EMORY NSCOR OVERVIEW PROGRESS

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The Emory University NSCOR grant entitled “Mechanisms underlying the risk of HZE particle-induced solid tumor development” (NNX11AC30G) started January 1, 2011. The main purpose of this NSCOR is to investigate the mechanisms by which high charge and energy (HZE) particles, a component of space radiation, induce lung cancer. The central hypothesis of this NSCOR is that this broader stress response amplifies the carcinogenic risk from a primary DNA damage event and microRNA-21 (miR-21) plays a key role in coordinating the HZE particle-associated stress response. We have used genetic, epigenetic, and biochemical approaches to address the role of miR-21 dependent and independent stress responses in HZE particle-induced lung cancer through four projects. To study the mechanism of space radiation-induced genomic instability and carcinogenesis in HZE particles irradiated human cells or mice, this NSCOR will answer the question concerning whether and how different qualities (LET) of radiation affects lung tumorigenesis. In addition, project 1 is focused on the regulation of miR-21 and other related miRNAs with their targets; project 2 is focused on the choice of different DNA repair pathways; project 3 is focused on the change of oxidative stress response; project 4 is focused on the specific DNA methylation profile. The four projects are synergized on studying the mechanism underlying how mammalian respond to HZE particle-induced DNA damage, which contributes to tumor development. So far, we have finished all the animal radiation exposure for observing tumorigenesis. The mouse strains include wild type C57BL/6 mice, miR-21 knock-in mice, Gprc5a-/- mice, miR-21 knock-in and Gprc5a-/- double mutant mice, miR-21-/- mice. We will examine the tumorigenesis at 1.5 years after the mice are exposed to radiation (including X-ray, Fe, Silicon and Oxygen). The final results about tumorigenesis frequency will be obtained by the end of next year (2014). Also, our four projects have collaborated to obtain some expected results that are reflected in seven research articles published in peer-reviewed journals and three submitted manuscripts.