290C>T	p.Arg764Ter	R764X
c.2453delT	p.Leu818TrpfsTer3	2585delT
c.2464G>T	p.Glu822Ter	E822X
c.2490+1G>A	p.?	2622plus1
c.2491G>T	p.Glu831Ter	E831X
c.2538G>A	p.Trp846Ter	W846X>TGA
c.2551C>T	p.Arg851Ter	R851X
c.2583delT	p.Phe861LeufsTer3	2711delT
c.2657+5G>A	p.?	2789plus5
c.2668C>T	p.Gln890Ter	Q890X
c.2780T>C	p.Leu927Pro	L927P
c.2834C>T	p.Ser945Leu	S945L
c.2875delG	p.Ala959HisfsTer9	3007delG
c.2908G>C	p.Gly970Arg	G970R
c.2988G>A	p.?	3120G>A
c.2988+1G>A	p.?	3120plus1G>A
c.2989-1G>A	p.?	3121min1
c.3067_3072del	p.Ile1023_Val1024del	3199del6
c.3140-26A>G	p.?	3272min26
c.3154T>G	p.Phe1052Val	F1052V

HGVS Nomenclature		
Variant Name (cDNA)	Variant Name (Protein)	Legacy Mutation Name
c.3194T>C	p.Leu1065Pro	L1065P
c.3196C>T	p.Arg1066Cys	R1066C
c.3197G>A	p.Arg1066His	R1066H
c.3205G>A	p.Gly1069Arg	G1069R
c.3209G>A	p.Arg1070Gln	R1070Q
c.3230T>C	p.Leu1077Pro	L1077P
c.3266G>A	p.Trp1089Ter	W1089X
c.3276C>G	p.Tyr1092Ter	Y1092X>TAG
c.3276C>A	p.Tyr1092Ter	Y1092X>TAA
c.3302T>A	p.Met1101Lys	M1101K
c.3310G>T	p.Glu1104Ter	E1104X
c.3454G>C	p.Asp1152His	D1152H
c.3472C>T	p.Arg1158Ter	R1158X
c.3484C>T	p.Arg1162Ter	R1162X
c.3528del	p.Lys1177SerfsTer15	3659delC
c.3587C>G	p.Ser1196Ter	S1196X
c.3611G>A	p.Trp1204Ter	W1204X>TGA
c.3612G>A	p.Trp1204Ter	W1204X>TAG
c.3700A>G	p.Ile1234Val	I1234V
c.3718-2477C>T	p.?	3849plus10kb
c.3731G>A	p.Gly1244Glu	G1244E
c.3744delA	p.Lys1250ArgfsTer9	3876delA
c.3752G>A	p.Ser1251Asn	S1251N
c.3764C>A	p.Ser1255Ter	S1255X
c.3764C>T	p.Ser1255Leu	S1255L
c.3773dupT	p.Leu1258PhefsTer7	3905insT
c.3846G>A	p.Trp1282Ter	W1282X
c.3873+1G>A	p.?	4005plus1
c.3876delA	p.Val1293TyrfsTer35	4006delA
c.3889dupT	p.Ser1297PhefsTer5	4016insT
c.3909C>G	p.Asn1303Lys	N1303K
c.3937C>T	p.Gln1313Ter	Q1313X
c.3964-78_4242+577del	p?	dele22.23
c.4077_4080delTGTTinsAA	p.Val1360ThrfsTer3	4209TGTT>AA
c.4251delA	p.Glu1418ArgfsTer14	4382delA