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City of Hope®

UNIVERSITY of ROCHESTER MEDICAL CENTER

Welcome-Day 1

Introduction to the CARG Infrastructure Grant

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CANCER & AGING RESEARCH GROUP

Infrastructure Grant

Funded by NIH/NIA

Grant No. 1R21AG059206

Thank YOU from all of us!

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CARG Infrastructure Grant Goals

- **Increase high-impact research** to reliably identify older patients at highest risk for adverse outcomes from cancer and its treatments
- **Develop effective interventions** to improve outcomes for vulnerable older adults and their caregivers
- **Mentor the next generation** of aging and cancer researchers
- **Disseminate the findings** widely to inform clinical practice

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CARG Infrastructure Grant Specific Aims

Aim 1	• ***Solidify the Infrastructure and Expertise***
Aim 2	• ***Utilize the Sustainable Infrastructure***
Aim 3	• ***Support and Guide High-Priority Research Projects***
Aim 4	• ***Identify, Cultivate, and Mentor Investigators***
Aim 5	• ***Disseminate through Effective Communication Strategies***

Goals of Conference 1

- Conference Invitees: oversight board, organizational liaisons, patient advocate board, junior investigator board
- Identify mechanisms to translate U13 research priorities (Table 1) into actionable research (Delphi)
- Define the Cores
  - Finalized set of standard operating manuals for each Core will be created
  - Core infrastructure will be evaluated
  - Refinements will be made

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Table 1: U13 Conference Results: Highlights of Recommendations for Aging and Cancer Research

Conference 1: Biological, Clinical, and Psychosocial Correlates in Aging and Cancer Research[18]	Conference 2: Clinical Trial Designs for Older and Frail Adults with Cancer[1]	Conference 3: Developing Intervention Studies for Older Patients with Cancer[7]
A. Consistently incorporate validated Geriatric Assessment (GA) measures into oncology research. Trials enrolling substantial numbers of older adults should include: 1) Routinely validated GA measures. 2) Additional endpoints, such as maintenance of functional abilities and quality of life, which should be considered as important as mortality. 3) Precise measurement of mental health and/or cognitive changes. B. Consistently incorporate aging biomarkers in oncology trials. 1) Aging biomarkers may identify older adults at increased risk for cancer treatment toxicity. 2) Tumor samples from patients of all ages are needed to assess whether tumor biology changes with aging. 3) Studies are needed of the pharmacokinetics/dynamics of cancer therapeutics in older adults. C. There is a need for more studies of vulnerable older adults and/or those age ≥ 75. 1) A need exists for trials in older adults with comorbidities, functional losses, cognitive impairment, and frailty. 2) A need exists to recruit those age ≥ 75 to clinical trials for whom there are virtually no data. D. Research infrastructure should incorporate age-associated support. 1) A need exists to better tailor oncology trials to the specific needs of older, more vulnerable patients. 2) It is essential to have more consistent and earlier research collaboration between geriatrics and oncology researchers when designing trials. 3) Data collection from remote locations (ie, home) needs more study.	A. Research design. Several clinical trial design opportunities exist depending on the potential objectives and outcomes. The pros and cons for each are detailed in the original manuscript. 1) Single-arm trial: Current gold-standard design for phase II clinical trials of novel therapeutics (all older patients receive treatment under the study with no randomization). 2) Randomized controlled trials (RCTs): Study participants are randomly assigned among different treatment arms; pros and cons discussed regarding an elderly specific study vs. a study for patients of all ages. 3) Extended trial: Building upon the RCT results, the study expands the cohort of older patients to be treated on the superior treatment arm without randomization. 4) Embedded study (correlative or ancillary study): GA measures and biomarkers of aging are placed within the parent study infrastructure. 5) Prospective cohort study: Assessment of treatments received as standard of care to evaluate geriatric oncology outcomes. B. Considerations for dosing schema. Start low and go slow: reduce the first dose, and then escalate to standard dosage if the patient tolerates the treatment. C. Trial designs to predict treatment tolerability. Inclusion of a GA can reduce heterogeneity and provide information on independent predictors of outcomes. 1) All-comers design: Enrolls all eligible patients to identify the characteristics of patients who are at risk for toxicity. 2) Enrichment design: The trial will oversample for patients with specific characteristics (ie, age ≥ 75 or risk factors for toxicity). 3) Marker by treatment interaction design: Compares the risks and benefits of 2 treatment strategies for 2 groups of older patients (those predicted to be at low risk vs. high risk for toxicity).	A. The percentage of older adults enrolled in standard clinical trials should reflect the percentage of older patients in the general population. B. Studies are needed to better understand how cancer and its treatments interact with underlying vulnerabilities, which in turn impacts understanding of the feasibility, safety, and efficacy of interventions for this population. C. Extrapolating evidence from intervention studies (e.g., falls, cognitive impairment, delirium) of older adults without cancer is beneficial. Nevertheless, studies are needed to determine how to tailor these interventions for older patients with cancer. D. Studies should incorporate knowledge regarding trial design, infrastructure support, and methodology that is known from existing research focused on the aging population without cancer. E. Partnership with stakeholders, including older patients, caregivers, and interdisciplinary team members with geriatric expertise should occur at the very beginning of research development. F. Issues that should be considered during study development include how the intervention will be delivered in the community and cost considerations. G. More studies should be designed up-front by interdisciplinary teams with expertise in aging and cancer in partnership with patient and caregiver stakeholders to overcome the known barriers and fundamental design dilemmas.

