

1.0 Specific Aims

The goal of our research is to speed the development of cancer drugs through the development and application of human imaging techniques. While extraordinary advances in drug discovery have been made, critical problems remain in the development process. Development of new drugs reportedly costs as much as \$800M and takes up to 12 years. There is a possibility that all cancers becoming orphan diseases due to genotyping. Add the proliferation of yet-to-be-validated drug targets, and these developments suggest a new drug development paradigm emphasizing significant improvements in drug efficacy, development cost, and time to market will be needed to turn improved discovery approaches into medicines that benefit cancer patients.

In this proposal we advance the notion that proper use of validated imaging biomarkers can lead to more effective development of cancer therapeutics, and that a dedicated partnership between academia, drug developers, and imaging companies can more effectively promote such use. There is now suggestive evidence that in certain oncology settings, the judicious use of validated imaging biomarkers can result in considerable insights into drug mechanism of action and pharmacokinetics, reduce cohort size, provide indicators of drug activity, improve the likelihood of drug approval, and allow “fast fail” termination of unpromising projects. Despite these encouraging reports, however, enthusiasm for imaging biomarkers has been tempered by some failures, such as instances of inadequately understood relationships between biomarkers and outcomes that have resulted in erroneous conclusions based on surrogates. This in turn has led to confusion over the best role for biomarkers. We propose that imaging biomarkers are a powerful tool, and like any powerful tool, should be used with care. In the case of cancer drug development, we believe this requires close cooperation between those caring for patients (academic medical centers and patient advocates), those developing new drugs (pharma and biotech companies) and the tool builders (academia and imaging companies). Therefore, the purpose of the partnership proposed herein is four-fold:

- To promote, and to develop a scientific program around, the rigorous understanding, validation, and utilization of imaging biomarkers, with the goal of demonstrating substantial improvement in the rate at which new cancer drugs can be clinically tested, without compromising patient/subject safety;
- To develop a highly multidisciplinary partnership comprised of academic research, biopharmaceutical firms, imaging system developers, government, and patient advocacy groups focusing on the opportunity to use imaging to accelerate development of oncology pharmaceuticals;
- To develop an imaging biomarker validation process that can be readily generalized to work with new compounds and new targets, thereby impacting numerous forms of cancer; and
- To quantify the tangible benefits of integrating the use of imaging biomarkers during a drug development process.

Given these objectives, our specific aims revolve around the creation of an environment and process in which plans for an AP4 Center can be developed and implemented:

Specific Aim 1: Develop a productive and cohesive partnership with appropriate administrative structure and broad representation

- Aim 1.1: Establish criteria for selection of industrial, academic, and public parties.
- Aim 1.2: Develop suitable forums for interacting, brainstorming, communicating, and planning.
- Aim 1.3: Form partnership with agreed-upon guidelines and structures.

Specific Aim 2: Select compelling projects that demonstrate the objectives of this partnership

- Aim 2.1: Establish criteria for projection selection.
- Aim 2.2: Select and prioritize a small set of projects that meet the objectives of the Center.

Specific Aim 3: Deliver to the membership a 5-year operating plan for the Center

- Aim 3.1: Reach consensus on general terms of non-disclosure, material transfer, sponsored-research, and intellectual property agreements.
- Aim 3.2: Obtain firm industrial support commitments.
- Aim 3.3: Set a timetable for establishing an operating structure.