Towards a molecular map of cystic fibrosis mechanisms

Catarina Pereira[1,2], Alexander Mazein[3], Margarida D. Amaral[2] André Falcão[1,2]

University of Lisboa, Faculty of Sciences, BioISI-Biosystems and Integrative Sciences Institute, Campo Grande, 1749-016 Lisboa, Portugal[1], LASIGE, Faculdade de Ciencias, Universidad de Lisboa, 1749-016 Lisboa, Portugal[2], European Institute for Systems Biology and Medicine, CIRI UMR5308, CNRS-ENS-UCBL-INSERM, Universite de Lyon, 50 Avenue Tony Garnier, 69007 Lyon, France[3]

Background. Cystic fibrosis (CF) is a monogenic genetic disease caused by more than 2000 mutations identified in the CF transmembrane conductance regulator (CFTR) gene, although one single mutation -F508del- occurs in ~85% of patients worldwide. This gene encodes CFTR protein, an anion (Cl-/HCO32-) channel which when mutated results in a multi-organ disease that affects mostly the lungs and is ultimately life-shortening. The growing omics studies relative to disease states provide the opportunity to integrate data from different sources and to analyse with a greater context the mechanisms and interactions involved in the development of a disorder like CF (Clarke et al., 2015, PMID 26225835).

Goal and objectives. This work aims to create a disease map for CF describing the existing in an organized way by integrating current data on CF and to use this map as a resource to discover new interactions and new therapeutic targets.

Methods. Data from the literature and pathway databases is used to build a network of interactions for normal (wt) and mutant (F508del) CFTR via the Systems Biology Graphical Notation standard (SBGN, www.sbgn.org). The construction is designed in collaboration with CF domain experts.

Results. MetaCore pathways on wt- and F508del-CFTR were updated by publicly available databases and literature searches for the creation of the CF-MAP. This map represents interactions among more than 300 proteins with focus on the life cycle and the immune response triggered in the lung when the F508del mutation is present.

Conclusion. CF-MAP represents an updated repository containing the current pathways implicated in the pathogenesis of CF. The organized knowledge present in this map may serve as basis for further computational analyses using a transferable and scalable technology that can be applied to different projects do address multiple questions. The CF-MAP thus supports research communities in CF field allowing an easier exploration and analysis of complex data and the identification of key players in the disease, leading to the discovery of new therapeutic targets.

Keywords: CF-MAP; cystic fibrosis; omics; data integration; computational model; SBGN

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