

The role of glycosylation in the emergence of animal multicellularity

All life on Earth, including humans and other animals, descended from a common ancestor. While the human body consists of several trillions of cells, this ancestor consisted of a single cell. One of the important steps in evolution was therefore acquisition of multicellularity – the transition from single-celled organisms to those built up of many cooperating cells.

Sugars, also called glycans, belong to the key molecules of life. They help accumulate and transport information (e.g. ribose in RNA – ribonucleic acid, or deoxyribose in DNA), energy (e.g. glucose) or shape the physical form of an organism (e.g. cellulose in plants). They also allow cells to communicate with one another – neighbors can be recognized as friends or foes depending on the sugars present on their surface. I am particularly interested how sugars helped the animal multicellularity to emerge and how the functions of sugars evolved. These are fundamental questions about our evolution and recent advances made them more feasible than to be answered than ever. The aim of the project is to answer them.

In order to grasp at these questions, I will use a close relative of animals, a protist *Capsaspora owczarzaki*, as a model organism. It can exist as a single cell – an amoeba when food is plentiful or a round cyst when it starves – or aggregate into a multicellular form. I will characterize the entire repertoire of sugars (the glycome) of *C. owczarzaki* in each of its three life cycle stages and quantitate the differences between them. I will focus on three categories of sugars found in cells: N-glycans, O-glycans (both are linked to proteins) and glycosphingolipids (sugars connected to lipids). This will allow me to infer the changes in sugar usage that happened upon the transition from a single-celled animal ancestor to a multicellular organism – an animal. To broaden the picture, I will then compare the *C. owczarzaki* data with those from evolutionarily relevant organisms, including simple animals such as a sponge and a sea anemone.

Another section of the project will be devoted to the evolution of glycosylation (sugar modification) machinery in animals. I will compare the repertoires of proteins acting on sugars from a broad selection of animals and their relatives, including those less closely related to animals than *C. owczarzaki*. This approach will reveal the evolutionary points at which specific activities were gained or lost and help view the origins of animal multicellularity in a new light.

Once I determine which proteins and sugars were important for the transitions between single-cell and multicellular life forms, I will manipulate the sugar-making machineries to either increase, decrease or completely remove their activities. By making observations on how the form of *C. owczarzaki* changes after these manipulations, I will test the roles of individual sugars in these transitions. In this part of the research I will apply innovative genetic manipulation procedures, as *C. owczarzaki* is a relatively new model organism with a yet to be established toolbox of tested techniques.

In the wild, *C. owczarzaki* lives inside a freshwater snail species *Biomphalaria glabrata*. The snail can also host a parasitic worm, *Schistosoma mansoni*, which causes a human disease called schistosomiasis. Approximately 230 million people every year are affected by schistosomiasis and it is one of the diseases recognized by World Health Organization as Neglected Tropical Diseases. It was observed that *C. owczarzaki* can kill the parasite form that replicates inside the snail, but the mechanism of this phenomenon remains unknown. As sugars are often responsible for cell-cell recognition, they may be relevant in the interaction between *C. owczarzaki* and the parasite. Understanding of the sugar usage of *C. owczarzaki* can help explain how it eradicates the parasite. This, in turn, could contribute to the development of preventive measures aiming at eliminating the worm before it reaches the human hosts.