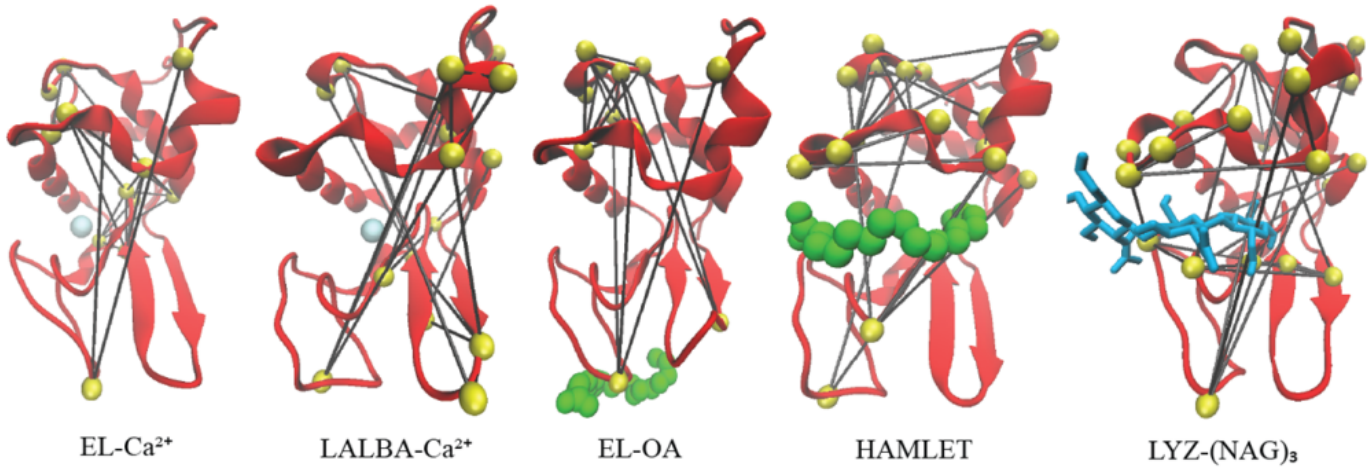
Understanding the evolution of protein dynamics can lead to more effective non-toxic drug therapies

Proteins are macromolecules that play important roles in all living organisms. They protect the body from viruses and bacteria, control chemical reactions, transmit signals between cells and organs, and transport other molecules to places in the body where they are needed. Many diseases ranging from Alzheimer's to some forms of arthritis are directly related to protein *mis*-function. Consequently, a large number of existing drugs target proteins. Kristina N. Woods and Jürgen Pfeffer from Carnegie Mellon University in Pittsburgh (Pennsylvania, USA) focus in their work published in the prestigious Journal “Molecular Biology and Evolution” on proteins in the lysozyme family that provide a historical retrospective on the evolution and adaption of immunity in humans. They represent an ancient class of structurally related proteins that are crucial for our immune response in that they have the ability to fight off foreign bodies that enter cells but they also form the basic nutritional aspects of human breast milk.



Network representation of the most important nodes of the selected protein–ligand system mapped onto a cartoon representation of the protein.

The authors combine computational methods (Molecular Dynamics Simulation, Evolutionary Network Analysis) with Terahertz spectroscopy experiments to identify molecular mechanisms that are responsible for the adaptation and evolution of individual proteins within the lysozyme family. All of the proteins in the family are structurally similar but have developed different present day functions due to their evolved dynamics. In particular, Woods and Pfeffer are interested in understanding the mechanism that allows certain members of the lysozyme protein family to selectively kill a broad range of tumor cells while at the same time sparing healthy cells. They show evidence that when these proteins are complexed with small molecules that are found naturally in human breast milk (oleic acid) they adapt their dynamical characteristics which allows them to

selectively bind with cancerous cells. A better understanding of the adaptations in immunity that formed the function of individual proteins in the protein family may help to facilitate the design of a more effective line of non-toxic cancer therapies in the near future.

Publication

Using THz Spectroscopy, Evolutionary Network Analysis Methods, and MD Simulation to Map the Evolution of Allosteric Communication Pathways in c-Type Lysozymes.
Woods KN, Pfeffer J
Mol Biol Evol. 2015 Sep 3