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 Center for Molecular Discovery

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BUMC

Boston University Medical Campus

BU CRC

Boston University Charles River Campus

BU NEIDL

Boston University National Emerging Infectious Diseases Laboratories

OTHER AREAS OF INTEREST

The BU-CMD research team is also currently developing small molecules that specifically target:

Multiple Myeloma

Chordoma

Medulloblastoma

Renal failure

Cryptococcal meningitis

Smallpox

Schizophrenia

NEMO deficiency syndrome

Cystic fibrosis

Multiple sclerosis

Neglected tropical diseases

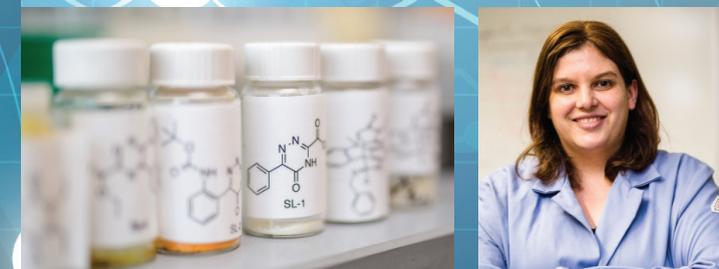
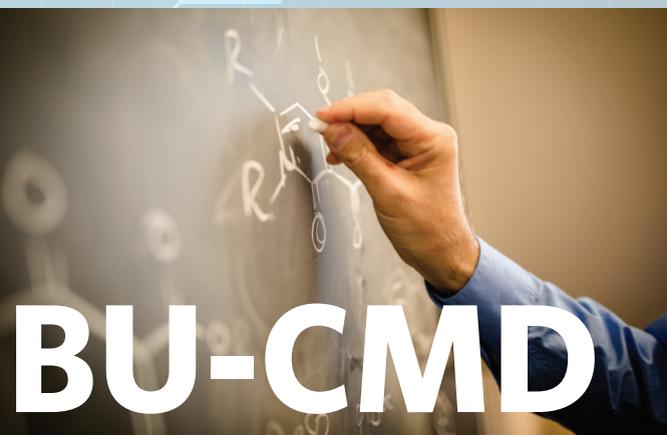
Alzheimer's disease

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 Center for Molecular Discovery

Life Science and Engineering Building
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Boston, MA 02215

 Center for Molecular Discovery



WHO WE ARE

The **Boston University Center for Molecular Discovery** (BU-CMD) is a laboratory connecting chemists who make molecules with biologists who wish to test them for activity against diseases. We foster and seed collaborative research projects, with the goal of advancing curative research for challenging biological disease areas.

HOW WE ARE UNIQUE

- We are an **open-access** compound and medicinal chemistry resource for biological discovery.
- We curate and distribute a diverse collection of screening molecules to biological researchers **free of charge**.
- The molecules we distribute are **crafted** by leading innovators in the art of organic synthesis. These molecules are **structurally more complex** than the “flat” molecules that are often found in mass-produced, commercial screening collections.
- When a bioactive compound is identified, we can **instantly connect** the biomedical researcher with the chemist who created it. This chemist is **uniquely equipped** with the skill and expertise to collaboratively support new research.

WHY BU-CMD IS IMPORTANT

The steady decline in novel small molecule drug approvals over the past decade underscores the **need for new approaches in drug discovery**. The BU-CMD's unique approach couples a rich variety of molecules with new and innovative approaches to combatting disease that are currently being pursued in universities, hospitals, and screening centers across the globe. The end result is **collaborative and multidisciplinary research that can specifically target human diseases** such as cancer, CNS disorders, and neglected tropical diseases.

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PROTECTING AGAINST NEUROLOGICAL DISORDERS

Neurodegenerative Diseases: Alzheimer's disease affects approximately 36 million people worldwide and is a debilitating and ultimately deadly disease. A key feature of Alzheimer's disease is cholinergic neuron loss, leading to cognitive decline. It has been shown that nerve growth factor (NGF) stimulates basal forebrain cholinergic neuron function, and reduces memory impairment. There has been much interest in using NGF as an Alzheimer's disease treatment; however, NGF therapy would be expensive and invasive. One of the main focuses of research in The Beeler Group is synthesis and medicinal chemistry of small molecules which induce the same effects as NGF. The group develops efficient and scalable processes to synthesize these small molecules, which will be therapeutic leads toward developing new drugs for Alzheimer's disease.

Project Leader: Aaron B. Beeler, Ph.D. (pictured)



TARGETING CANCER AND ITS CAUSATIVE MECHANISMS

Liver Cancer:

Hepatocellular carcinoma (HCC), the prevalent form of primary liver cancer, is one of the six most common cancers worldwide. Nearly 90% of HCC patients succumb to the disease within 5 years of diagnosis. Just one systemic chemotherapy is available for advanced HCC; moreover, it only improves survival by a few months. The goal of this BU-CMD project is to develop a novel, first-in-class treatment of HCC that targets the oncogene protein LSF, a controller of HCC growth. This approach was validated by the discovery of a compound family that targets LSF and significantly inhibits HCC growth in mouse models. The lack of toxicity at the effective doses is a hallmark of targeting an oncogene, a key indicator for effective drug development. *Project Leaders: Scott E. Schaus, Ph.D. (pictured) and Ulla Hansen, Ph.D.*



DEVELOPING NEW TREATMENTS FOR INFECTIOUS DISEASES

Leishmaniasis: Leishmaniasis is an insect-transmitted, parasitic, neglected tropical disease that manifests in different clinical forms ranging from skin ulcers and mucosa destruction to fatal organ damage. It affects 98 countries, with over 2 million current cases and 350 million people at risk. The spread of leishmaniasis is of particular concern in the southern US and to military troops stationed in regions where the disease thrives. The development of new, affordable drugs to treat the different clinical forms of leishmaniasis is in urgent demand and is a significant unmet medical need. To address this problem, BU-CMD works jointly with the University of California, San Diego's Center for Discovery and Innovation in Parasitic Diseases and GlaxoSmithKline to develop new antileishmanial drugs *Project Leaders: Lauren E. Brown, Ph.D. (pictured) and Scott E. Schaus, Ph.D.*



HARNESSING NATURAL PRODUCT DERIVATIVES TO FIGHT LEUKEMIAS

Blood Cancers: Multiple myeloma (MM) is a cancer formed by malignant cells found in the bone marrow. This cancer and other hematopoietic malignancies, including acute myeloid leukemia (AML), are highly aggressive and deadly. The effectiveness of chemotherapies for MM and AML are limited, as cells become resistant over time. Accordingly, there is an urgent need for new agents. BU-CMD's work is focused on developing a novel class of natural products and derivatives, rocaglates, which strongly inhibit translation of oncogenic proteins. Collaborative studies with clinical oncologists have shown that these inhibitors are effective in numerous cancers, including MM and AML. In addition, rocaglates have also shown very high efficacy against viruses, including hepatitis C virus (HCV), by acting as inhibitors of viral entry. *Project Leaders: John A. Porco, Jr., Ph.D. (pictured) Aaron B. Beeler, Ph.D., and Igor Kramnik, M.D./Ph.D.*

