Cancer Immunoprevention Network (CIP-Net)

RFAs: UG3/UH3s and U24 (Clinical Trials Not Allowed)

Co-sponsored by the
Division of Cancer Prevention and the Division of Cancer Biology

New Program for Immunoprevention

NIH NATIONAL CANCER INSTITUTE

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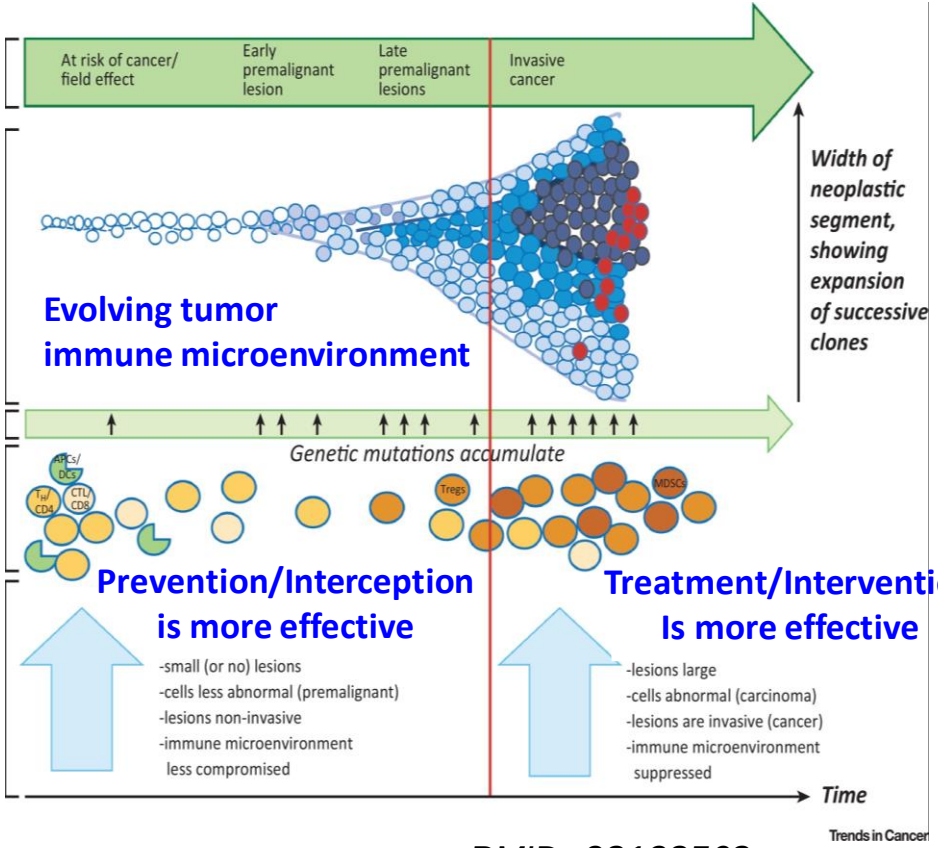
Carcinogenic Progression in Common Adult Epithelial Tumors: Opportunities for Immunoprevention

