UNIVERSITY of GUELPH

COLLEGE of BIOLOGICAL SCIENCE

DEPARTMENT OF MOLECULAR AND CELLULAR BIOLOGY

MCB Seminar SPEAKER SERIES

2023 - 2024

MAR **WED 6** **10 30 AM**

Summerlee Science Complex
SSC 2315

DR. JAMES HOUGLAND

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Hungry like the GOAT: The chemistry, biology, and endocrinology of ghrelin O-acyltransferase

James Hougland (Syracuse University) is a Professor of Chemistry and Biology at Syracuse University and holds an adjunct appointment in the Department of Biochemistry & Molecular Biology at SUNY Upstate Medical University. He earned his B.A. at Northwestern University (Chemistry / Integrated Science double major) where he pursued research in organic photochemistry with Prof. Frederick Lewis. Dr. Hougland's doctoral studies at the University of Chicago with Prof. Joseph Piccirilli focused on catalytic strategies employed by RNA-based enzymes such as the group I ribozyme. As a NIH Postdoctoral Fellow at the University of Michigan with Prof. Carol Fierke, he studied the enzymology and substrate selectivity of protein prenyltransferases prior to his faculty appointment at Syracuse (2010-present) where he serves as director of the undergraduate Biochemistry program (2015-present). The Hougland research group studiess the enzymology and biological chemistry of posttranslational protein lipidation with support from the National Institutes of Health, the American Diabetes Association, and the March of Dimes.

Ghrelin is a peptide hormone involved in appetite stimulation, energy balance regulation, glucose homeostasis, and a range of other physiological and neurological pathways including those associated with addictive behaviors. Ghrelin requires octanoylation of a serine side chain, a unique posttranslational modification within the human proteome, to bind its cognate receptor and activate signaling. The enzyme that catalyzes this acylation, ghrelin O-acyltransferase (GOAT), was identified in 2008 as a protein-modifying member of the membrane-bound O-acyltransferase (MBOAT) enzyme superfamily alongside Hedgehog acyltransferase (Hhat) and PORCN. Ghrelin and GOAT are targets for treating diabetes, obesity, appetite dysregulation, and other diseases connected to ghrelin signaling. Ghrelin is the only predicted substrate for GOAT, suggesting that blocking ghrelin acylation using GOAT inhibitors potentially offers a specific and targeted therapeutic avenue to treat conditions impacted by ghrelin signaling.

We are applying chemical, biochemical, and computational approaches to investigate the mechanism of ghrelin acylation by human GOAT (hGOAT) and the biological impact of this modification at the cell and organismal level. Using structure-activity analysis of substrates and inhibitors, we've identified multiple functional groups within ghrelin recognized by hGOAT. Defining the hGOAT active site and substrate binding sites through computational and biochemical analyses offers insight into the structure and mechanism of this integral membrane acyltransferase and related enzymes while providing guidance for designing and optimizing hGOAT inhibitors. Creation of GOAT-specific ligands has identified molecular determinants for ghrelin recognition between GOAT and the ghrelin receptor, enabling investigation of unanticipated roles of GOAT in ghrelin signaling. Moving beyond the classical view of ghrelin as the "hunger hormone", our work provides a molecular foundation for understanding the multiple endocrine roles played by this secreted peptide within the body.

All welcome to attend
Light refreshments will be served

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