2. CYSTIC FIBROSIS: CURRENT THERAPEUTIC TARGETS BASED ON SYMPTOMS OCCURRED DUE TO SPECIFIC CFRT GENE MUTATIONS

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Introduction. Cystic fibrosis (henceforth CF) is autosomal recessive disease involving mucus and sweat producing cells affecting multiple organs with lungs most severely affected leading to death in 90% of patients . A mutation in Cystic fibrosis trans-membrane conductance regulator (henceforth CFTR) gene changes a protein (a regulated chloride channel), which regulate the activity of other chloride and sodium channels at the cell surface epithelium.This mutation and some others, have attracted much attention in recent years due to significant advances in the pharmacological targeting. However, increasing evidence points to the reduced efficacy of single treatments, thus reinforcing the need to combine several therapeutic strategies to effectively target the multiple basic defect(s).Also mechanistic subdivisions of some of the major classes of mutations can be a good support in order to improve the success of drug-selection strategies.

Aim of study. Study about cystic fibrosis manifestation based on classes of CFRT mutations, and get acknowledged about currently approved drugs and exploration of future clinical development pipeline therapeutics for cystic fibrosis, and possible limitations in their use.

Methods and materials. Extensive literature search using individual and a combination of key words related to cystic fibrosis therapeutics.

Results. Cystic fibrosis is an autosomal recessive disorder results from mutation of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. The gene was identified in 1989, but more than 20 years later, the regulatory mechanisms controlling its complex expression are still not fully understood. Over the years, scientists have used several different ways of grouping these mutations into different classes. The most recent classification system groups mutations by the problems that they cause in the production of the CFTR protein: Protein production mutations (Class 1);Protein processing mutations (Class 2);Gating mutations (Class 3);Conduction mutations (Class 4);Insufficient protein mutations (Class 5) For many of the identified mutations, the disease liability is unknown, but efforts are under way to assess their functional consequence and clinical severity. Respiratory system and GIT are primarily involved but eventually multiple organs are affected leading to life threatening complications. Management requires drug therapy, extensive physiotherapy and nutritional support. Previously, the focus was on symptomatic improvement and complication prevention but recently the protein rectifiers are being studied which are claimed to correct underlying structural and functional abnormalities.

Conclusion. The ultimate goal of theratyping is to achieve optimal correction of a specific mutant defect by selecting the most efficacious CFTR modulator(s), including correctors(s), potentiator(s), and/or read-through drugs, or a combination of these drugs. Based on accumulating observations, however, mechanistic subdivisions of some of the major classes of mutations (classes I, II, and III) may be necessary to further improve the success of drug-selection strategies.