

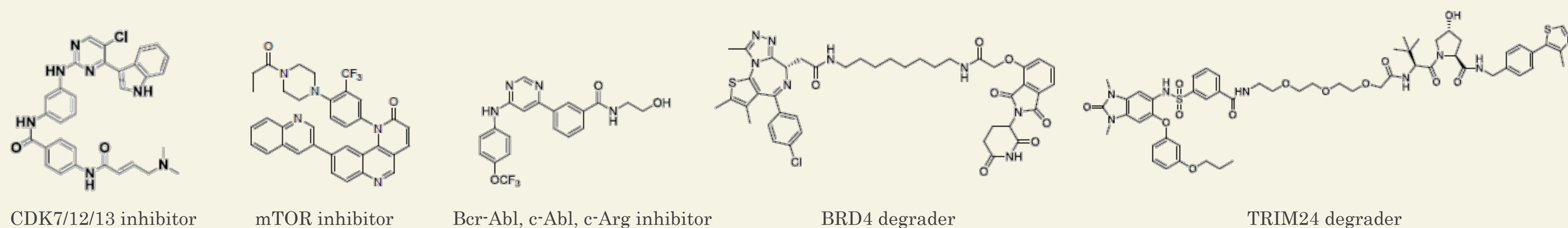
# MEDICINAL CHEMISTRY & STRUCTURAL BIOLOGY CORES @DFCI

When it comes to small molecule inhibitor development, it is very unlikely that a lead that emerges from a target-based high-throughput and/or virtual screen is the best possible inhibitor for that target. More often than not, the initial hits have liabilities such as off-target activity, poor cell penetration, unacceptable pharmacokinetic and pharmacodynamic properties, or poor plasma stability or oral bioavailability. Scientists at Dana-Farber's Chemical Biology Program are experts in optimizing small molecules towards targeted therapies. Critical to these efforts are structural biology analysis that allows us to visualize how a small molecule engages its target, and medicinal chemistry that enables to modify a small molecule into new and improved compounds. We formed a Structural Biology Core and a Medicinal Chemistry Core in order to share our expertise in these areas with a broader research community.

## Medicinal Chemistry Core @ DFCI

Contact: David Scott, PhD

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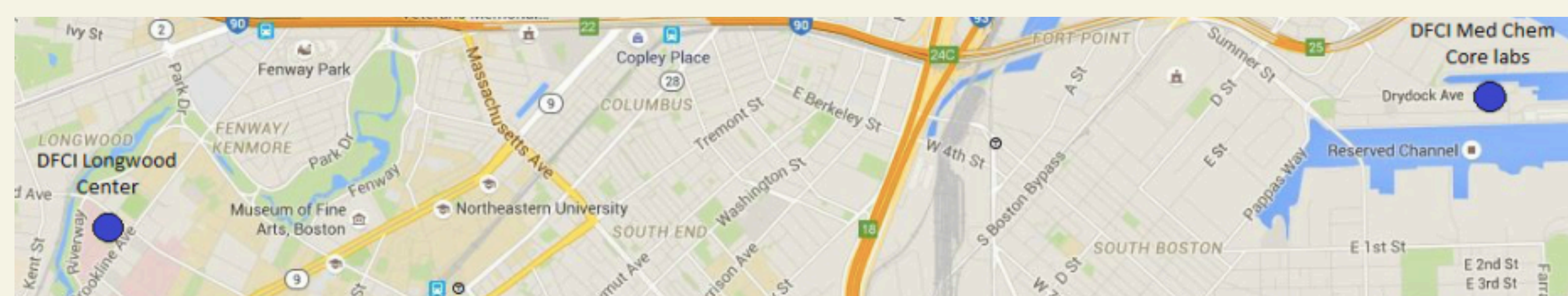
### Mission:

The mission of the Medicinal Chemistry Core is to collaborate with researchers to advance their understanding of disease, and to accelerate the development of novel therapeutic agents. We can assist with all chemistry-related needs, from the provision of suitable small molecule probes to interrogate basic biology, to the optimization of promising lead compounds for *in vivo* studies.

### People and Equipment:

We are experienced medicinal and synthetic chemists, and our lab space is located in Dana-Farber's Harbor Campus. The labs are fully equipped to perform synthetic organic chemistry on a small to multi-gram scale, with LCMS, reverse phase chromatography, and access to the NMR facilities at DFCI and Harvard Medical School.

*Note: we come to the Longwood Medical Area twice to three times a week and happy to meet locally.*



### Services:

#### • Provision and consultation on the use of tool compounds

We can help you identify and secure the most suitable small molecule chemical probes for your *in vitro* testing or animal studies. If the required compound is not commercially available, the Core can arrange for its custom synthesis. The core can also provide access to a collection of kinase inhibitors maintained by Nathanael Gray's lab, and can make available many of the published compounds generated in the Chemical Biology Program @DFCI.

