European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:
SWATH LABEL-FREE PROTEOMICS FOR CYSTIC FIBROSIS RESEARCH

Authors:
Clarissa Braccia[1,4], Valeria Tomati[2], Emanuela Caci[2], Nicoletta Pedemonte[2] and Andrea Armirotti[3]

Affiliations:
[1]D3Pharmachemistry, Fondazione Istituto Italiano di Tecnologia, Via Morego 30, 16163 Genova, Italy;
[2]U.O.C. Genetica Medica, IRCCS Istituto Giannina Gaslini, Via Gerolamo Gaslini 5, 16147 Genova, Italy
[3]Analytical Chemistry Lab, Fondazione Istituto Italiano di Tecnologia, Via Morego 30, 16163 Genova, Italy
[4]Dipartimento di Chimica, Università degli Studi di Genova, Via Dodecaneso 31, 16146 Genova, Italy

What was your research question?
SWATH is a particular way of doing proteomics (i.e. measure how much of a given protein is in a cell or tissue). It is one of the most widely used methods worldwide. Can we optimize it and make it suitable to investigate the surfaces of the airways and lungs for Cystic Fibrosis (CF) research?

Why is this important?
Many papers have shown that using SWATH enables a high level of precision and accuracy when measuring proteins. This technique has never been used before in CF research. The core of SWATH are the so-called “ion libraries” (IL): a sort of encyclopedia of data on thousands of fragments belonging to thousands of proteins of a given organism. These libraries, made publicly available, can be shared and used by virtually any proteomics lab in the world. Our work produced an IL highly optimized to investigate the surfaces of the airways and lungs. This will allow many other groups, worldwide, to use SWATH for CF research.

What did you do?
We extensively investigated the proteome (all the proteins that are or can be expressed by a cell, tissue, or organism) of the surfaces of the airways and lungs and we collected data on

hundreds of proteins highly specific for this tissue. We then added the data for these proteins to the Pan Human ion library, the most complete IL published so far. We then successfully used this tool (and SWATH) to compare the proteomes of the surfaces of the airways and lungs of four people with CF with that of four corresponding individuals without CF.

What did you find?

We found that 154 proteins were significantly altered by CF. Among them, we observed some protein known to work together with the cystic fibrosis transmembrane conductance regulator (CFTR). These proteins have a role in CFTR degradation and protein transport. For example, we found that the amount of protein STUB1 is decreased in CF. This protein is involved in CFTR maturation, and it works together with two other proteins (ANAPC1 and RAD23), both reduced by CF. Since these three proteins participate to CFTR degradation, we suggest that this phenomenon, observed on the surfaces of the airways and in the lungs of people with CF, is an adaptive mechanism to contrast the disease.

What does this mean and reasons for caution?

In our SWATH experiments on the surfaces of the airways and in the lungs, we collected data from more than 4000 proteins per each single sample. Our data demonstrate that the protocol is reliable and that the optimized IL is perfectly fit for proteomics in CF research. On the other hand, the limited number of biological samples we tested (4 CF versus 4 non-CF) prevents us from drawing definitive biological conclusion from our evidence and further experiments on broader groups of individuals should be carried out.

What's next?

The next step is to expand the use of SWATH proteomics in the CF field. We will perform further experiments on other cell types and other individuals' lung tissues. The ultimate goal of our research is to shed new light on the CF biology and hopefully to pave the way to new drug treatments.

Original manuscript citation in PubMed

https://www.ncbi.nlm.nih.gov/pubmed/?term=SWATH+LABEL-FREE+PROTEOMICS+FOR+CYSTIC+FIBROSIS+RESEARCH

cfresearchnews@gmail.com