A considerable amount of work has been done to develop stochastic mathematical formalisms that embody major biological processes thought to control the emergence of a cancer after exposure to environmental insults, such as radiation. A conceptually simple example is the one employing the "initiation-promotion-conversion" paradigm of malignant transformation, the Two-Stage Clonal Expansion Model. The hypotheses of this model are: (1) two (or more) events (presumably genomic) must occur within a cell (or its progeny) to produce a malignant cell, (2) at some point between the first and last event, a cell clone emerges with average increased net growth rate, and (3) a cell in this clone can further sustain one (or more) spontaneous or induced genomic events that lead to a malignant cell. The three processes are called "initiation", "promotion" and "malignant conversion", respectively. Although such a picture is undoubtedly simplified over the realistic situation in a complex tissue, some interesting general conclusions can be drawn that are not dependant on the details of the model, but emerge from the conceptual framework of the initiation-promotion-conversion process and the analysis of cohorts exposed to both high- and low-LET radiation. These conclusions point to the relative importance of each of the above processes in producing a malignant cell as a function of such parameters as attained age, age at exposure, and exposure duration.

A review is presented of analyses of lung cancer in cohorts of Colorado Plateau miners (high-LET alpha particles from radon inhalation), and Canadian radiation workers (low-LET gamma radiation), as well as a cohort of the US population (the SEER registry) for colorectal cancer. The two lung cancer studies conclude that radiation-induced initiation is not as important as either radiation-induced promotion or malignant conversion in lung cancer induction after extended exposures of either high- or low-LET radiation. Interesting time dependences of the hazard function that vary markedly for different exposure scenarios emerge as a function of attained age. The colorectal cancer cohort study suggests that two rare events plus a high-frequency event are necessary to produce an initiated cell. These and other results of these analyses are discussed in terms of long term space flight. One important general conclusion is that since different processes are important at different ages, it would not be surprising if different LET dependences of the risk exist at different ages. Also, unique models of tumor induction will probably be necessary for each of the various radiation-induced cancers of importance in estimating risk on long missions.