Solidify the Infrastructure

- Evaluation and Metrics:
  - Staff hired (program manager, biostatistician, science writer)
  - Development of a comprehensive inventory of aging and cancer researchers
  - Establishment of the Cores including a membership roster and operating manuals for Core structure and function
  - Revision of Core function and procedures based on evaluation by Core members, conference attendees, and grantees
  - Frequency of participation of Core members in calls, webinars, and conferences
  - Publications summarizing the key aspects of the infrastructure development

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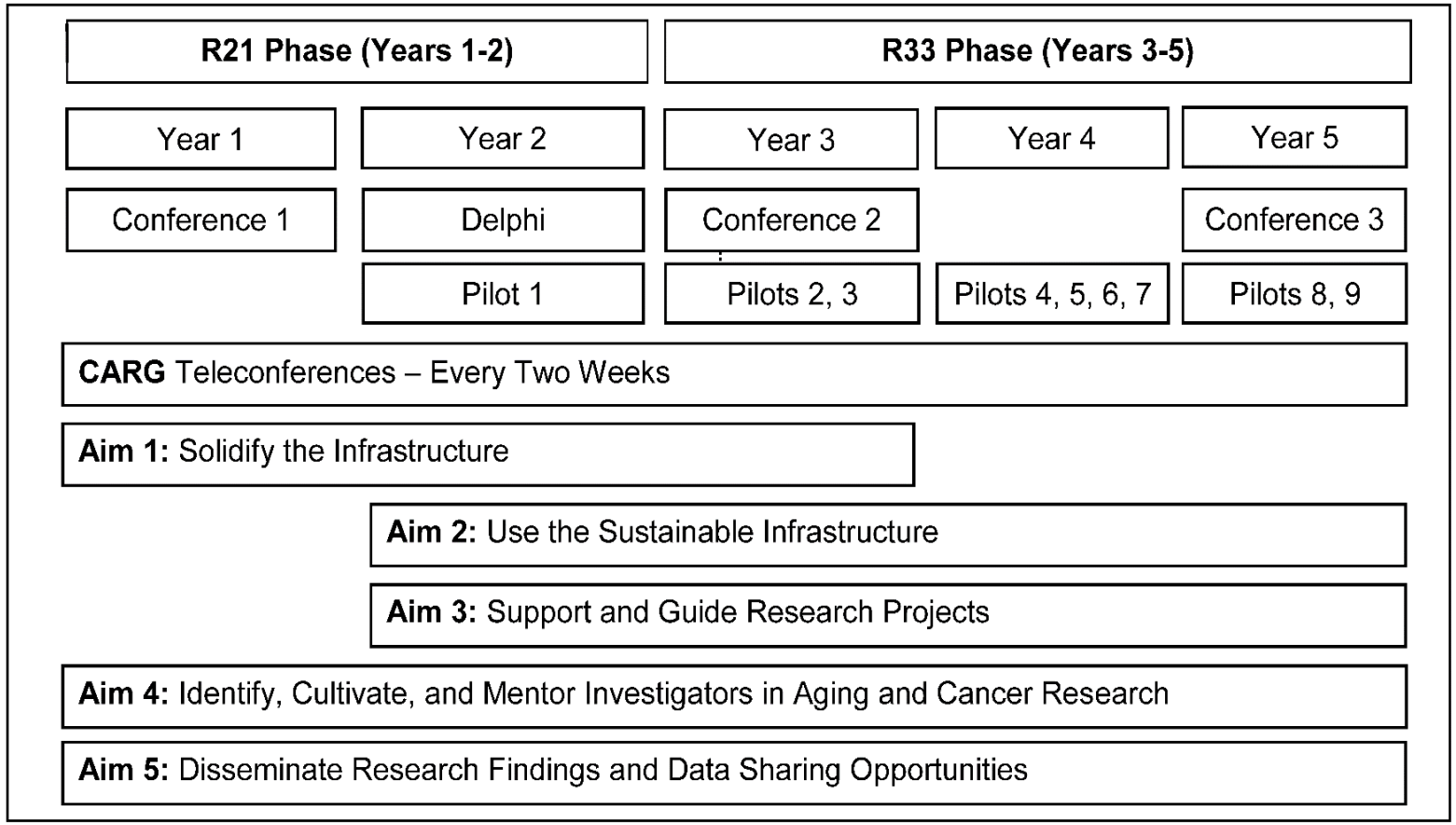
Setting the Foundation

Figure 1: Schema of Events for "Geriatric Oncology Research Infrastructure to Improve Clinical Care"



How This Proposal Will Propel Aging and Cancer Research Forward

This proposal will establish the infrastructure, infused with our current supportive, collaborative culture, needed to:

1) Accelerate high-quality research at the aging and cancer interface
2) Attract and mentor investigators
3) Combine aging and cancer research to form a pipeline of sustainability for the field of geriatric oncology
4) Disseminate these results to a broader community to nationally improve the care of older adults with cancer

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Scenarios

1. Junior Investigator
2. Senior Investigator
3. Large group from a single organization (*optional*)
4. Others?

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