Elevated Cholesterol Impairs Water and Gas Transport in Red Blood Cells

By Siddhartha Jena

I have always had a great interest for the science of the microscopic. Many great problems in science have been solved by simply examining them on the small scale. Heart disease is the most prevalent disease affecting Americans and individuals all over the globe, claiming more lives than cancer on an annual basis, but comparatively little is known about its causes and precursors. Heart disease causes are often misleading; for instance, obesity has been demonstrated to be linked to heart disease for decades, yet many who suffer from cardiovascular ailments are slim and hardly fit this profile. After doing some research I found that the majority of these “healthy” individuals in fact have very high levels of cholesterol (hypercholesterolemia). The accumulation of this fatty substance in the arteries, a condition known as atherosclerosis, causes difficulties in breathing, dizziness, and fatigue with the mildest of physical exertion. Additionally, I found a study dating back to the early 1970’s where doctors found that increasing the concentration of plasma cholesterol in humans had an adverse effect on oxygen transport into the red blood cell. Based on these studies, I wanted to attempt to analyze heart disease on the biochemical level, by observing the effect of a prominent risk factor, cholesterol, on the cellular level of the cardiovascular system, namely the red blood cell. I was already a laboratory intern at Wayne State University in Detroit, MI, so when I approached my mentor with my idea she was excited and helped me design experiments to test my theories. Over the course of the last three years, I have successfully identified cholesterol as an impediment to water and gas transport through the Aquaporin-1 water
channel protein in red blood cells. Aquaporin-1 is like a pump that moves water and gases rapidly in and out of the cell. Interestingly, I found that the negative effects of cholesterol are specific to Aquaporin-1, which led me to identify the mechanism of Aquaporin-1 function and regulation. My results suggest that in the future scientists could find preventive therapies to cholesterol-associated cardiovascular disease based on this newfound knowledge, and I even found two novel possible candidates for cardiovascular drugs based on my studies.