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Discovery of 3 New Natural Killer (NK) Cell Populations & CD4+/CD8+/NK Cell-Specific Radiation Response Signature using Single-Cell Transcriptomics

Dr. Preethi Gunaratne is a Moores Professor in the Department of Biology & Biochemistry at the University of Houston (UH) with adjunct appointments in the Department of Molecular & Cellular Biology, Human Genome Sequencing Center and Dan L. Duncan Cancer Center at Baylor College of Medicine (BCM). She obtained her B.Sc. (Zoology Hons), from the University of Colombo, Sri Lanka and Ph.D. in Genetics, from Cornell University, New York. Following postdoctoral fellowships at the Lurie Cancer Center, Northwestern University and Department of Human & Molecular Genetics at BCM, Dr. Gunaratne received Board Certification in Clinical Molecular Genetics and Medical Genetics (ABMG) in 1999. After serving as Assistant Director, Baylor-DNA Diagnostic laboratory, she joined the International Human Genome Project (HGP). As Director, of the cDNA Sequencing Team, at the Baylor-Human Genome Sequencing Center (Baylor-HGSC), she contributed to the sequencing and annotation of Human Chromosomes 3, 12 and X and led her team to make the largest single contribution to the Mammalian Gene Collection (MGC) in Phase I. Dr. Gunaratne also served as one of the leaders of the microRNA and LncRNA-Analysis Working Groups for the NCI-The Cancer Genome Atlas (TCGA), TCGA-Pan Cancer Atlas, NHGRI-Zebrafinch and Marmoset Genome Projects.

In 2006 Dr. Gunaratne, joined the University of Houston (UH) and went on to establish a functional genomics platform focused on discovering new druggable targets through the microRNA-regulated transcriptome. Through >120 co-authored articles Dr. Gunaratne and collaborators have laid the groundwork for determining the role of the microRNAs and microRNA-regulated genes in cancer, schizophrenia, asthma, COPD/emphysema, and song response in the auditory forebrain of songbird. In 2015, Dr. Gunaratne was appointed Director, UH-Genome Sequencing Core (UH-SNEC, http://seqnedit.nsm.uh.edu/). Major projects spearheaded by Dr. Gunaratne, include, 1) Decoding the 45% of disease variants mapping in the non-coding genome to discover new druggable targets and diagnostic markers for congenital disorders and complex diseases; 2) Developing Single Cell Sequencing technologies for remote sensing disease onset and progression; and 3) Discovering immunogenic peptides from RNA-fusions in cancer cells and RNA viruses including COVID-19. Dr. Gunaratne has served as an Expert Peer Reviewer for over 25 scientific journals and 10 grant review panels; including National Institute of Health (NIH-USA), U.S. Department of Defense-CDRMP, National Health and Medical Research Council (NHMRC)-Australia, Cancer Research Council-UK, Netherlands-Research Foundation Flanders (FWO) Cancer and COVID-19 panles, Israel Science Foundation, Florida Department of Health (F-DOH), Pennsylvania Department of Health (PA-DOH), US Food and Drug Administration (FDA). In addition to her research accomplishments, Dr. Gunaratne is an inventor/co-inventor on 3 US patents applications and served on a National Science Foundation-ADVANCE committee to advance women and minorities in the faculty. As one of the Directors, of the US Army Research & Engineering Apprenticeship (USAEOP/REAP) program (2008-Present) focused on advancing minorities in Science, Technology, Engineering & Mathematics (STEM) fields, she has provided internships to 70 high-school interns and mentorship opportunities to 30 undergraduate students.

Abstract: To reveal the full extent of the Natural Killer (NK) cell repertoire during viral infection we performed single cell RNA-sequencing (scRNA-seq) on unstimulated and interleukin (IL)-2–activated NK-cells from healthy cytomegalovirus (CMV)-negative donors. Three novel human blood NK cell populations were identified including; Type I interferon–responding CD56neg-NK subpopulation, and two other NK cell subpopulations characterized by 1) cytokine-induced memory-like phenotype and 2) cellular activation phenotype showing high levels of immediate early response genes. In order to model the DNA damage response in astronauts exposed to radiation during space exploration missions we performed scRNA-seq on human immune cells 3 h after ex vivo exposure to 2-Gy gamma rays. Comparing 700 irradiated and ~700 nonirradiated control cells, we found that TP53 responsive genes were up regulated in all groups of immune cells. By contrast, IRF1, STAT1, and BATF were only upregulated in the CD4+ and naïve groups, but were unchanged in the CD8+/NK group, which suggests that the interferon-gamma pathway does not respond to radiation in CD8+/NK cells. The unexpected NK cell-diversity revealed through single cell sequencing provides a new framework for incorporating NK cell responses to viral infection and environmental exposures.