FACILITIES AND RESOURCES (Molecular Design and Synthesis Center, MDSC)

RESEARCH LABORATORY SPACE-MDSC

The Vanderbilt Institute of Chemical Biology (VICB) Molecular Design and Synthesis Center (MDSC) is housed on the twelfth floor of Medical Research Building IV. Each staff member is assigned bench space including a 6-foot fume hood, a variety of storage areas and desk space. Ten fully equipped hoods with associated rotary evaporators, stirring hot plates, etc. are assigned to the MDSC. One of the hoods is designated for cGMP (current Good Manufacturing Practice) synthesis with equipment and glassware used specifically for the practice of cGMP syntheses.

OFFICE

Drs. Kim (Director), Christov (Assistant Director), Sulikowski (Scientific Director) and Waterson (VICB, Associate Director for Medicinal Chemistry and Director for Vanderbilt Center for Cancer Drug Discovery) each occupy individual offices. Remaining MDSC staff scientists share an office suite adjacent to open lab space as well as individual lab desks adjacent to assigned hood space.

PERSONNEL

Kwangho Kim, Ph.D, Director
Plamen Christov, Ph.D., Assistant Director and Drug Discovery Scientist, senior
Somnath Jana, Ph.D., Drug Discovery Scientist
KyuOk Jeon, Ph.D., Drug Discovery Scientist, senior
Ian Romaine, Ph.D., Drug Discovery Scientist
Benjamin Guttentag, B.S., Research Assistant, senior
Sydnee Ellmore, M.S., VICB Lab Manager
Alex G. Waterson, Ph.D., Director for Vanderbilt Center for Cancer Drug Discovery (VCCDD)

Rates 2023-2024 Chemical synthesis projects, including lead optimization (medicinal chemistry), are supported by one or more staff members at a rate of $133.55 per hour, $2,671 per week, $10,684 per month, or $128,208 per year. This rate includes labor plus consumable lab supplies and reagents, while project-specific chemicals and analyses are charged separately. All core members have extensive experience in chemical synthesis and drug discovery.

OVERVIEW OF LEAD OPTIMIZATION PROCESS In addition to providing services focused on the synthesis of single targets, the VICB MDSC has established a process to support extended lead optimization campaigns, often in collaboration with the (VICB) High-Throughput Screening (HTS) core. The molecular design process incorporates principles of modern medicinal chemistry and typically starts from compound(s) that were identified in the initial (HTS) screen(s) or fragment and progressed though hit validation activities. The VICB Associate Director for Medicinal Chemistry (Alex Waterson, Ph.D.) leads hit prioritization and analog design. In conjunction with the core Director (Kwangho Kim, Ph.D.) and other MDSC staff, synthetic schemes and specific analogs are prioritized based on medicinal chemistry design principles, existing activity data, synthetic accessibility and commercial availability of monomers, as well as patent and literature searches assisted by search engines such as Scifinder.

Scheduled team meetings that include participation from both the “designers” and “synthesizers” are led by Waterson and serve to share and review structure-activity relationship (SAR) data to support subsequent analog design/synthesis cycles aimed at further lead refinement. Concepts of structure-based or property-based drug design are utilized where applicable, and all available assay and physical properties and ADME data are considered to both inform the iterative optimization process and drive progression of individual molecules toward translational program goals.

VANDERBILT COMPOUND COLLECTION The MDSC, established in 2007, is now approaching twenty years of supporting the organic synthesis, chemical probe design-development, and medicinal chemistry needs of researchers across Vanderbilt's campus as well as external collaborators. Over its lifetime, MDSC has produced a diverse array of small molecules with functional activity. Some of these have been previously reported in the scientific literature, while others are novel, designed and synthesized in collaboration with other research groups. The breadth and diversity of functional small molecules produced by the MDSC since its founding was illustrated in a review article published in 2021 (*ACS Chem. Biol.,* **2021**, *16*, 787–793). Examples include well-characterized selective small-molecule protein modulators of enzymes, ion channels, GPCRs, kinases, cell death, etc. Many of these compounds are available from milligram to multi-gram quantities, as needed, to support *in vitro* or *in vivo* studies. Indeed, the MDSC maintains a catalog of over **500 compounds available on demand** to Vanderbilt and external investigators. Many of these compounds have been pharmacologically characterized, and many may have as yet unknown activities. Selected examples of available small molecule probes with potential utility in biochemical and biological studies is provided below. The MDSC also has the ability, in collaboration with VUII radiochemistry group, to provide access to ^{18}F-labeled chemical probes for imaging studies.