

Exploring the landscape of cell receptors

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Professor Scott Prosser and post-doc Libin Ye

Ever wonder how caffeine works so marvelously to give you that extra boost you need the night before your final exam?

The caffeine molecule—much loved by students the world over—binds to a receptor, preventing the action of the sleep-inducing molecule adenosine, giving you those extra few hours to prep for your exam in the morning.

The class of receptors responsible for regulating [neuronal function](#) are part of the focus of a recent study by Professor Scott Prosser in the Department of Chemical & Physical Sciences at U of T Mississauga. Their paper, "Activation of the A2A adenosine G-protein-coupled receptor by conformational selection," appears in the latest edition of the prestigious international science journal, *Nature*. The research also involved UTM postdoctoral scientist, Libin Ye, and Oliver Ernst in the Department of Biochemistry at U of T.

There is a great deal of interest in understanding this class of cell signaling receptors called GPCRs (G-Protein-Coupled Receptors), which are responsible for basic processes such as vision, taste, smell, chemical signaling in the brain and

immune defense. Roughly 30 to 40 per cent of current drugs target these receptors, which essentially serve as gatekeepers for cell signaling. "With our latest findings, we can begin to design the next generation of GPCR drugs," says Prosser.

He explains that GPCRs are often likened as molecular switches, which are blocked or turned on or off by drugs. Since 2007, a technique called X-ray crystallography has revealed a wealth of high-resolution structures of these "switches." Prosser's studies allow researchers to understand the molecular underpinnings of many pharmacological effects.

"This work delves further into the conformational landscape of these neuronal [receptors](#), which are some of the most important drug targets in inflammation, cancer, sickle cell disease, diabetes, and brain disorders such as Parkinson's disease," says Prosser.

More information: Libin Ye et al. Activation of the A2A adenosine G-protein-coupled receptor by conformational selection, *Nature* (2016). [DOI: 10.1038/nature17668](https://doi.org/10.1038/nature17668)

Provided by University of Toronto

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