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



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Background

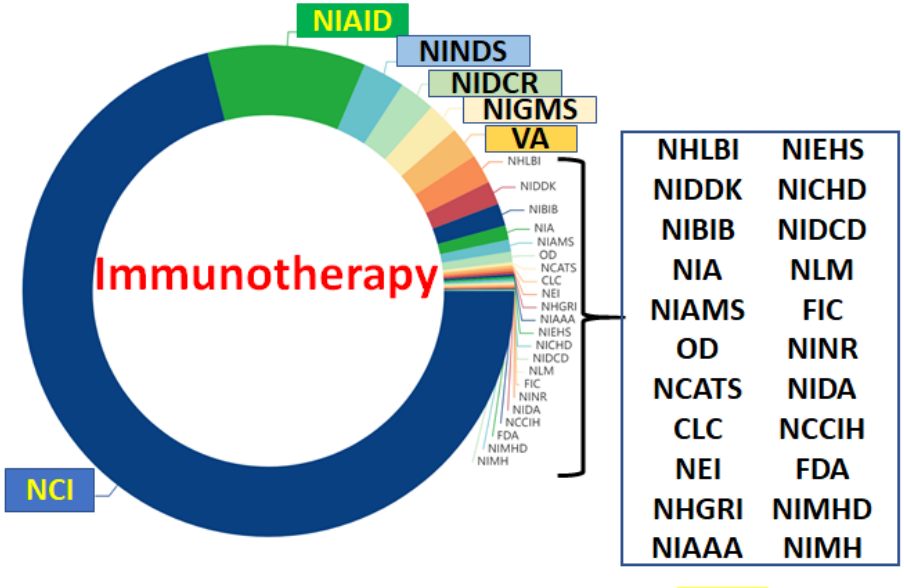
- While cancer immunotherapy research has expanded and has seen major advances in the past decade, cancer immunoprevention research has been quite limited.

- The only FOAs supporting cancer immunoprevention were published 2017/2018 as part of the **Cancer Moonshot** Immuno-Oncology Translation Network (IOTN): 5 projects funded (3 U01s and 2 UG3/UH3 grants).

- There are **no current** NCI programs or initiatives supporting this type of activity.

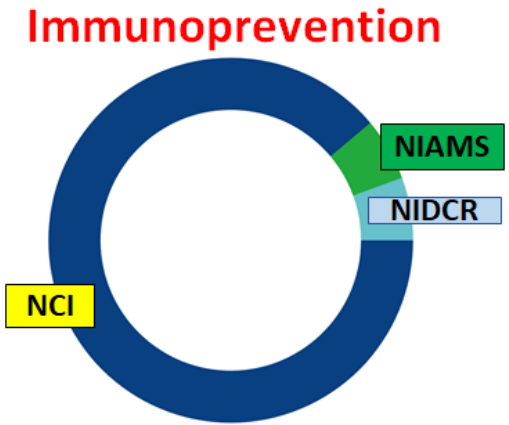
Portfolio Analysis

NIH Immunoprevention awards are only 0.67% of Immunotherapy awards (18 vs 2,654)



NHLBI	NIEHS
NIDDK	NICHD
NIBIB	NIDCD
NIA	NLM
NIAMS	FIC
OD	NINR
NCATS	NIDA
CLC	NCCIH
NEI	FDA
NHGRI	NIMHD
NIAAA	NIMH

Total projects	2,654
NCI projects	1,885



Total projects	18
NCI projects	16

Scientific Objectives

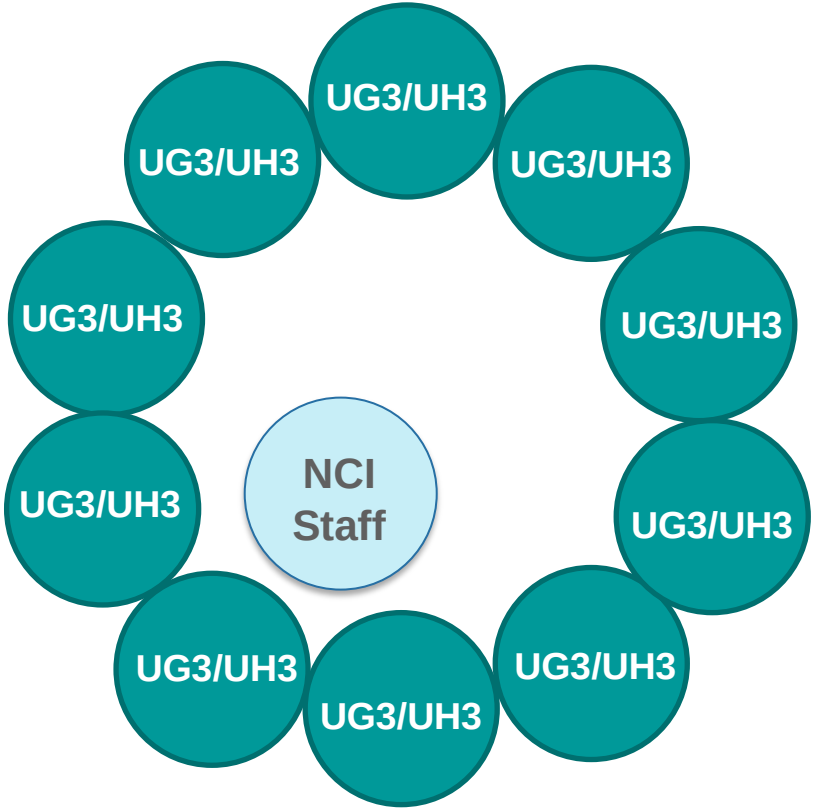
- The overarching goal of Cancer Immunoprevention Network (CIP-Net) is to support a deeper understanding of basic mechanisms of immunoprevention**,** discover novel immunoprevention strategies, and foster a community of cancer immunoprevention researchers.

