UNIVERSITY OF NEW ENGLAND
Office of Research and Scholarship

In Vitro Drug Screening Core

Service Mission: The In Vitro Drug Screening Core is part of a continuing effort by the Research and Scholarship Office to develop complementary groups of core services that UNE faculty, staff and students can utilize in the conduct of their research. Building upon strengths in the various academic programs and centers of excellence, the broader vision for these cores includes:

1. Medicinal chemistry to produce novel lead molecules that can be refined and optimized to become drug candidates;
2. In vitro drug screening to quickly and efficiently find and characterize the most promising of these candidates;
3. In vivo behavioral testing of the best candidate drugs to establish their preclinical effectiveness and side effect profiles; and
4. Pharmacokinetics and formulation expertise as part of the final steps prior to initiating a clinical development plan.

The core is thus an integral part of a program designed to move therapeutic drugs from initial conception to clinical testing, all within the framework of an academic setting. In addition, the Core offers services and expertise that will improve the capabilities and opportunities for collaborative research in Maine, the Northeast and beyond. The core services and faculty expertise will be open to extramural academic researchers as well as pharmaceutical and biotechnology companies. By serving both academia and industry, the Core can act as a bridge to bring together academic and industrial institutions to foster interaction and collaboration, to the benefit of both.

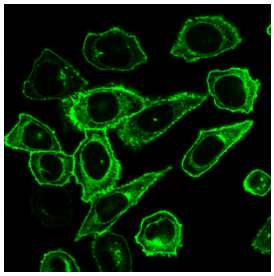
Specifically, the Core will provide:

1. Consultation or direct service, at the discretion of the investigator, in all aspects of target selection, cell line/model creation, assay and experimental design.
2. A flexible service model that allows for the investigation of most receptor targets.
3. Medium throughput drug screening, starting with radioligand binding and GTPγS coupling in cells or animal tissues.
4. Consultation or direct service, as desired, in all aspects of statistical data analysis and interpretation.

Model and Assay Creation: The Core has extensive expertise in the use of cell line models for drug characterization, with both traditional cell lines and primary cells (consultation is available for primary cell models, but the Core is unable to provide primary cells at this time). The Core can provide service or advice for which targets to select, which cell line or cell model to use (a number of cell lines will be on hand), creation of cell lines, and the creation and use of assays for drug action.

Services:

1. Cloning and amplification of DNA expression vectors for the target of choice.
2. Transfection, selection, sub-cloning and validation of stable cell lines.
3. Assay design and creation. The Core has experience with multiple assay types, including transporter assays, receptor binding and coupling assays, signaling kinase activation, whole cell activation (i.e. CellKey or Epic system) and so forth.



Target Flexibility: Due to the flexible nature of the assays and cell culture systems in use, the Core is able to investigate most receptor targets (even orphan receptors). It may also be

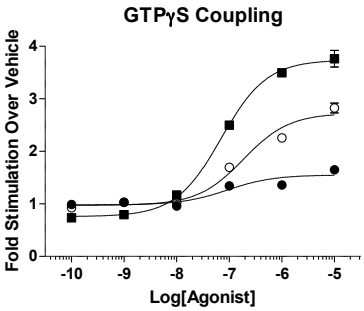
possible to investigate non-receptor targets, such as signaling kinases or enzymes, depending on the particulars of the protein involved. For instance, the use of ELISA to investigate changes in enzyme synthesis activity or Western blot to investigate signaling kinase activity changes in response to novel compounds.

Medium Throughput Drug Screening: The primary purpose of the Core is served by evaluating the activity of multiple novel compounds (potentially into the hundreds) against the target of choice. Furthermore, in addition to traditional agonist and antagonist testing, the Core can test novel compounds for inverse agonism or allosteric modulation (positive or negative).

Services:

1. Radioligand binding. The Core can test novel compounds in competition radioligand binding against a known and labeled ligand of the desired target. Can be performed in cells or animal tissue.
2. GTPγS coupling, a functional assay of G protein activation and recruitment. Can be performed in cells or animal tissue.
3. Signaling kinase (i.e. ERK MAPK) activation by In Cell Western.
4. Qualitative β-arrestin recruitment by confocal imaging.
5. Many other potential assays.

Data Analysis and Interpretation: The Core offers services and expertise in data analysis and interpretation. This includes non-linear curve fitting and the derivation of pharmacological properties (potency, efficacy, etc.) and the determination of statistical significance (curves as well as parameters).



Education and Training: The Core will gladly offer training opportunities on all aspects of the services it provides to interested investigators. If there is sufficient interest, the Core may also provide more structured mini-courses on cell and molecular biology, drug screening strategy and techniques, receptor biology, and similar topics.

Pricing: For internal users, the Core is offering its services for the cost of reagents and materials only, without charging for the time and expertise of Core personnel or use of capital equipment. As collaborations with investigators develop, we request that direct monetary support for the Core be written into grant proposals as appropriate. As the Core matures, it will eventually transition to a self-sustaining fee structure. For external partners, the fee structure covers costs of materials and personnel along with the University's standard indirect cost rates.

Contact:

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