NEW MUTATIONS PER GENERATION

In humans, the mutation rate per nucleotide per generation is approximately 1.59 times 10 to the negative eight that is ±48 mutations per genome per generation (1).

To address the inherent limitations in humans, López-Cortegano et al. (2) conducted experiments in mice. They used 12 inbred mouse lines derived from three commonly used inbred strains maintained for 8-15 generations in a "mutation accumulation" experiment. "Mutation accumulation" means that the lines are maintained under conditions that minimize selective pressure, often with a small number of individuals per generation. This reduces selection against deleterious mutations, enabling their accumulation. Individuals are propagated over many generations, during which new mutations accumulate.

In this way they were able to calculate:

- **Single nucleotide mutations** (~20 per haploid genome/generation).
- **Insertions and deletions** (~24.4 per genome/generation).
- **Structural mutations** (~1 per genome/generation).

These mutations are favored by **repetitive DNA sequences** (insertions, deletions, and contractions/expansions); **microsatellite instability** (90% of indels); **insertion of transposable elements** (they also mediate structural mutations); **nonallelic homologous recombination** (usually triggered by interspersed repeats or by transposable elements); **methylated CpG sites** (favoring C→T transitions).

1. https://www.cell.com/ajhg/fulltext/S0002-9297(22)00065-9?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0002929722000659%3Fshowall%3Dtrue
2. https://genome.cshlp.org/content/early/2024/12/02/gr.279982.124