- This FOA builds on IOTN's progress toward the aspirational Cancer Moonshot Immunology Working Group goal "**to prevent cancers before they occur**" and the extraordinary success with recent mRNA vaccines makes it timely to address cancer immunoprevention strategies.

- 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.

- This initiative directly addresses the recommendations in the BSA Ad Hoc Working Group Report to encourage "**novel and innovative research designs….to expedite progress in precision prevention**"

CIP-Net Structure



UG3/UH3 Research Projects:

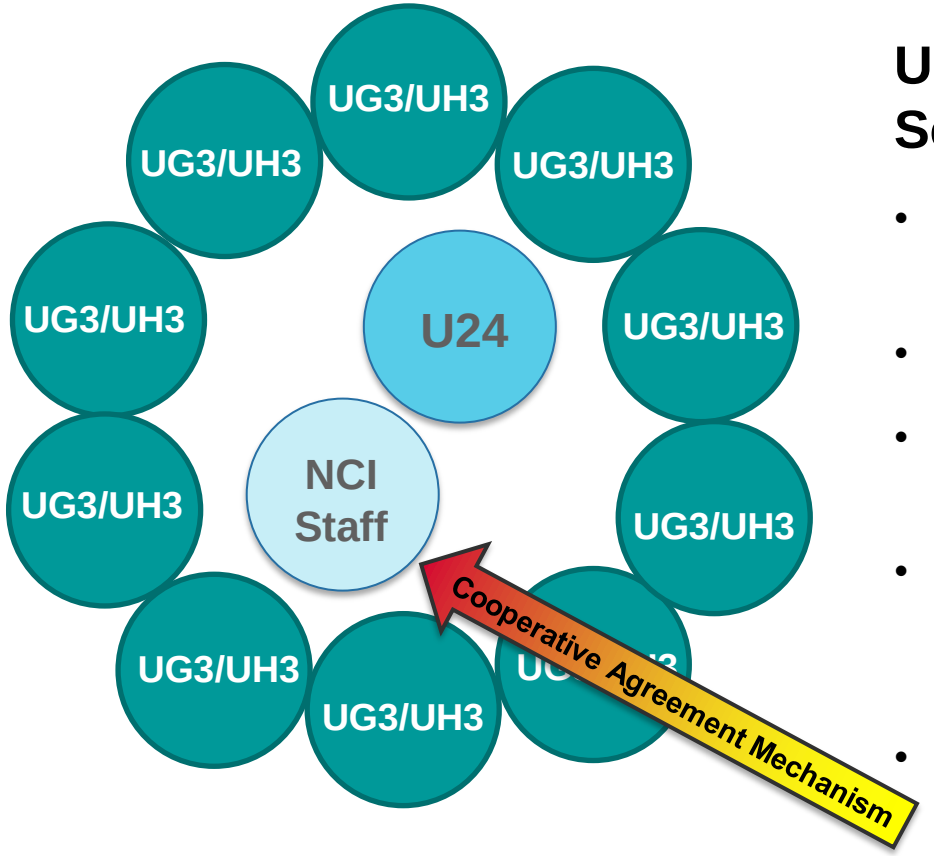
- **UG3:** Discovering and investigating novel immune pathways, mechanisms, and innovative targets for immunopreventative intervention
- Milestone driven transition evaluation by NCI Staff
- **UH3:** Validation and deeper mechanistic interrogation of pathways, development, or preclinical testing to evaluate mechanisms, efficacy and potential side-effects

