Cancer Immunoprevention Network (CIP-Net)

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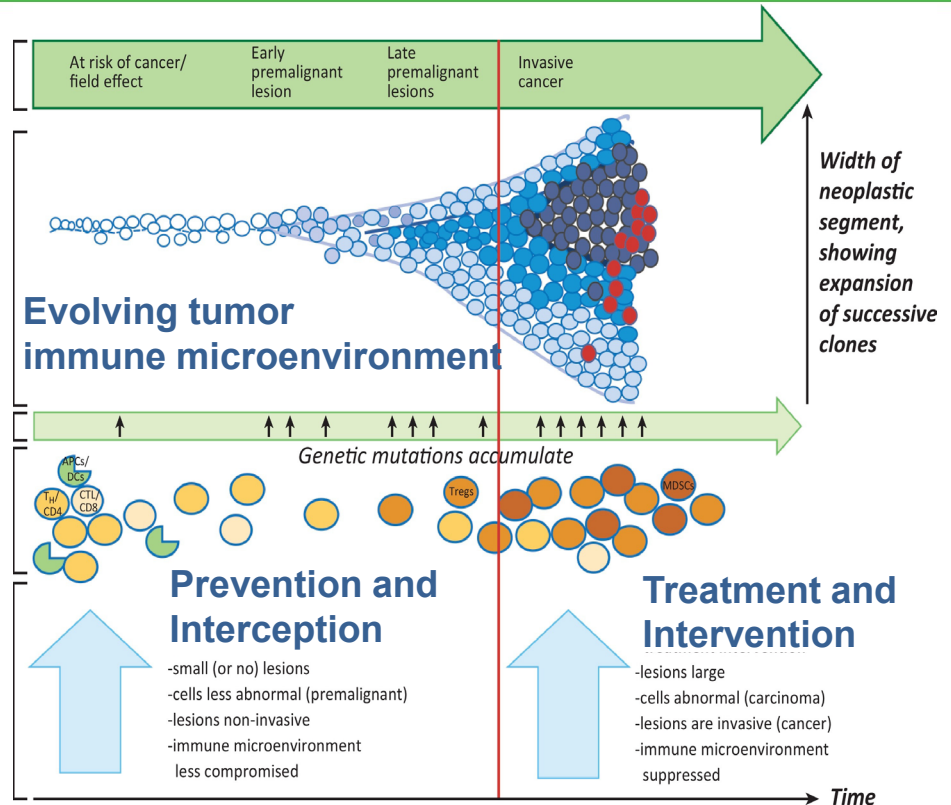National Cancer Institute

Disclosure Information

No financial relationships to disclose.

High Risk Cohorts

1) Inherited cancer predisposition individuals

2) Individuals with precancers

3) Individuals exposed to occupational/ environmental carcinogens

4) Special populations (e.g., MGUS)

5) Cancer survivorship cohorts

At risk of cancer/ field effect | Early premalignant lesion | Late premalignant lesions | Invasive cancer

Width of neoplastic segment, showing expansion of successive clones

Evolving tumor immune microenvironment

Genetic mutations accumulate

APCs/ DCs
T_H/CD4
CTL/CD8
Tregs
MDSCs

Prevention and Interception
-small (or no) lesions
-cells less abnormal (premalignant)
-lesions non-invasive
-immune microenvironment less compromised

Treatment and Intervention
-lesions large
-cells abnormal (carcinoma)
-lesions are invasive (cancer)
-immune microenvironment suppressed

Time

PMID: 28138568

Trends in Cancer

Scientific Objectives

- The overarching goal of the Cancer Immunoprevention Network (CIP-Net) is to support a deeper understanding of basic mechanisms of immunoprevention, discover novel immunoprevention strategies, and foster a community of cancer immunoprevention researchers

- This initiative builds on the aspirational Cancer Moonshot Immunology Working Group goal "**to prevent cancers before they occur**"

- Meets an **emerging scientific opportunity** to complement recent immunoprevention clinical trials (in humans and dogs) by building a research pipeline of discovery science in basic mechanisms of immunoprevention

Key Definitions for CIP-Net

- **Cancer immunoprevention:** Cancer immunoprevention is the prevention of invasive cancer onset (not recurrence) with immunological means such as vaccines or immunomodulatory agents.

- **Cancer interception**: Cancer interception is defined as the disruption of the oncogenic process during the precancer stage before the development of invasive cancer (not recurrence).

- **Higher-risk populations, higher-risk cohorts**: These are individuals with an increased risk of cancer such as those with hereditary cancer syndromes (HCS) and precursor abnormalities that place individuals at higher risk of cancer, e.g., precancer.

