P-2.27

A Numerical Model to Evaluate the Interplay of Key Parameters in the Transport Process of Small Synthetic Chloride Carriers

Sara Boi [1], Giacomo Picci [1], Claudia Caltagirone [1], Roberto Quesada [2], Mariano Andrea Scorciapino [1]

[1] University of Cagliari, Monserrato, Italy

[2] Universidad de Burgos, Burgos, Spain (2)

The investigation of small-molecule chloride ion transporters is receiving significant interest as a potential therapeutic strategy for cystic fibrosis. Defective chloride transport in cystic fibrosis due to malfunction of transport proteins result from mutations that vary among patients. Unlike traditional therapies targeting specific mutations, small synthetic transporters could replace the lost activity of defective proteins, offering a more general approach. Several promising transporters have been identified, yet the interplay of the key physicochemical properties, such as, lipophilicity,

size, charge distribution and conformational plasticity, remains unclear. A computer algorithm, initially developed to simulate the non-electrogenic uniport mechanism, is being extended to include osmosis and counterions transport, beside membrane partitioning, and passive diffusion. Chloride release assays from lipid vesicles have been performed for different transporter classes, including squaramides, thioureas, tambjamines and prodiginines, enabling the comparison of their molecular properties. Also, the effect of membrane composition including cholesterol or negatively charged lipids was investigated.