Structure-based approaches to study the functions and dysfunctions of CFTR and to develop personalized medicine for cystic fibrosis.

CFTR (Cystic Fibrosis Transmembrane conductance Regulator) is a member of the ABC (ATP-Binding Cassette) transporter superfamily that functions as an ATP-gated ion channel and whose dysfunctions lead to cystic fibrosis. Development of specific CFTR modulators represents a challenge in the era of personalized medicine, as CFTR mutations lead to a variety of phenotypes, which likely require different, specific treatments. CF drug development is also complicated by the need to preserve the right balance between stability and flexibility that is required for optimal function of the CFTR protein.

I will highlight here how structural data, especially coming from theoretical approaches (molecular modeling and molecular dynamics simulations), can be exploited in this context to understand the molecular mechanisms of disease-associated mutations, to characterize the mechanisms of action of known modulators and to rationalize the search for novel, specific compounds.