- **Precision cancer prevention and interception:** Precision cancer prevention-interception refers to an approach employing cancer preventive-interceptive interventions individually tailored for different higher-risk populations as defined above.

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CIP-Net Structure: U24 and UG3/UH3
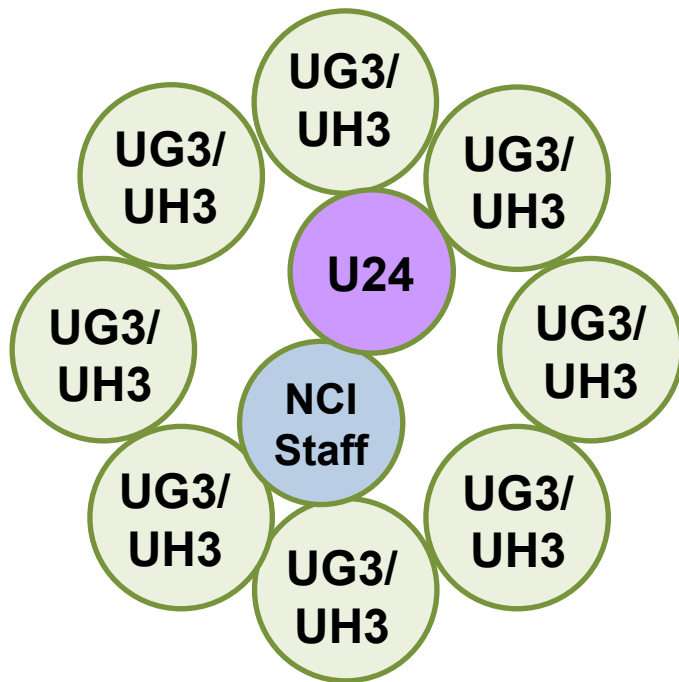
U24 Data and Resource Coordinating Center:

- Enhance CIP-Net data, resource sharing (e.g., biospecimens), and collaborations
- Provide bioinformatic and analytical support
- Increase awareness through scientific communications and meetings
- Conduct scientific outreach to build immunoprevention bridges across complementary cancer research communities
- Foster early career scientist development

CIP-Net UG3/UH3 Research Projects
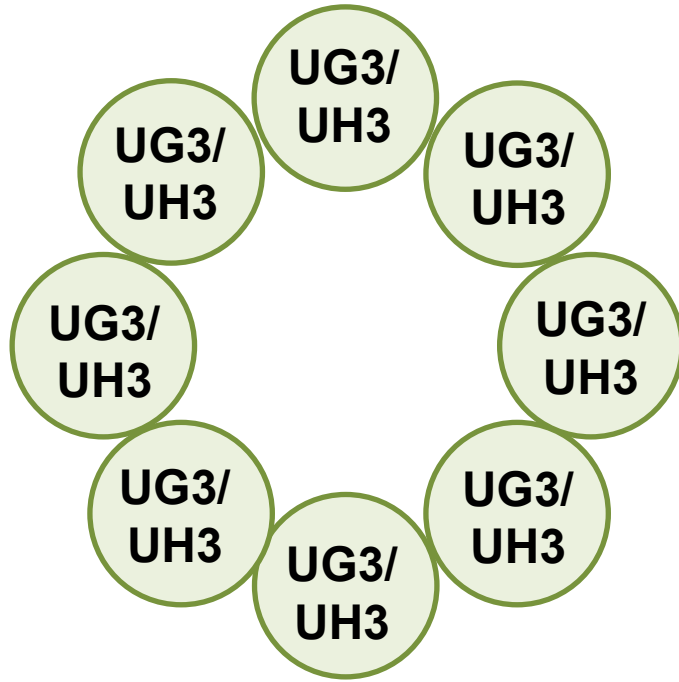
UG3/UH3 Research Projects:

- UG3: Discover and investigate novel immune pathways, mechanisms, and innovative targets for immunopreventative intervention

- Milestone driven transition evaluation by NCI staff

- UH3: Validation and deeper mechanistic interrogation of pathways, development, or preclinical testing to evaluate mechanisms, efficacy and potential side-effects

