With the development of effective therapeutic regimens, most of the cancers are now treatable. Though radiotherapy has been in practice to control the progression of cancer effectively, an often-associated complication with radiotherapy is its side effects on other organ systems. Testis is one of the most important radiosensitive tissues because even very low doses of radiation deteriorate testicular functions. Leydig cells, which reside in the interstitium of the testis, contribute about 75% of the total testosterone produced by normal adult male to support spermatogenesis, and to maintain masculinity. In boys with acute lymphoblastic leukemia (ALL), the main site of leukemic relapse is the testis (Sather et al., 1981; Brauner et al., 1988; Didi et al., 1994) and the direct testicular irradiation is being the effective treatment, these children often fail to undergo normal pubertal development due to Leydig cell dysfunction. In healthy adult men, single dose of 600 rad of radiation directed to the testis lowered the testosterone and raised luteinizing hormone (LH) levels indicating Leydig cell failure (Rowley et al., 1974). Pelvic radiotherapy for prostatic carcinoma with doses between 10 and 25 Gy drastically changed the levels of serum testosterone and LH (Tomic et al., 1983; Shapiro et al., 1985). Elevated levels of gonadotrophins (both FSH and LH) recorded following radiation treatment for carcinoma of the prostate (4.5-6 Gy over 7-8 weeks) demonstrate Leydig cell failure (Grigsby and Perez, 1986).
Total body irradiation for bone marrow transplantation also showed Leydig cell dysfunction as incidental elevation of serum LH was recorded in these cases (Bakker et al., 2000). Radioiodine therapy for thyroid carcinoma is associated with transient impairment of testicular functions (Pacini et al., 1994) and is also resulted in decreased testosterone/LH ratio (Wichers et al., 2000). In pubertal and adult rats, radiation induces both acute and chronic damage to Leydig cells, and is followed by decreased testosterone secretion, increased gonadotrophins secretion with loss of Leydig cells (Delic et al., 1986a, b). Delic et al. (1985) also reported that the threshold dose for induction of Leydig cell dysfunction in prepubertal rats is about 5 Gy, which is similar to pubertal and adult rats. In this study, they observed biphasic response of the testis to radiation after two weeks as the number of Leydig cells increased at 1-5 Gy and decreased between 5 and 15 Gy.

Therapeutic or experimental radiation exposures impair Leydig cell function. However, the mechanisms by which radiation induces such changes are unknown. Therefore, dose-dependent effects of gamma radiation on Leydig cell LH/hCG receptor expression, signal transduction and steroidogenesis were studied to understand the molecular mechanism behind radiation-induced Leydig cell dysfunction.