due to impairing of the phenotypic plasticity that causes cells to adopt stem cell and pro-migratory characteristics. Further mechanistic studies are focusing on alterations to stem cell subpopulations after radiation and superadded notch inhibition.

PO-0991 Chromosomal radiosensitivity and genomic instability of Fanconi anaemia patients in South Africa

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Purpose or Objective
Fanconi anaemia (FA) is an autosomal recessive disorder characterised by defects in DNA repair associated with chromosomal instability. FA cells exhibit cellular hypersensitivity to DNA cross-linking agents such as mitomycin C (MMC). The clinical manifestations include congenital and developmental abnormalities and haematological defects. It has previously been shown that FA patients undergoing radiotherapy display increased clinical radiosensitivity by exhibiting adverse normal tissues side-effects. Evidence suggests that FA patients are chromosomally radiosensitive to ionising radiation, however, with very limited data.
The aim of this study is to investigate chr omosomal radiosensitivity and genomic instability of hom ozygous and heterozygous carriers of FA mutations compared to healthy individuals using the micronucleus (MN) assays.
Material and Methods
For the G0 MN assay, heparinised blood in culture medium was irradiated at 0Gy (Baseline), 2Gy and 4Gy followed by the immediate stimulation of lymphocytes using phytohaemagglutinin (PHA). Cytochalasin B was added 23 hours later to inhibit cytoplasmic division. Cells were harvested 70 hours post irradiation.
The S/G2 MN assay is a modified version of the G0 MN assay. To initiate the assay, the cultures are stimulated with PHA and then irradiated with the same radiation doses 72 hours after stimulation. To detect DNA damage in the S/G2 phase of the cell cycle, the cells were harvested 8 hours post irradiation.
The third assay is similar to the G0 MN assay except the cell damage is induced using MMC.
Subsequent to harvest, all slides were prepared and stained with acridine orange and micronuclei were scored using a fluorescent microscope.
Results
When compared to parents and healthy controls, spontaneously occurring micronuclei are significantly higher in FA patients indicating genomic instability. A similar trend is noticed in the micronuclei frequency of irradiated FA cells signifying chromosomal radiosensitivity. This sensitivity is evidently pronounced in the S/G2 phase. Elevated chromosomal damage was also detected with MMC treatment in the FA patients.
Conclusion
Chromosomal radiosensitivity and genomic instability of FA mutation carriers are notably higher when compared to healthy individuals.

PO-0992 Low-dose whole lung irradiation plus Re-188-liposome eliminates lung metastasis of esophageal cancer

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Purpose or Objective
External beam radiotherapy (EBRT) treats gross tumors and local microscopic diseases. Radionuclide therapy by isotopes can control tumors systemically. Rhenium 188 (^{188}Re)-liposome, a nanoparticle undergoing clinical trials, emits gamma rays for imaging validation and beta rays for therapy with biodistribution profiles preferential to tumors. We designed a unique combinatory treatment and examined its effects on lung metastasis from esophageal cancer, a malignancy with poor prognosis.
Material and Methods
Human esophageal cancer BE-3 cells with luciferase gene for optical imaging were injected into tail vein of nude mice to induce lung metastasis. The radiochemical purity of ^{188}Re-liposome exceeded 95%. Molecular imaging by NanoSPECT/CT (NanoSPECT/CT PLUS, Mediso, Alsotorokvesz, Budapest, Hungary) showed that lung metastatic lesion could uptake the ^{188}Re-liposome. For biodistribution, the radioactivity of ^{188}Re-liposome was detected by Auto-Gamma counter (Packard Cobra II, Canberra, Germany), and the uptake of ^{188}Re-liposome in each organ was expressed as the percentage of injected dose per gram of tissue (% ID/g). Low-dose whole lung EBRT with 3 consecutive daily fractions of 1 Gy was delivered by linear accelerator with 6-MV photon (Clinac iX, Varian Medical Systems, USA) followed by intravenous ^{188}Re-liposome (250 μCi) administration 2-h after last teletherapy. Flow cytometry was used to estimate the amount of myeloid derived suppressor cells and macrophages.
Results
The combination of EBRT and ^{188}Re-liposome inhibited tumor burden of lung metastasis faster and better than each treatment alone (Figure 1 and 2). Combination treatment did no cause additive adverse effects on white blood cell counts, body weight, or liver and renal functions. EBRT significantly reduced the uptake of ^{188}Re-liposome in lung, kidney, bone marrow and blood. In spleen, ^{188}Re-liposome administration declined the amount of myeloid derived suppressor cells and increased the amount of M1 and M2 macrophages.

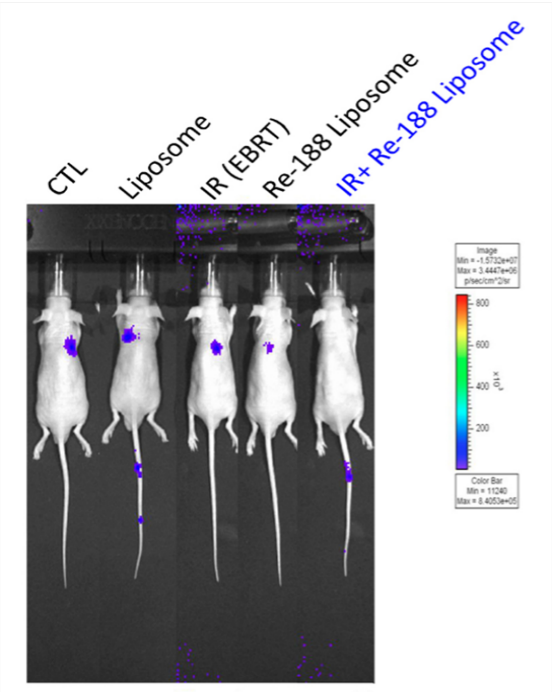

Figure 1. The therapeutic efficacy of ^{188}Re-liposome