CIP-Net UG3/UH3 Research Project Examples

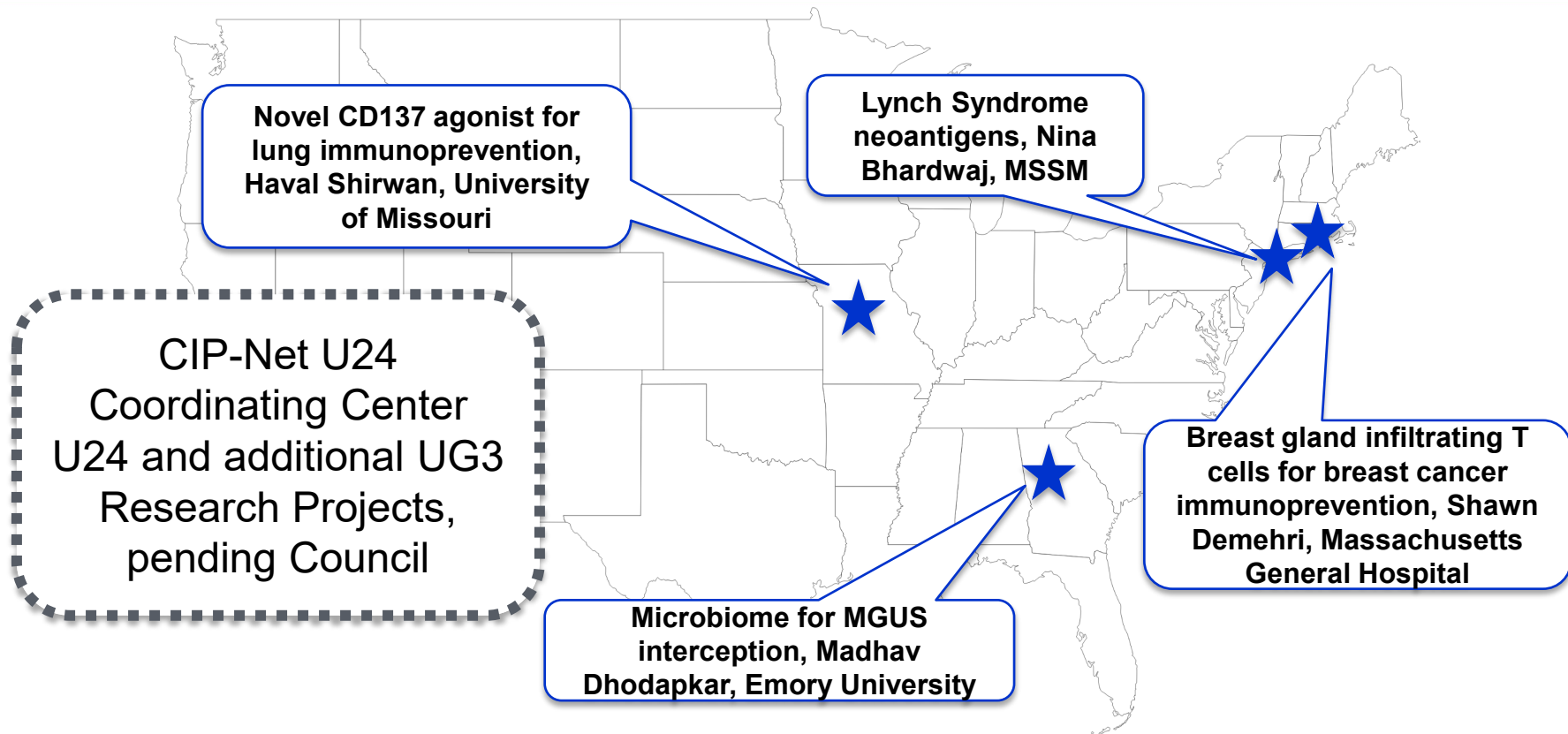*Research may include, but not limited to:*

- Discover novel immunoprevention pathways and targets

- Elucidate immune responses to the earliest stages of carcinogenesis

- Preclinical development and testing of interventions (agents/vaccines)

- Investigate mechanisms of efficacy and potential side-effects of precision cancer prevention-interception strategies

