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Intrinsic base substitution patterns in diverse species reveal links to cancer and metabolism

LE JEUDI 30 SEPTEMBRE 2021 À 12 H 30

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Analyses of large-scale sequencing data reveal that mutagenic processes create distinctive patterns of base substitutions, called mutational signatures. To determine whether similar patterns exist more generally, we analyzed substitutions from seven model species and single nucleotide polymorphisms (SNPs) in 42 species, totalling >1.9 billion variants. We found that base substitution patterns for many species most closely match single base substitution (SBS) mutational signature 5 in cancers, and that the pattern of human SNPs is almost exactly the same as this signature. SBS 5 is ubiquitous in cancers and normal human cells, suggesting that similar patterns of mutation across species are likely due to conserved biochemistry. We present evidence from yeast that sugar metabolism is linked to this form of DNA damage. Finally, we propose that conserved metabolic processes in cells are coupled to continuous generation of mutations, which are acted upon by genetic selection to drive the evolution of species, and cancers.

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