Space Radiation Can Enhance the TGFβ Induced Epithelial–Mesenchymal Transition

Minli Wang[1], Megumi Hada[1], Janice Huff[1], Janice M. Pluth[2], Jennifer Anderson[3], Peter O'Neill[3] and Francis A. Cucinotta[4]

[1]USRA Division of Life Sciences, Houston TX USA; [2]Lawrence Berkeley National Laboratory, Berkeley CA, USA, [3]Gray Institute for Radiation Oncology & Biology, University of Oxford, UK, [4]NASA, Lyndon B. Johnson Space Center, Houston TX, USA

TGFβ is a key modulator of the Epithelial–Mesenchymal Transition (EMT), important in cancer progression and metastasis, which involve classic Smad or non-Smad signaling pathways, leading to the suppression of epithelial genes and promoted expression of mesenchymal proteins. Ionizing radiation was found to specifically induce expression of TGF-β1 isoform, which can modulate late post-radiation changes and increase the risk of mesenchymal transition in epithelial cells and as a result the development of tumor and metastasis. Interactions between TGFβ induced EMT and DNA damage responses have not been elucidated, particularly at low doses and of different radiation qualities. Further characterization of their relationship to cancer processes is warranted. We investigated the activation of DNA damage induced by simulated space radiation on TGFβ dependent EMT, using hTERT immortalized human esophageal epithelial cells (EPC-hTERT). In this study, we have observed morphologic and molecular alternations consistent with EMT after EPC cells were treated with TGFβ, which can be efficiently inhibited by using TGFβRI inhibitor (SD208). Similar effect was observed with non-transformed Mink lung epithelial cells (Mv1Lu). Silicon particle (Energy 170 MeV/u, with a LET of 99 keV/μm) alone was shown to cause the mild induction of EMT, and TGFβ induced EMT phenotype was greatly enhanced when cells were irradiated at a low dose of 0.4 Gy. Further increase of EMT signals was achieved by using higher dose, with a dose of 2 Gy silicon particles. TGFβRI inhibitor was able to reverse the EMT induced by the combination of TGFβ and high LET radiation. These studies indicate that high LET radiation, even with a low dose, may trigger the process of TGFβ–induced EMT, and the components involved in the mechanism need to be further studied.