

Responses to Questions, (RTQ) Pertaining To The “Twin Studies” Solicitation (i.e. HERO – Appendix D; RFA NNJ13ZSA002N-TWINS, Entitled “Differential Effects on Homozygous Twin Astronauts Associated with Differences in Exposure to Spaceflight Factors “)

Updated November 18, 2013

Question (1): During the period of the one year mission will it be possible to perform periodic blood sampling on Scott and Mark Kelly?

Answer: Yes, phlebotomy is currently routinely performed on the International Space Station, (ISS), and therefore blood draws will certainly be possible during ISS-12, (i.e. the one year mission).

Question (2): During the period of the one year mission will it be possible to perform hi-tempo blood sampling e.g. phlebotomy events spaced at 12, 8 or even 6 hour intervals?

Answer: Such 12, 8 or 6 hour sampling intervals are possible, if the astronauts consent and if they can be scheduled within and among the primary activities of the year-long mission.

Question (3): During the period of the one year mission will it be possible to perform multiple (e.g. ~ 5 times) hi-tempo blood sampling experiments - with each blood sampling experiment comprising a plurality of phlebotomy events separated by just a few hours?

Answer: Yes multiple hi-tempo blood sampling experiments – each involving multiple phlebotomy events are possible, if the astronauts consent and if they can be scheduled within and among the primary activities of the year-long mission.

Question (4): Before and after the one year mission will it be possible to perform blood sampling activities involving the Kelly Twins?

Answer: Yes blood sampling activities are possible before and after the one year mission, if the astronauts consent.

Question (5): Should proposers suggest the scheduling of specific physiological data / physiological measurements / physiological experiments at essentially the same time as biofluids are sampled - in order to correlate phenotype with genotype?

Answer: Yes – proposers should absolutely suggest specific physiological and/or neurobehavioral experiments that can be performed at times juxtaposed to biofluid, (e.g. blood) sampling – in order to correlate physiology with the underlying genetics.

Question (6): Are Post-Doctoral Fellows eligible to submit proposals in response to the “Differential Effects on Homozygous Twin Astronauts Associated with Differences in Exposure to Spaceflight Factors” (i.e. HERO – Appendix D) solicitation?

Answer: Yes. All categories of United States (U.S.) institutions are eligible to submit proposals in response to this NRA. Principal Investigators may collaborate with universities, Federal Government laboratories, the private sector, and state and local government laboratories. In all such arrangements, the applying entity is expected to be responsible for administering the project according to the management approach presented in the proposal.

The applying entity must have in place a documented base of ongoing high quality research in science and technology, or in those areas of science and engineering clearly relevant to the specific programmatic objectives and research emphases indicated in this NRA. Present or prior NASA support of research or training in any institution or for any investigator is not a prerequisite to submission of a proposal.

Question (7): The solicitation document details a \$50 K limit/year for up to 3 years, per funded investigation. Does this \$50 K limit include both direct and indirect costs?

Answer: The funding level of \$50K/year should cover both direct and indirect costs. NASA understands that \$50K/year represents a relatively small amount of funding, but this level of funding is appropriate for such a preliminary –omics based investigation - which is not the primary objective of the mission. NASA hopes that this funding will encourage investigators to focus on the most important and meaningful –omics measurements.

Question (8): Will biofluid samples derived from the Kelly Twins be provided by NASA?

Answer: All biofluid samples will be provided to funded investigators by NASA. NASA will utilize the existing biofluid sample collection and preservation capabilities currently used on the ISS.

Question (9): Is it feasible to request urine samples at regular intervals before, during, and after the one year mission?

Answer: Yes – urine sampling activities are possible before, during and after the one year mission, if the astronauts consent. Proposers should detail the sample types and ideal cadence for urine collection that are needed to achieve experimental objectives and address specific aims of the study.

Question (10): If blood is sampled and analyzed, CBC-panel data may help account for changing blood cell number and therefore be relevant to the final –omics analyses. Accordingly does NASA Medical Operations conduct regular CBC-panel assays, and can data sharing be requested?

Answer: Yes – NASA Medical Operations does conduct regular CBC-panel assays and data sharing is possible for funded investigators. As such, proposers should detail the assays and data-sharing activities that are needed to achieve experimental objectives and address specific aims of the study.

Question (11): For inflight blood draws, will the crew have access to a centrifuge to spin down the blood samples?

Answer: Yes – centrifugation of blood is currently routinely performed by the crew on the ISS.

Question (12): The stabilization of RNA samples is often achieved on Earth via use of high salt type solutions, e.g. the commercially available reagent “RNAlater” which prevents degradation of RNA. Accordingly are there plans to fly RNA stabilization kits such as RNAlater to the ISS and use these reagents during spaceflight?

Answer: RNAlater (or equivalent reagents) is not currently qualified to fly into space – however proposers should detail those reagents and technologies that are needed to achieve experimental objectives and address specific aims of their studies, as it may be possible to qualify these reagents for spaceflight ahead of the one year mission.

Question (13): Is there a link to a general document providing a high level overview of the environment of space and its effect on human physiology, e.g. radiation, g-transitions, bone and muscle loss, neurobehavioral decrements etc.?

Answer: The following reference posted on the NSBRI website entitled "Human Physiology in Space" and written by Barbara F. Lujan and Ronald J. White provides an overall reference regarding the environment of space and its effect on the human body, viz:
<http://www.nsbri.org/HumanPhysSpace/>

Question (14): Why is Mark Kelly an ideal “ground control” for Scott Kelly – who will be flying the one year mission, (ISS-12)?