- Immunoprevention models development and optimization

- Immune mechanisms of preventive cancer vaccines and immunomodulatory agents
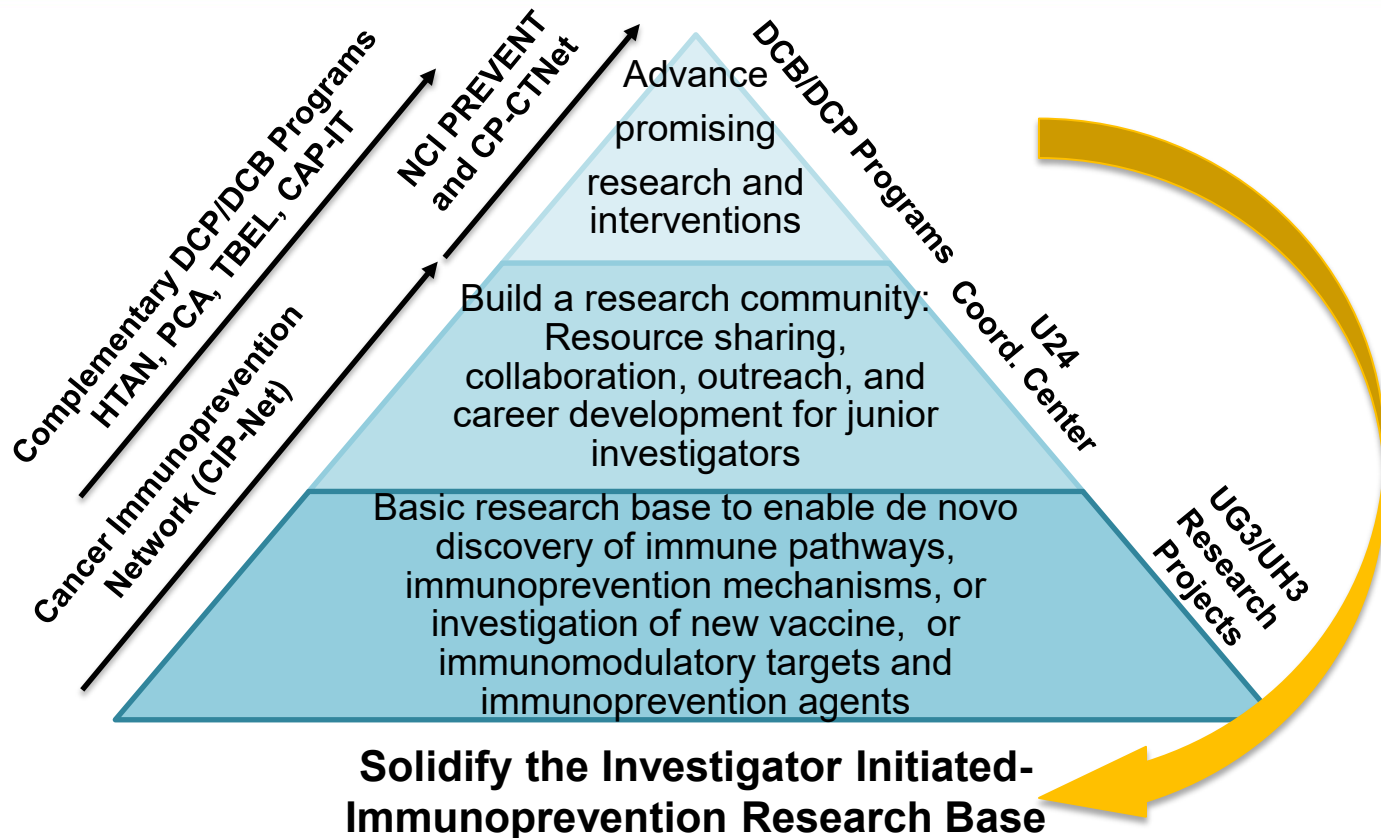
CIP-Net UG3 Phase to UH3 Phase Transition

- Utilization of milestones is a key characteristic of this NOFO

- Applications must include well-defined milestones for the UG3 phase and annual milestones for the UH3 phase

- Milestones for the UG3 phase must be objectively defined and quantifiable with clear go/no-go criteria to demonstrate the proposed milestones were met at the time of the transition request

- UG3 to UH3 transition criteria include:

  - ✓ successful completion of established milestones during the UG3 phase;
  - ✓ demonstration of the feasibility for the proposed UH3 research; and
  - ✓ extent to which UG3 phase activities support the aims of the UH3

Building a Cancer Immunoprevention Network (CIP-Net)

Novel CD137 agonist for lung immunoprevention, Haval Shirwan, University of Missouri

Lynch Syndrome neoantigens, Nina Bhardwaj, MSSM

CIP-Net U24 Coordinating Center U24 and additional UG3 Research Projects, pending Council

Breast gland infiltrating T cells for breast cancer immunoprevention, Shawn Demehri, Massachusetts General Hospital

Microbiome for MGUS interception, Madhav Dhodapkar, Emory University

Building a Cancer Immunoprevention Research Continuum

Building a Cancer Immunoprevention Community

CIP-Net aims to **build immunoprevention bridges** across complementary cancer research communities, future directions:

- Integration of immunoprevention research advocates

- Communications, engagement, and outreach with AACR, SITC, AAI, et al.

- Early career scientist development

- Associate membership

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Contact Us! CIP-Net@mail.nih.gov

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National Cancer Institute

CIP-Net UG3/UH3 Phased Innovation Structure

- **UG3 phase research projects:** de novo discovery of immune pathways, immunoprevention mechanisms, or preclinical investigation of new vaccines or immunomodulatory targets or agents with the potential for the development of immunopreventive interventions

- Achievement of the UG3 milestones will be necessary for the transition to the UH3 phase.

- **UH3 phase research projects**: further evaluation of efficacy, immune mechanisms of action, validation of actionable targets, and/or further preclinical development