



## Scientific Abstract

### SU2C-LUNGeity Foundation-American Lung Association Lung Cancer Interception Dream Team:

#### **“Intercept Lung Cancer Through Immune, Imaging, and Molecular Evaluation (InTIME)”**



*[This abstract was provided by the scientists when their application was accepted.]*

We lack effective lung cancer interception approaches due to our incomplete understanding of the earliest molecular events associated with lung carcinogenesis, as well as the challenge in developing personalized tools for early detection and prevention. Our multidisciplinary Dream Team proposes a series of interrelated aims that will address these barriers and establish a critical foundation for lung cancer interception, with the potential for direct and immediate clinical impact. The proposal is based on the hypothesis that premalignant lesions bear specific genomic and transcriptomic aberrations, and a subset of these lesions escape immune surveillance and progress to invasive cancer.

Our team, in collaboration with a number of existing industry partners, will apply novel molecular, imaging, and immunological approaches to biospecimens that are being collected prospectively from unique patient cohorts, to understand the biology of lung cancer precursor lesions and their response or resistance to therapies, and to develop biomarkers that predict these outcomes.

Our first aim will build a genomic, transcriptomic and immune atlas of premalignant lung adenocarcinoma and squamous cell carcinoma lesions that will serve to 1) identify novel targets for disease interception including personalized immune-related approaches; 2) develop genomic biomarkers for early detection in noninvasive samples e.g. nasal swabs and 3) develop companion diagnostics to identify subjects at high risk for progression to invasive carcinoma who would benefit from interception trials as well as surrogate markers of efficacy in those trials.

Our second aim will develop and validate early detection biomarkers that would directly impact two growing needs: 1) integrated imaging and non-invasive molecular diagnostics for indeterminate pulmonary nodules that would allow physicians to avoid unnecessary invasive procedures in patients with benign lung disease and 2) circulating cell-free DNA biomarkers for detecting preclinical recurrence and guiding precision adjuvant therapy.

Our third aim will leverage two industry-sponsored interception trials to discover companion biomarkers that are predictive of response to immunotherapy, enabling precision lung cancer interception. Critical to the success of the proposal is the multidisciplinary expertise of the team, involvement of patient advocates and the extensive preliminary data supporting the feasibility of the proposed approaches. The insights gained from successful completion of this project and the data that will be made available to the research community will serve as a foundational resource for other investigators in the field and will result in a significant and sustained impact on the interception of early stage lung cancers.

