

**NCI Guidelines for ARRA Research and Research Infrastructure
Grand Opportunities:
NCI Molecular Target Discovery and Development Centers Pilot Program**

Updated May 8, 2009

Announcement Number: [RFA-OD-09-004](#)

Title: Recovery Act Limited Competition for NIH Grants: Research and Research Infrastructure “Grand Opportunities” (RC2)

The NCI is participating in the Research and Research Infrastructure Grand Opportunities (GO) Program ([RFA-OD-09-004](#); RC2 grant), which has been issued by the NIH to support research on high impact ideas that lend themselves to short-term, non-renewable funding, and may lay the foundation for new fields of investigation. Through its participation on this and other related funding initiatives, the NCI is committed to fulfilling the goals of the American Recovery and Reinvestment Act (ARRA) to help stimulate the economy through support of biomedical and behavioral research. Additional information the Recovery Act and related NIH opportunities is available through the Office of Extramural Research.

Areas of Scientific Priority:

As part of its participation on Recovery Act Limited Competition for NIH Grants: Research and Research Infrastructure “Grand Opportunities” (RC2), the NCI is interested in leveraging recent progress in the multi-dimensional genome characterization and deep analysis of cancer-relevant genomic changes from statistically robust cohorts of tumor and normal samples. Recent reports from The Cancer Genome Atlas (TCGA) and other large scale genomic studies have shown these alterations are present at all levels inclusive of rearrangements expression, changes in the epigenome and point mutations. The integration of data from these multi-dimensional data sets, when placed in biological context, is producing new insights into cancer genomes, affirming, confirming genomic alterations that were heretofore suspected, but not definitive and providing new direction for developing molecular-based subclassification systems for tumors that have generally regarded and treated as single diseases. Perhaps of most importance recent findings from TCGA and other large scale sequencing studies are pointing to new directions for identifying and developing new targets for cancer therapeutic, diagnostic, and preventive interventions.

Given the genomic associated complexity of cancer driven in large measure by somatic and a limited number of inherited mutations, it is increasingly important to place this array of genomic alterations in biologic context to determine their relevance to the initiation and progression of cancer. It is also critical that the area of cancer target discovery and development move quickly to develop the tools and approaches that will facilitate incorporation of new data and knowledge to discover new targets and rethink how they are qualified and validated. This is a complex goal, but based on TCGA and other large scale genome characterization efforts, the NCI believes that

there is sufficient data to begin building a new generation of centers to undertake this effort. These centers will drive a new molecular-based paradigm that gives consideration to comprehensive genomic data, biological context, and the clinical picture of specific tumors.

The complex nature of developing this infrastructure requires that the development of these centers be undertaken as a pilot program. Moreover, it will be critical that the centers selected employ different overall concepts, approaches, and models that although different will in the aggregate inform the next phase and potential scale up of this new network. This program will require regular interaction amongst the centers and an open data and other resource sharing approach is expected to ensure the success of the pilot program.* Although not mandatory, preference will be given to centers that include other institutions and associated experts to build on respective strengths vs. re-inventing existing infrastructure, expertise and capabilities. To qualify for participating in this program centers applications must include, but are not limited to, at least three of the following activities in an integrated plan that establishes the overall direction and expected outcomes from a specific center. New ideas for other value added center functions not included are encouraged. The success of each center will ultimately depend on new targets qualified, validated, and shared among the network and broader cancer research communities. The recommended focus areas include, but are not limited to, the following:

1. Robust approaches to identify appropriate targets/biomarkers from multi-dimensional genomic data sets such as TCGA and others considering target identification in the context of pathways vs. single genomic alteration based targets.
2. Innovative and new approaches to algorithm development and computational approaches that will inform target discovery and development from large multi-dimensional data sets such as TCGA.
3. Innovative and new approaches to chemical genomics (inclusive of unique probes and chemistry) that emphasizes targeting heretofore “un-druggable” targets for pathways.
4. Value added innovation in the area of small molecule screening.
5. New approaches to compound synthesis that optimizes production based on a thorough understanding of the biology of the cancer at all levels.
6. New and innovative models to qualify and validate new targets that optimize both the biological context of the potential target and relevance to the clinical situation.
7. New approaches to validate the wide array of potential targets that are emerging from current molecular discovery programs.

*All participants in this initiative will be expected to make data broadly available through a publicly available web site.

Funding Priorities:

Overall, NCI expects to make awards for a period of up to 2 years to establish 2-4 new centers. NCI may devote up to 3 million for each successful “Molecular Target Discovery and Development Center” in this pilot program.

The budget cap for each award proposal is \$3M in total costs per year.

Application Guidelines:

Applications for NCI funds supporting the scientific areas listed above **MUST** follow the guidelines listed in [RFA-OD-09-004](#).

Key Dates ([RFA-OD-09-004](#)):

Letters of Intent Receipt Date: April 27, 2009
Application Receipt Date: May 27, 2009
Peer Review Date: June/July 2009
Council Review Date: August 2009
Earliest Anticipated Start Date: September 30, 2009
Expiration Date: May 28, 2009

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