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On the absence of mutations in nucleotide excision repair genes in sporadic solid tumors

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ABSTRACT. In general, stochastic tumors show genomic instability associated with the proliferation of DNA point mutations, that is, a mutator phenotype. This feature cannot be explained by a dysfunctional mismatch repair alone, and indicates that nucleotide excision repair (NER) and/or base excision repair should be suppressed. However, mutations in NER genes are not causally implicated in the oncogenesis of sporadic solid tumors, according to the Cancer Gene Census at http://www.sanger.ac.uk/genetics/CGP/Census/. This brings up an apparent paradox: how to explain the recurrent non-existence in NER genes of somatic mutations causally related to cancer? In a recent study, we have shown that the origin of point mutations in cancer cell genomes can be explained by a structurally conserved NER with a functional disorder generated from its

entanglement with a disabled apoptosis gene network. In the present study, we further characterize NER gene network properties and show that it has a highly connected architecture. This feature suggests that the absence of mutations in NER genes in sporadic solid tumors is a result of their participation in many essential cellular functions.

Key words: Nucleotide excision repair; Cancer; Gene network; Sporadic solid tumors

