

Establishment of Working Group to Evaluate The NCI RAS Initiative

FNLAC 11th Virtual Meeting

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The NCI RAS Initiative Vision and History

- Overarching goal of mobilizing the cancer research community to develop ways to understand and target cancers driven by mutant KRAS in an open research model of collaborations among government, academic, and industrial investigators
- 2013: The NCI RAS Initiative was established
 - Addressed critical knowledge gaps that impeded RAS as a drug target
 - Provided detailed RAS biology/structure and RAS reagents to the community
- 2017: The NCI RAS Initiative was reviewed and renewed for FY19-23
 - Increased focus on advancing RAS therapeutic compounds and provided an increasingly sophisticated biophysical model of RAS activation and signaling at the membrane
- 2022: The NCI RAS Initiative Research Team is seeking an additional 5-year renewal
 - Push valuable new preclinical and clinical drug candidates into clinical trials
 - Broaden RAS-directed therapeutics to additional RAS alleles, regulatory/effector proteins and other innovative strategies and technologies

RAS Initiative Evaluation Team (RIET) Working Group

- To judge the scientific merit, productivity, and innovation of the RAS Initiative, the FNLAC will convene an ad hoc RAS Initiative Evaluation Team (RIET) Working Group (WG) to conduct its review of the Renewal package.
- The NCI RAS Initiative Renewal package components:
 - Report and recommendations of existing FNLAC RAS ad hoc Working Group
 - Full written proposal provided by the RAS Initiative Research Team
 - In-person session provided by the RAS Initiative Research Team
 - RAS Initiative progress (FY19-22)
 - Engagement with the extramural RAS community
 - Future research and therapeutic development plans

RIET WG Remit

- The RIET WG will advise the Frederick National Laboratory Advisory Committee to the National Cancer Institute and the Director, NCI
- The technical review of the RAS Initiative Renewal Package will be conducted by the RIET WG
- This review will be critical to:
 - Ensure the appropriateness of the proposed future research
 - Optimize the functionality, output, and balance of partnerships with the extramural RAS community
 - Provide their overall assessment of the NCI RAS Initiative Renewal and future research and therapeutic development plans
- The RIET WG will produce a written technical report and recommendation to be presented at the February 27, 2023 FNLAC meeting.
- Upon FNLAC acceptance, the RIET WG report and recommendation will be provided to the NCI Director

Proposed Composition of the RIET WG

- The RIET WG shall be composed of highly regarded scientists recruited from both the academic research community and the private sector
- Scientific excellence and domain expertise will be drawn from:
 - Academic RAS and cancer biology researchers
 - Structural biologists
 - Biopharmaceutical/research institute experts with relevant drug discovery and development experience
- Balanced for gender, racial, and ethnic demographics



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