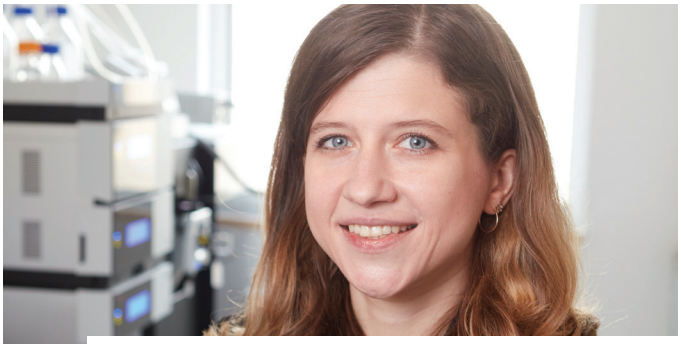

Ekaterina V. Vinogradova, Ph.D.

ASSISTANT PROFESSOR, LABORATORY OF CHEMICAL IMMUNOLOGY AND PROTEOMICS

A remarkable array of proteins—and the interplay between them—mediate the immune system's response to external pathogens and internal damage, and determine the difference between health and disease. Vinogradova combines tools from chemistry, chemical proteomics, and cell biology to modulate and study the functions of immune proteins. The work is illuminating innovative ways to treat immune-related disorders.

Despite major advances in our understanding of the role of the human immune system as both a guardian against and cause of many human disorders, the majority of immune-relevant proteins lack chemical probes, which are critical tools for understanding and controlling immune responses in vivo. The Vinogradova lab aims to discover and develop chemical probes that selectively engage specific sites in proteins to thereby perturb their activity, interactions, and expression in human immune cells. They will then use these probes to study the molecular pathways involved in immune regulation in healthy and disease states.

The amino acid cysteine in proteins plays a critical role in regulating immune signaling pathways as well as sensing electrophilic and oxidative stress. During her postdoctoral work, Vinogradova and colleagues generated the first global atlas of cysteine druggability in primary human T cells by developing an integrated chemical proteomic and phenotypic screening strategy. The study revealed a remarkable number of cysteines across many proteins with human genetic links to immunological disorders that can be targeted with small molecule electrophiles. Most of the identified protein targets lack chemical probes and thus represent a rich resource for medicinal chemistry programs.

The Vinogradova lab applies synthetic chemistry, chemical biology, and proteomics methods toward the goals of discovering and characterizing (a) novel selective chemical probes that perturb the functions of key proteins regulating immunological and neuroimmunological processes; (b) new mechanisms for small molecule-induced protein degradation; and, more broadly, (c) the pharmacological landscape and signal transduction pathways in immune and neuroimmunological disorders. Achieving these objectives is enhanced through the development of new chemical scaffolds targeting cysteine and other nucleophilic residues.

By developing and applying innovative chemical proteomic profiling technologies, Vinogradova's lab aims to enrich our understanding of the molecular differences between pathologic and physiologic states in immune cells and cells of the nervous system (including microglia and oligodendrocytes, which are implicated in the autoimmune disorder multiple sclerosis). The lab also plans to explore how those differences can be further leveraged from a pharmacological perspective for the development of new therapies that not only target specific immune cell subtypes, but also the defined activation states of these cells.

EDUCATION

M.Sc. in chemistry, 2010
Higher Chemical College of the Russian Academy of Sciences

Ph.D. in organic chemistry, 2015
Massachusetts Institute of Technology

POSTDOC

The Scripps Research Institute, 2015–2020

POSITIONS

Assistant Professor, 2021–
The Rockefeller University

AWARDS

International Precious Metals Institute Bright Futures Award, 2014

American Chemical Society Young Investigator Award, 2015

Life Sciences Research Foundation Postdoctoral Fellowship, 2015

IUPAC-Solvay International Award for Young Chemists, 2016

Irma T. Hirschl/Monique Weill-Caulier Trust Research Award, 2021

Searle Scholar, 2021

C&EN Talented 12, 2021

Damon Runyon-Rachleff Innovation Award, 2022

Kellen Women's Entrepreneurship Fund Proof-of-Concept Award, 2022

SELECTED PUBLICATIONS

Scott, K. A. et al. Protein state-dependent chemical biology. *Israel J. Chem.*, e202200101 (2023).

Scott, K. A. et al. Stereochemical diversity as a source of discovery in chemical biology. *Curr. Res. Chem. Biol.* 2, 100028 (2022).

Vinogradova, E.V. et al. An activity-guided map of electrophile-cysteine interactions in primary human T cells. *Cell* 182, 1009–1026 (2020).

Zambaldo, C. et al. 2-sulfonylpyridines as tunable, cysteine-reactive electrophiles. *J. Am. Chem. Soc.* 142, 8972–8979 (2020).

Senkane, K. et al. The proteome-wide potential for reversible covalency at cysteine. *Angew. Chem. Int. Ed.* 58, 11385–11389 (2019).