#### • Medicinal chemistry consulting/advice

We can provide input for grant applications, search the chemistry and patent literature for a preliminary assessment of a compound's patentability, and assist with the collection of selectivity, pharmacokinetic and safety data.

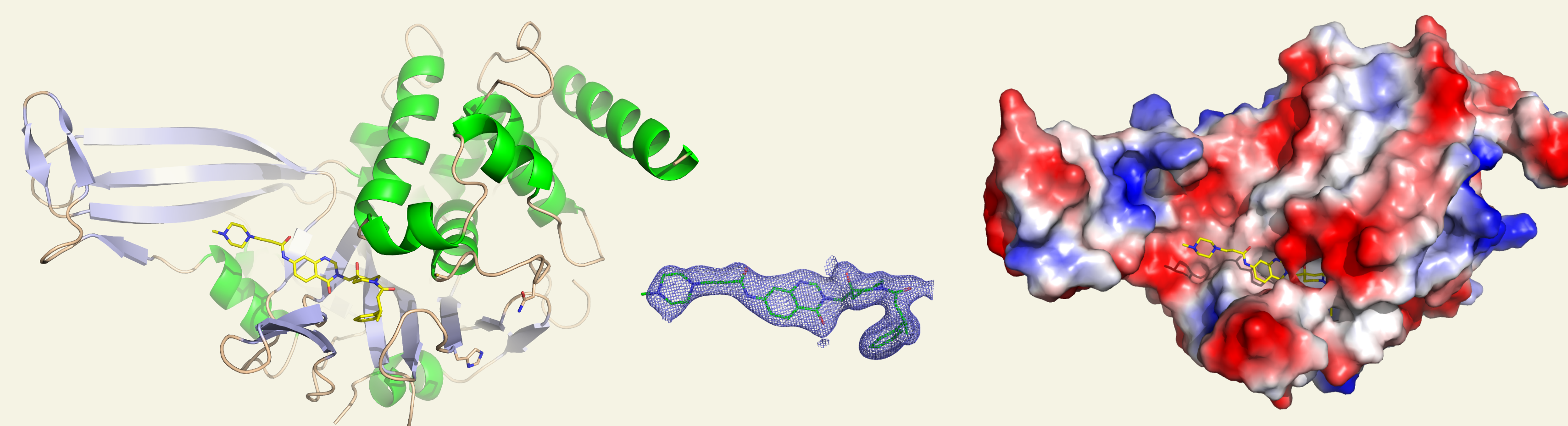
#### • Drug discovery

For researchers pursuing novel therapeutics, or wishing to develop chemical tools for new targets, the Core can assist with hit identification strategies, the analysis and prioritization of HTS data, and the optimization of initial lead molecules for potency, selectivity and pharmacokinetics. With appropriate funding, the Core can more fully collaborate with researchers, designing compounds and synthesizing them, either in its own labs or through a chemistry CRO.

## Structural Biology Core @ DFCI

Contact: Sirano Dhe-Paganon, PhD

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### Mission:

The mission of the Structural Biology Core @DFCI is to collaborate with researchers to advance their understanding of normal and disease biological processes and to accelerate development of novel therapeutic agents. We can assist with *in-vitro* level experimentation, including protein sample preparation, biochemical & biophysical characterization, structure determination, and computer-assisted drug discovery. For example, we conduct screening assays, hit-validation, and protein crystallography for structure-guided medical chemistry. Collaborations are engaged via joint grants, subcontracts, and project-based services.

### Equipment:

#### • In-house X-Ray system (Microstar and Mar345)

An in-house generate and detector system is available for rapid data-set collection or for rapid crystal evaluation. Training and certification is provided and required before use.

#### • Crystallization robots (Phoenix and NT8)

Three-seat 96-well Intelli-plates and 384-well clear polystyrene plates (hanging drops) are provided, as well as common sparse-matrix source screens.

#### • Custom formulators (Formulator and NT8)

Expansion or optimization plates are prepared using either the Formulator or the NT8. Common stock primary precipitant solutions and stock buffers are provided and maintained.

#### • Automated plate microscopy/storage (Rock Imager 1000)

We use Rock Imager to store and handle crystallization plates. Users will be setup with their own, secure account in RockMaker software.

#### • Bacterial and Insect/Baculoviral incubators

A dedicated baculovirus and insect-cell room with full supporting equipment.

#### • Protein purification systems (FPLCs)

A pair of AKTA Pure 25L equipped to process high-throughput serial & tandem purification schemes.