Examples of Potential Research Projects

- 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

*The complete list as indicated in the concept document will be included in the RFA

CIP-Net Structure



U24 Resource Coordinating Center Scientific Objectives:

- 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 junior investigator career development

RFA Justification

- There is no NIH parent announcement for the UG3/UH3 or U24 mechanisms
- The RFA mechanism will enable the incorporation of NCI cooperative agreement terms of the award and specific language for the UG3/UH3 milestone transition
- Despite the recent CSR ENQUIRE evaluation and update of standing study sections, immunoprevention is still not designated in any of the 13 new study sections, thus a dedicated NCI Special Emphasis Panel (SEP) will be required for CIP-Net applications

Justification for Cooperative Agreement

- The CIP-Net UG3/UH3 and U24 awards will require programmatic stewardship above and beyond normal investigator-initiated grants
- NCI Program Staff will
  a) negotiate and monitor milestones for the UG3/UH3 transition,
  b) develop and ensure open communication across CIP-Net
  c) ensure rapid deposition of all CIP-Net generated data into appropriate databases, and
  d) facilitate CIP-Net communications and collaborations to leverage complementary NCI research programs such as HTAN, TBEL, PREVENT, CP-CTNet, and other DCP/DCB initiatives

Evaluation Criteria for an RFA

- It is anticipated CIP-Net projects will develop promising immunoprevention candidates that will advance into the NCI DCP PREVENT and CP-CTNet programs
- Success of CIP-Net will be quantified by tracking new investigator-initiated R01s, publications, patents, data depositions, and trainee career development
- CIP-Net investigators will promote the growth of immunoprevention research through sponsoring immunoprevention sessions at international scientific conferences (e.g., SITC, AACR, ASCO, et al.)