Answer: Setting aside the reality of recently discovered genetic mosaicism, (i.e. multiple genomes present in a single organism) and also likely differences in copy number variants - the genomes of Scott and Mark Kelly are to a first order of approximation – “identical.” This similarity in their genetic material provides an ideal starting point for analyzing the question of “nature versus nurture.” Accordingly, because Scott and Mark Kelly are essentially genetically identical – the effects of the space environment on Scott Kelly can be directly compared to the effects of the terrestrial environment on Mark Kelly – over the same one year time window.

Question (15): Can proposers respond to a plurality of research emphases solicited for in the Twins RFA?

Answer: Each proposal should respond to one or more of the discrete research emphases. Proposers who choose to respond to multiple research emphases within a single research proposal must adhere to the specified page limit and other proposal constraints while still providing adequate information for a rigorous review of the proposal.

Question (16): Can proposers reference other complementary research proposals submitted by other Principal Investigators and form “virtual teams”?

Answer: Proposers may reference one or more other complementary research proposals that are submitted by colleagues, i.e. the referencing of so-called “virtual teams” is permissible. Note however that the referencing of complementary proposals submitted by other PI’s is NOT a requirement for participation in this funding opportunity. Following scientific peer review and evaluation of scientific relevance, NASA will assemble an integrated portfolio of the selected proposals and form a Team. The ability of different research groups to collaborate and work together in a team spirited fashion is therefore a helpful and relevant parameter, but will NOT be a primary determinant in selection.

Question (17): How will proposals submitted in response to the Twins Solicitation (viz. RFA NNJ13ZSA002N-TWINS) be evaluated?

Answer: All proposals deemed to be substantially responsive to one or more of the research emphases will undergo peer review to determine scientific merit. NASA will select the most programmatically relevant proposals in each of the research emphasis areas, representing the highest quality scientific research consistent with the programmatic, operational and practical constraints of this research opportunity.

Question (18): What is the age difference between Mark Kelly and Scott Kelly?

Answer: Mark Kelly was born 6 minutes before his twin brother Scott Kelly.

Question (19): Who developed the idea for this Twins Study?

Answer: Mark and Scott Kelly themselves originated the idea to conduct this Twins Study.

Question (20): Will biofluid samples be available essentially immediately, i.e. from year 1 of the studies, onwards. Stated differently, are there samples already collected and stored from prior experiments that funded investigators will have access to?

Answer: Mark Kelly and Scott Kelly have both provided a series of biofluid samples during the course of their astronaut careers that can be requested from NASA for longitudinal –omics studies via the LSDA program. However, those specimens are frozen and were not necessarily collected using a reagent such as RNA*later*.

Question (21): Who will pay for the shipping of biofluid samples to funded investigators?

Answer: NASA will pay for the track-able shipping of biofluid samples to funded investigators.

Question (22): As a necessary adjunct to these –omics studies will the twins, (Mark and Scott Kelly) be provided with genetic medical counseling?

Answer: Yes – NSBRI is facilitating and paying for genetic medical counseling for the Kelly Twins – in close consultation with NASA Flight Surgeons and NASA’s Human Research program.

Question (23): In regards to the question of Cost Sharing - can faculty time be used as a match?

Answer: The HERO Solicitation –Appendix D states: “If an institution of higher education, hospital, or other non-profit organization wants to receive a grant from NASA, cost sharing is not required. However, NASA can accept cost sharing if it is voluntarily offered. If a commercial organization wants to receive a grant, cost sharing is required unless the commercial organization can demonstrate that they are unlikely to receive substantial compensating benefits for performance of the work. If no substantial compensating benefits are likely to be received, then cost sharing is not required but can be accepted. Acceptable forms of cost sharing are located at: http://www.hq.nasa.gov/office/procurement/regs/1816.doc#OLE_LINK3.”

Question (24): Is it feasible at all to cryopreserve biological samples while working in space e.g. on the International Space Station?

Answer: Yes - it is certainly possible to store biofluids at at minus 80 degrees Celsius - and repatriate these samples to Earth - whilst still frozen. In fact this activity of storing and repatriating biofluid samples from space is now relatively routine - or at least as routine as spaceflight can ever be.

Please note however that there is the likelihood that these frozen samples may warm up somewhat during the return to Earth - as sometimes it takes "additional" time beyond that normally scheduled to secure and off-load the returning spacecraft containing the biofluid samples.

Question (25): To make the study 100% controllable - will both twins be placed on the same or a similar diet, as expression of many genes might be alerted by a simple dietary change.

Answer: NO - Mark Kelly and Scott Kelly will NOT be on the same diet during the period of the 1 Year Mission, (ISS-12). Nor will they be experiencing the same levels of Carbon Dioxide. Nor will they be sleeping on the same schedule. In short - Mark Kelly will go about his "normal" life here on Earth - whilst his Twin Brother - Scott Kelly is in space.

Of course we acknowledge that this schema is not ideal and we would like to better control all these potentially confounding variables - but at least for this particular Twin Study, that will not be possible.

Question (26): Please explain how civil servant salaries and travel should be included in the proposal.

Answer: Civil Servant Salaries must be included in all proposals, however, the expectation is that the Senior Scientist spends no more than 30% of their time on any one proposal. Civil Servants

are not expected to cover 100% of their salary on a proposal. That is not realistic in academia, thus is not expected here.

They should also include the travel required for the proposal, including conference attendance, regardless of Civil Servant conference restrictions. Travel on a Civil Servant proposal should be comparable with that on external University proposals.