Frederick National Laboratory Advisory Committee NCI RAS Initiative Evaluation Team Ad Hoc Working Group

Mission Statement

The National Cancer Institute (NCI) RAS Initiative is the first National Mission Program sponsored by the NCI. It began in 2013 with the 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 industry researchers. In this funding model, the state-ofthe-art facilities at the Frederick National Laboratory for Cancer Research (FNLCR) serves as a hub for the initiative, while multiple collaborating laboratories function as the spokes. The initial funding cycle of the RAS Initiative addressed critical knowledge gaps that had impeded or discouraged the exploitation of RAS as a drug target. The program was reviewed and renewed in FY17 with a recommended increased focus on identifying and advancing RAS therapeutic compounds and to develop a biophysical model of RAS activation and signaling in the membrane.

Based upon the accomplishments and productivity of the NCI RAS Initiative, the Research Team is seeking an additional 5-year renewal to push valuable new preclinical and clinical drug candidates into clinical trials and to broaden the scope of RAS-directed therapeutics to include additional mutant RAS alleles, other RAS regulatory and effector proteins, and other innovative strategies and technologies to address this formerly "undruggable target".

To judge the scientific merit, productivity, and innovation of the NCI RAS Initiative, the Frederick National Laboratory Advisory Committee (FNLAC) will convene an ad hoc RAS Initiative Evaluation Team (RIET) Working Group (WG) to conduct the review. This Working Group will have at its call a report and recommendations of the existing FNLAC RAS ad hoc Working Group, which has provided oversight for the RAS Initiative since its inception. The RIET WG will be provided a full written proposal from the RAS Initiative team and will conduct an in-person session to hear the progress of the RAS Initiative in early 2023. It will also evaluate the engagement of the extramural community and convey their overall enthusiasm for the RAS Initiative Renewal and future research and therapeutic development plans. The technical review conducted by the RIET WG will be critical to ensure the appropriateness of proposed future research and to optimize the functionality, output, and balance of partnerships with the extramural RAS research community.

The RIET WG shall be composed of highly regarded scientists recruited from both academic research community and the private sector. Scientific excellence and relevant domain expertise will be drawn from academic RAS and cancer biology researchers, structural biologists and molecular modelers, and biopharmaceutical and/or research institute experts with experience in relevant drug discovery and development.

The RIET Working Group will advise the Frederick National Laboratory Advisory Committee to the National Cancer Institute and the Director, NCI.