

# **Request For Applications: Cancer Systems Biology Pilot Project Program**

Sponsored by The Cancer Cell Map Initiative, UCSF and UC San Diego Health Sciences

## **Overview**

The Cancer Cell Map Initiative (CCMI; [www.ccmi.org](http://www.ccmi.org)) has funds to support up to two pilot projects in cancer systems biology. Project proposals are solicited from faculty members at UCSF, UC San Diego and nearby universities and research institutes (within 30 miles of either campus) wishing to develop and apply systems biology approaches to address a compelling biomedical question in cancer in collaboration with CCMI investigators ([www.ccmi.org/about/investigators](http://www.ccmi.org/about/investigators)).

## **Goals**

Although much attention has been devoted to mapping tumor genomes, understanding cancer involves more than cataloging frequently mutated genes. It is critical to understand the many interactions between these genes and the corresponding proteins, and how these complex networks give rise to tumor initiation, progression and metastasis. The CCMI is applying systematic approaches to comprehensively map the molecular networks that underlie cancer and will use these maps as a key resource for precision medicine.

This pilot project program is intended to support the short-term exploration of innovative, high-risk concepts that complement existing CCMI research efforts ([www.ccmi.org/research/introduction](http://www.ccmi.org/research/introduction)). These could be related to the development of novel bioinformatics techniques to integrate datasets into predictive tools or the exploration of a promising new experimental approach in systems biology such as imaging or single cell genomics. Representative examples are provided below:

- Developing new methods for mapping protein-protein interactions, with an emphasis on capturing transient interactions,
- Generating systematic knowledge of hallmark cancer pathways by linking tumor genomes to patient outcomes and responses, and
- Integration of system-wide molecular data with advanced imaging techniques.

## **Review Criteria**

Proposals will be reviewed and ranked according to the following criteria: potential to provide significant advances in the area of cancer systems biology, innovation, appropriateness of the experimental design, feasibility, qualifications of the personnel, complementarity to the existing research within the CCMI, and potential to be developed into R21 or R01 grants. Investigators receiving funding will be required to attend the annual CCMI Symposium and submit an annual report of no more than two pages.

## **Submission Information**

Use the NIH's structure (Significance, Innovation and Approach) or a similar format to describe a single Specific Aim in three pages or less. Proposals should clearly state the significance of the biomedical problem in cancer, why it will benefit from a systems biology approach and how this work will enable future competitive grant proposals. The proposal should include a succinct description of the research plan along with proposed experiments, methods and analysis. Please describe the available reagents and assays needed to support the research or describe what will need to be

developed. Finally, provide a brief description of how this proposal is in collaboration with a CCMI investigator ([www.ccmi.org/about/investigators](http://www.ccmi.org/about/investigators)).

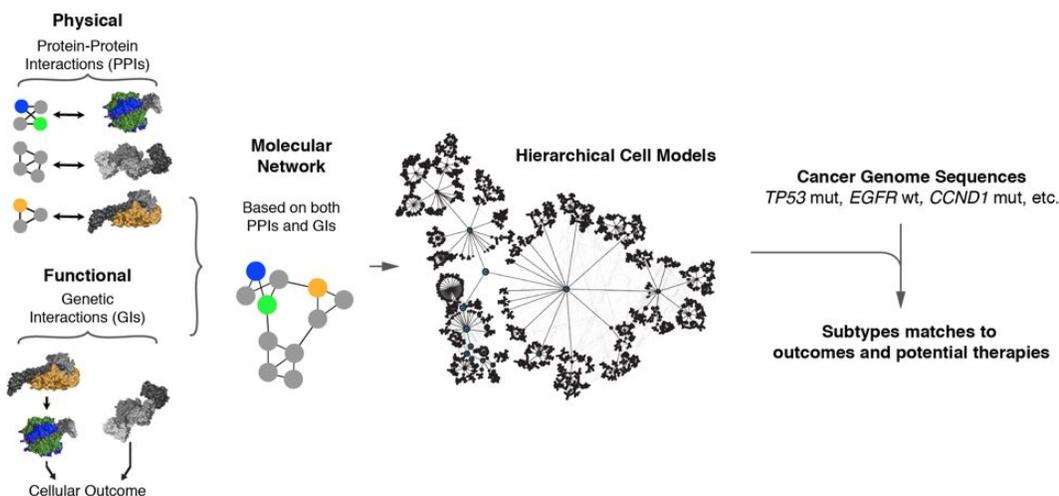
In addition to the three-page research proposal, please also provide an NIH biosketch (faculty members only) and a brief budget of no more than \$70,000 (direct costs) for one year.

**All documents should be submitted as one PDF to [hello@ccmi.org](mailto:hello@ccmi.org) by 11:59 PM PT August 20, 2017.** Please also direct any questions to [hello@ccmi.org](mailto:hello@ccmi.org).

## About The Cancer Cell Map Initiative (CCMI)

The CCMI is generating comprehensive maps of the key protein-protein and genetic interactions underlying cancer, and is developing computational methods using these maps to identify new drug targets and groups of patients with shared outcomes (**Fig. 1**). Protein-protein interaction maps – the complete set of proteins that bind to another protein – tell us about the physical structure of cancer cells. Genetic interaction maps – knowing how deleting one gene impacts how cells respond to the loss of another gene – tell us about how groups of genes function as pathways and networks. New drug targets and patient subtypes will then be identified using a variety of machine learning algorithms. Unsupervised methods such as clustering and network propagation will be used to identify patient subtypes and drug targets, respectively, and supervised methods like neural networks will be trained to predict outcomes based genetic information.

The CCMI's initial research efforts are focused on head and neck squamous cell carcinoma (HNSCC) and breast cancer. HNSCC is the sixth most common malignancy worldwide with only a 40% survival rate; breast cancer is the most common type of cancer in US leading to over 40,000 deaths. For both, we will generate unbiased, comprehensive physical interaction maps of the forty most commonly mutated proteins in that cancer type. Genetic interaction maps will be generated for the same forty genes plus an additional thirty druggable targets. These interaction maps will also be used along with other comprehensive datasets to infer data-driven cancer gene ontologies, hierarchical maps of the protein complexes, pathways and other subsystems present in cancer cells. These ontologies will then be used as features by sophisticated machine learning algorithms to predict patient outcomes like drug response.



**Figure 1 | Overview of the CCMI's research efforts.**