Radiation has emerged as the most critical issue to be resolved for long-term missions both orbital and interplanetary. Astronauts are constantly exposed to galactic cosmic radiation (GCR) of various energies at a low dose rate. Primarily late tissue sequelae like genetic alterations, cancer and non-cancer effects, i.e. cataracts and degenerative diseases of e.g. the central nervous system or the cardiovascular system, are the potential risks. Cataracts were observed to occur earlier and more often in astronauts exposed to higher proportions of galactic ions (Cucinotta et al., 2001). Predictions of cancer risk and acceptable radiation exposure in space are subject to many uncertainties including the relative biological effectiveness (RBE) of space radiation especially heavy ions, dose-rate effects and possible interaction with microgravity and other spaceflight environmental factors. The initial cellular response to radiation exposure paves the way to late sequelae and starts with damage to the DNA which complexity depends on the linear energy transfer (LET) of the radiation. Repair of such complex DNA damage is more challenging and requires more time than the repair of simple DNA double strand breaks (DSB) which can be visualized by immunofluorescence staining of the phosphorylated histone 2AX ($\gamma$H2AX) and might explain the observed prolonged cell cycle arrests induced by high-LET in comparison to low-LET irradiation. Unrepaired or mis-repaired DNA DSB are proposed to be responsible for cell death, mutations, chromosomal aberrations and oncogenic cell transformation. Cell killing and mutation induction are most efficient in an LET range of 90-200 keV/µm. Also the activation of transcription factors such as Nuclear Factor $\kappa$B (NF-$\kappa$B) and gene expression shaping the cellular radiation response depend on the LET with a peak RBE between 90 and 300 keV/µm. Such LET-RBE relationships were observed for cataract and cancer induction by heavy ions in laboratory animals, with varying maximal efficiencies. Furthermore, there is always the added risk of acute exposure to high proton fluxes during a solar particle event (SPE), which can threaten immediate survival of the astronauts in case of insufficient shielding by eliciting the acute radiation syndrome. Its symptoms depend on absorbed total radiation dose, type of radiation, the dose distribution in the body and the individual radiation sensitivity. After the prodromal stage with nausea and vomiting and a subsequent symptom-free phase, depending on dose, the hematopoietic syndrome with suppression of the acquired immune sys-
tem and thrombocytopenia (0.7-4 Sv), the gastrointestinal tract syndrome (5-12 Sv) or the central nervous system syndrome (> 20 Sv) develop and they are accompanied by exacerbated innate immune responses. Exposure to large SPE has to be avoided by warning systems and stay inside a radiation shelter during the event. Treatment options encompass e.g. the administration of colony-stimulating factors (CSF), growth factors and blood transfusions to overcome the hematopoietic syndrome and the administration of antibiotics against secondary infections. A concerted action of ground-based studies and space experiments is required to improve the radiobiological basis of space radiation risk assessment and countermeasure development.