**CFTR MUTATION CLASSES**

**Normal**
- CFTR protein is created, moves to the cell surface and allows transfer of chloride and water.

**Class I**
- No functional CFTR is created.

**Class II**
- CFTR protein is created, but misfolds, keeping it from moving to the cell surface.

**Class III**
- CFTR protein is created and moves to the cell surface, but the channel gate does not open properly.

**Class IV**
- CFTR protein is created and moves to the cell surface, but the function of the channel is faulty.

**Class V**
- Normal CFTR protein is created and moves to the cell surface, but in insufficient quantities.

### % of people with CF who have at least one mutation in that class

- **Class I**: 22%
- **Class II**: 88%
- **Class III**: 6%
- **Class IV**: 6%
- **Class V**: 5%

### MUTATION EXAMPLES

- **Class I**: G542X, W1282X, R553X (aka “nonsense mutations, splice mutations or deletions”)
- **Class II**: F508del, N1303K, I507del
- **Class III**: G551D, S549N (aka “gating mutations”)
- **Class IV**: D1152H, R347P, R117H
- **Class V**: 3849+10kbC→T, 2789+5G→A, A455E

### WHAT'S HAPPENING IN THE CELL

- **Class I**: New ribosome, newly folded CFTR, mature CFTR channel
- **Class II**: Misfolded CFTR, misfolded RNA, unstable, shortened RNA
- **Class III**: Channel gate does not open
- **Class IV**: Faulty channel
- **Class V**: Not enough CFTR

### POTENTIAL THERAPIES

- **Class I**: Correctors such as lumacaftor or tezacaftor help defective CFTR fold correctly
- **Class II**: Potentiators such as ivacaftor help open the CFTR channel, and also help increase the function of normal CFTR
- **Class III**: Read-through compounds may allow production of full-length CFTR for nonsense mutations
- **Class IV**: Potentiators such as ivacaftor help open the CFTR channel, and also help increase the function of normal CFTR
- **Class V**: Potentiators such as ivacaftor help open the CFTR channel, and also help increase the function of normal CFTR
Cystic fibrosis is caused by mutations, or changes, in the CFTR gene. This gene provides the code that tells the body how to make the cystic fibrosis transmembrane conductance regulator (CFTR) protein. The protein controls the salt and water balance in the lungs and other tissues. All people have two copies of the CFTR gene, and there must be mutations in both copies to cause CF. More than 1,700 mutations of the CFTR gene have been identified. Although some are common, others are rare and found in only a few people.

CFTR mutations are grouped into classes based on the way the mutations affect the CFTR protein. The reverse side of this sheet shows the most common CFTR mutation classes. In the future, mutations may also be classified by “theratype,” meaning which type of CFTR modulator therapy they respond to best. This is because mutations within the same class may respond to therapies differently, and not every mutation can be neatly assigned to one mutation class.

Certain types of CFTR mutations are associated with different disease complications. For example, some mutations are more likely to affect the pancreas than others. However, this correlation is not perfect, and knowing an individual’s CFTR mutations cannot always tell you how severe that person’s CF symptoms will be.

Although the potential therapies described on this sheet can be very effective for some people with CF, others may not experience the exact same benefit. Researchers continue to work in the lab and in clinical trials to find the best therapeutic approaches to target specific CFTR mutations or classes of mutations to improve the health of all individuals living with CF.