

Fighting neglected and non-communicable diseases

Carbonic anhydrases (CAs) catalyze the reaction between water and carbon dioxide to regulate pH and fluid balance *in vivo*. Deviations in CA activity have been shown to correlate with bone, lung and liver diseases, as well as obesity, type II diabetes and even epilepsy. Professor Areej Abuhammad and her team at the University of Jordan are interested in developing novel therapies to counteract imbalances in CA activity, using protein crystallography to investigate a wide range of potential inhibitors.

Carbonic anhydrases are a large group of zinc metallo-enzymes that can reversibly catalyze water and carbon dioxide – forming hydrogen and bicarbonate – to alter pH and carbon dioxide concentrations. Areej Abuhammad, an Associate Professor in Medicinal Chemistry at the University of Jordan, is combining her background in computer-aided drug design, structural biology and medicinal chemistry to investigate selective inhibitors for CA. Areej explained: “The function of carbonic anhydrases is to control the pH in the body and, through it, a variety of biological processes. They are therefore linked to the etiology of many different pathogenic diseases.”

“I have always been interested in neglected diseases; I did my Master’s degree on avian influenza and, during my PhD, I worked on drug discovery for tuberculosis in the Departments of Pharmacology and Biochemistry at the University of Oxford. I moved back to Jordan after finishing my PhD, and used the knowledge that I acquired to set up a protein crystallography lab to perform research on CAs, combining drug repurposing with fragment-based drug discovery.”

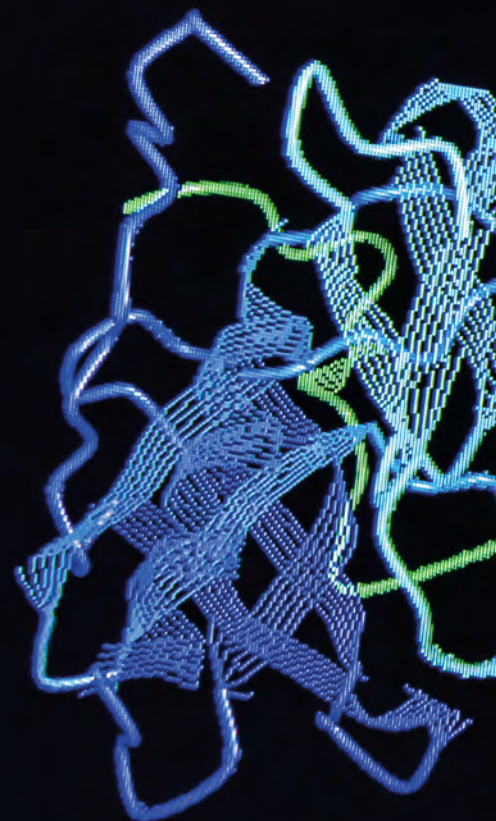
“I am working with isozymes of CAs, screening for the new inhibitors and testing their enzymatic activity. I am interested in knowing exactly how the inhibitors impact the enzyme; if they inhibit or activate it, and how the kinetics work. I also crystallize the proteins with the inhibitors and use

X-ray crystallography to investigate the structure of proteins, and how the ligands and inhibitors bind to them. This knowledge is very important for structure-based drug discovery, making it easier to make an informed decision on what needs to be altered, as well as finding out which functional groups are responsible for the activity.”

“A microplate reader is obviously a key instrument in our research, as we perform a lot of enzyme activity assays, screening a variety of different inhibitors and enzyme isoforms. I therefore needed an instrument that offers high sensitivity and can handle small sample sizes, which is essential to reduce the cost of screening. I also wanted a monochromators-based system, as we need the flexibility to perform a wide range of experiments, screening as many different conditions as we want without the limitation of filter sets.”

“After working with a Tecan instrument during my PhD, I decided to buy an Infinite® M Plex reader for our lab in Jordan, as this was the best for our lab. It offers the sensitivity and the accuracy level we need, while being easy to set up and use. This intuitive operation, together with the system’s robustness, is something that I really like about it. We have a lot of Master’s students – as well as offering some training to undergraduates – and they are naïve to the sensitivity of these instruments when they first enter the lab. Having a system that can withstand this without it compromising results is

great. And being very simple to set up, and offering versatile applications, it is perfect. Setting up a new lab is always difficult, especially when working with a tight budget, but the Tecan team and local distributor were very supportive,” Areej concluded.





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To find out more about Tecan's Infinite M Plex, visit www.tecan.com/infinite200pro

To learn more about Areej Abuhammad's research, go to www.researchgate.net/profile/Areej-Abuhammad