General Questions

**Q1:** What scope of research is appropriate for the R21/R33 mechanism?

A1: The R21/R33 phased innovation grant supports investigation of novel scientific ideas or new interventions, model systems, tools, or technologies that have the potential for significant impact on biomedical or behavioral and social sciences research and are related to aging and cancer biology, diagnosis, treatment, prevention, control, surveillance, epidemiology, genomics, healthcare delivery, implementation. Research projects will not only develop a research infrastructure, but also produce new knowledge, tools, or other tangible scientific results arising from specific research projects that are enabled by the new research infrastructure.

**Q2:** How do I know if my research question is appropriate for an R21/R33 versus an R01?

A2: For an R01 mechanism the aims are hypothesis driven, independent, and should be supported by preliminary data. For the R21/R33 mechanism, the aims are focused on infrastructure building, preliminary data is not required, and clear descriptions of aims (for both phases) and milestones should be included in the application. Also note that research proposed should investigate novel scientific ideas or new interventions, model systems, tools, or technologies that have the potential for significant impact on biomedical or behavioral and social sciences research. It is expected that applications funded through this FOA will not only develop a research infrastructure, but also produce new knowledge, tools, or other tangible scientific results arising from specific research projects that are enabled by the new research infrastructure. It is advised to consult with a program contact to discuss your proposed project.

**Q3:** PAR-20-070 will expire in November 2022. Will the PAR be reissued?

A3: We cannot say at this time, but if it is reissued, it will be published in The NIH Guide.

**Q4:** Can I apply for only R21 or only R33 funding through this mechanism?

A4: No, applications proposing R21 or R33 activities alone will be considered incomplete and will not be accepted.

**Q5:** Can I apply for 1 year of R21 support (rather than 2 years), followed by 3 years of R33 support?

A5: Technically yes, but it is not advised because shortening the length of the R21 period often proves difficult to execute in practice. However, individual circumstances vary, so it is advised to consult with a program contact to discuss your proposed project.
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Questions asked during the Informational Webinar

Q6: What does interdisciplinary mean in this case? Would combining epidemiology and environmental exposure to chemicals be considered interdisciplinary?

A6: NCI’s involvement in PAR-20-070 pertains to cancer and aging, but other disciplines may be involved, if appropriate for the project.

This FOA is intended to support establishment of new interdisciplinary collaborations or development of existing interdisciplinary collaborations in significantly new directions. Applications should have the appropriate expertise to carry out the work for the project. This may be accomplished through the development of new interdisciplinary collaborations or leveraging existing collaborations to move into a new direction. Multi-PI applications may be used to showcase interdisciplinary expertise, where one PI represents a specific discipline/field (e.g., aging/geroscience) and another PI provides different expertise (e.g., oncology). For existing collaborations, reviewers will evaluate closely whether the application represents a substantial development in scientific focus as opposed to simply maintaining existing operations.

Q7: NIA now sends all grants to a Special Emphasis Panel (SEP) and not a content specific section. Can you clarify?

A7: NIA’s review process is different from NCI’s. All applications responding to PAR-20-070 will first be submitted to NIA; cancer-relevant applications will be forwarded to NCI. If teams have an application that is under NIA’s purview, those grants will be assessed by a special emphasis panel. If the application is referred to NCI, the application will be reviewed by a Center for Scientific Review (CSR) study section of “best fit”. The PHS Assignment Request Form can also be used in the application to request up to three CSR- study section review groups. Helpful resources for finding a CSR study section are the study section guidelines (https://public.csr.nih.gov/StudySections/StandingStudySections), and the Assignment Request Tool (https://art.csr.nih.gov/ART/selection.jsp).

Q8: The topics are fairly R01 specific. So, I assume for this FOA, the goal is to develop infrastructure to advance these science areas?

A8: The R21/R33 phased innovation grant supports investigation of novel scientific ideas or new interventions, model systems, tools, or technologies that have the potential for significant impact on biomedical or behavioral and social sciences research and are related to aging and cancer biology, diagnosis, treatment, prevention, control, surveillance, epidemiology, genomics, healthcare delivery, implementation. Research projects will not only develop a research infrastructure, but also produce new knowledge, tools, or other tangible scientific results arising from specific research projects that are enabled by the new research infrastructure.

Q9: Could you provide some examples of aims that are focused on infrastructure building?

