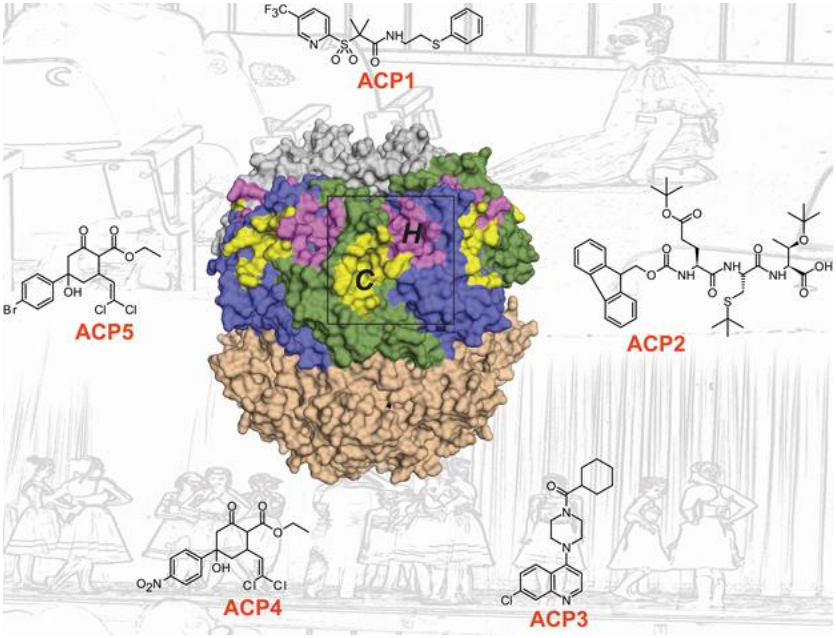
Walid A. Houry, PhD

- University of Toronto, Biochemistry, Professor

Our lab works with a proteolytic complex in bacteria called ClpP. It has been shown that modulating the activity of ClpP can affect bacterial viability. So, we are developing new compounds that target ClpP. Our first generation of these compounds show effectiveness against bacteria in plates and liquid culture. We are now further optimizing these compounds to carry out animal model studies. Using these compounds, we are hoping to target *Pseudomonas aeruginosa*, which is the major bacteria infecting Cystic fibrosis (CF) patients. We are hoping that eventually the compounds that we are developing can be used as antibiotics against bacterial infections in CF patients.

I enjoy science and doing research because of the aspect of discovery and having the freedom to study what you like, as well as the element of having the opportunity to discover something completely new that no one has identified before. I was able to start translating my research of basic biochemistry into research of CF when we started working on the ClpP system to understand its basic mechanism of function. This protease is present in many bacteria and is highly conserved, and therefore seemed to be a good target with respect to CF. An opportunity came around when there was a call for team grant from CIHR's Institute of Infection and Immunity to do something more translational. At that time ClpP was recognized as a potential drug target. Together with other researchers, we formed a group of six principle investigators and we submitted a grant to the institute to develop compounds against ClpP.



The structure of five activators of the ClpP protease, indicated as ACP1-5, are shown around a surface model of the protease. The proposed binding sites for these activators on ClpP are labelled as H and C. The ACPs allow ClpP to unspecifically degrade larger proteins, which eventually results in cell death. In the background, the resting ballet dancer at the top and performing dancers at the bottom are shown to convey this activation of ClpP.

Trainees:

Elisa Leung (research technician) has developed the technique for screening compounds targeting ClpP.

Adedeji Ologbenla (graduate student) and **Angela Yu (graduate student)** are working on understanding the basic biochemistry of how the ClpP protease works to degrade proteins into small peptides.

Click here for a complete list of Dr. Walid A. Houry's publications.

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