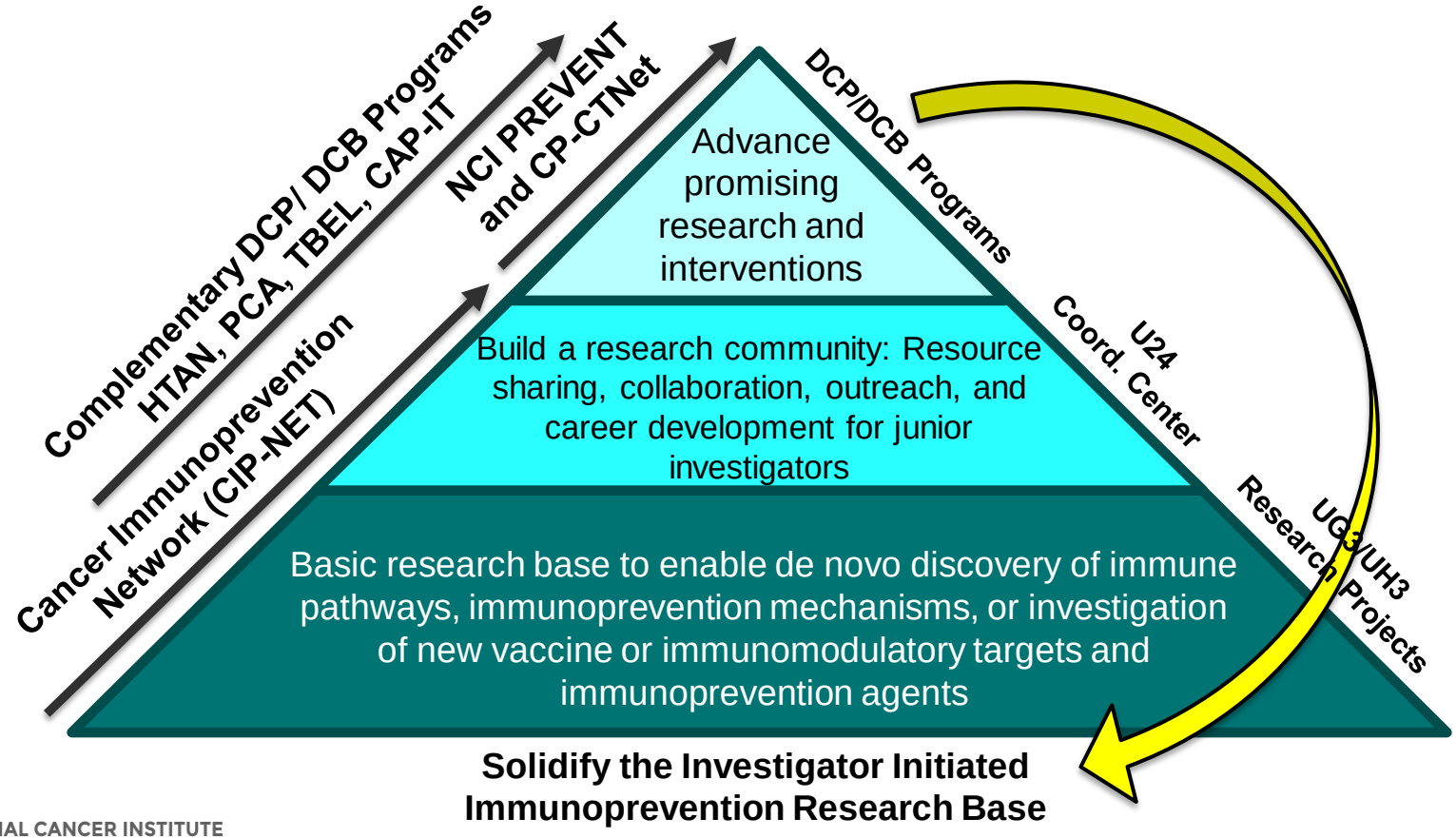
Budget Request

- Each UG3/UH3 and U24 capped at $500K direct costs, estimated ~$850K total costs
- Three receipt dates over two years, thus two opportunities for A1 resubmissions
- NCI controlled collaborative supplements in Years 2-4, with emphasis on UH3 projects

CIP-Net	FY2024	FY2025	FY2026	FY2027	FY2028	FY2029	Total Costs
UG3/UH3* (n≈10-12)	$4.25M	$8.5M	$8.5M	$8.5M	$8.5M	$4.25M	$42.5M
U24 Resource Coordinating center		$0.85M	$0.85M	$0.85M	$0.85M	$0.85M	$4.25M
Collaborative Supplements			$0.5M	$0.5M	$0.5M		$1.5M
Total Costs	$4.25M	$9.35M	$9.85M	$9.85M	$9.85M	$5.1M	$48.25M

*Estimated range of 10-12 awards total to be funded over two years, with 5-6 starting in FY24 and 5-6 in FY25

Building the Cancer Immunoprevention Research Continuum



Incorporating BSA Subcommittee Feedback

- **From Drs. Chan, Schreiber and Vonderheide:**
  - Clarify and refine specific definitions for prevention and immunoprevention research
  - Provide research examples: slide 8
  - Describe the milestone-based evaluation process for the UG3→UH3 transition
  - Clarify human subjects research vs. no clinical trials: clinical trials are not allowed but human subjects research (i.e., clinical samples) is strongly encouraged, and clinical trials will advance into CP-CTNet
  - Emphasize scientific engagement of U24 across CIP-Net activities: scientific collaboration and biospecimen collection and other relevant activities
- **BSA feedback will be incorporated into FOA language**

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