Microsatellite instability is found in other inherited and sporadic cancers

Microsatellite instability was quickly demonstrated to be a feature of a second cancer developing in HNPCC kindreds—endometrial cancer [23]. Microsatellite instability is therefore a manifestation of a general underlying carcinogenic defect inherited in these families (Table 1).

Simultaneous with the discovery of microsatellite instability in colon cancers in HNPCC families, it was demonstrated that this defect also occurs in about 15% of sporadic colon cancers [17••,24••–26••]. These observations were rapidly generalized to show that the RER phenotype is present in a high percentage of sporadic cases of many of the cancers that arise in HNPCC kindreds, and especially in endometrial and gastric cancers (Table 1).

Unexpectedly, RER is also found in some tumors that are not associated with HNPCC kindreds (Table l). Most notably, these include small-cell lung cancer and chronic myeloid leukemia in blast crisis.

Interestingly, the incidence of RER appears to vary among different sporadic cancers, from a high of 67% in pancreatic cancer to being relatively rare in liver and prostate cancers (Table 1). It is tempting to speculate that this tissue specificity reflects the sensitization by the RER phenotype to the actions of tissue-specific mutagens, or the existence of tissue-specific genes that are targets of spontaneous mutations accelerated in the RER phenotype and whose mutation confers a growth advantage to that specific cell type.