



**Figure 2. Knudson's two-hit hypothesis for tumourigenesis involving a tumour suppressor gene (TSG) (Ref. 10).** One pair of chromosomes is depicted, with one TSG [the normal gene (grey), the mutated gene (red), and deletion of the gene (absence) are shown]. (a) Normal individuals have two normal copies of the TSG, so two independent 'hits' (mutations) are required in the same cell to initiate a cancer. (b) Individuals with a germline mutation of the TSG already have a first 'hit' in every cell and require only one subsequent 'hit' in a cell to initiate a cancer (**fig002frb**).