A9: Examples include any activities that you could use to build infrastructure. For example, consensus building, agenda setting, or data harmonization. Clinical trials are also admissible for this FOA, so one example could be to conduct a pilot study to test intervention feasibility in the R21 phase and then use the R33 phase to establish intervention efficacy. Looking at examples of aims from funded projects may be useful and can be found on NIH RePORTER.
Q10: PAR-20-070 R21/R33 is considered relevant to Notice of Special Interest (NOSI) NOT-CA-21-031 entitled, ‘Understanding the effects of cancer and cancer treatment on aging trajectories and aging outcomes’. Can you please tell us: (i) what does it mean to have an application relevant to an NIH/NCI published NOSI, AND (ii) how do we determine whether an application is relevant to both PAR-20-070 and NOT-CA-21-031?

A10: An application is considered responsive to a published NOSI if the focus of the application is aligned with the purpose and research objectives of the NOSI. An application responsive to NOT-CA-21-031 can be submitted to PAR-20-070 (see list of funding opportunity announcements in NOT-CA-21-031). To be considered for NOT-CA-21-031, applicants must include NOT-CA-21-031 in the Agency Routing Identifier field (box 4b) of the SF424 R&R form.

Q11: For biospecimen work, is human preferred or are non-human primate tissues considered eligible?

A11: There is no limit to the type of animals or species included in this study. Individuals can also apply models where cancer and aging is relevant.

Q12: Can you clarify about the criteria for transition from R21 to R33 phase.

A12: Prior to funding an application, program staff will contact the applicant to discuss the proposed milestones. The Program Director and the applicant will negotiate and agree on a final set of milestones. These will be incorporated into the terms and conditions of the award and will be the basis for judging the success of the R21 work.

Prior to the end of the R21 phase, awardees will submit a package that requests transition to the R33 phase. This package will include a progress report that describes progress towards each of the initial milestones and a clear description of how research during the R33 phase will be impacted by attainment of the R21 milestones. These materials will be reviewed by program staff and then, if selected, the grant will be transitioned to an R33 award without the need to submit a new grant application. Decisions on transitioning to the R33 phase will be based on the original R21/R33 peer review recommendations, successful completion of the milestones, program priorities, and availability of funds.

Q13: Can you share with us a currently funded research project under this mechanism?

A13: We would encourage you to visit NIH RePORTER to see a wide range of projects that have been funded through this mechanism.

Q14: Will only studies in older adults be considered? Or can we focus studies on accelerated aging outcomes in younger cancer survivor populations?

A14: There is no age criterion associated with this FOA. In fact, see https://grants.nih.gov/policy/inclusion/lifespan.htm

Q15: In addition to infrastructure, does it need to have a hypothesis testing scientific aim?

A15: Yes, there should be a unifying and testable hypothesis that transcends both the R21 and the R33 phases. The unified hypothesis should emphasize the new research infrastructure built in the early phase to produce new knowledge tools, or other tangible scientific results arising in the R33 phase.

Q16: Can we ask for an NIA assignment for our cancer-relevant aging-focused investigation when applying to PAR-20-070? NIA has an in-house aged wild-type mouse
repository that is free and available for shipping to NIA-supported PIs that the NCI does not. “Free” aged mice potentiates a research program to be more rigorous and robust as it relates to an aging-focused cancer-relevant research program.

A16: Your application will first be sent to NIA. If you complete the PHS Assignment Request Form, you can request the institute that you would prefer.

Q17: If the R21 does the feasibility work for the intervention in cancer survivors, and the R33 tests it, what would the infrastructure component of the R33 be? To build up a biobank to serve future R01 analyses? Or does the R33 need to actually test an aging-related outcome hypothesis?

A17: If feasibility work is completed in the R21 phase, the R33 phase should expand upon the R21 phase work. This could include testing intervention efficacy, for example. The utility of the R21/R33 is to scale up or expand the work completed in the R21 phase.

Q18: Is a specific study an infrastructure? Much of the answers make it sound like the study is to get preliminary data and have a project, which is not an infrastructure?

A18: The R21/R33 phased innovation grant supports investigation of novel scientific ideas or new interventions, model systems, tools, or technologies that have the potential for significant impact on biomedical or behavioral and social sciences research. This includes research that will not only develop a research infrastructure, but also produce new knowledge, tools, or other tangible scientific results arising from specific research projects that are enabled by the new research infrastructure. Accordingly, reviewers will emphasize the conceptual framework, the level of innovation, and the potential to significantly advance our knowledge or understanding.

Q19: Can you provide the contact information from each participating NCI Division or Center?

A19:

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**Dr. Jennifer Guida is the NCI Scientific Contact listed on the FOA. For any general questions, or if you are unsure of the appropriate NCI contact, please reach out to Dr. Jennifer Guida.