

TwinStrand DuplexSeq™ Mutagenesis Solution



Mutagenesis is an important predictor of cancer risk in chemical and drug safety testing. Standard mutagenesis assays yield a limited amount of indirect information about a compound's mutagenic potential and/or are complex and cumbersome.

Duplex Sequencing™ Mutagenesis assays offer a fundamentally new NGS-based approach for mutational research that directly detect, quantify and characterize induced mutagenesis in the DNA of exposed organisms and cells. The unprecedented richness of data unlocks powerful opportunities for novel insights and discoveries.

Duplex Sequencing for Mutagenesis

The first Next-Generation Sequencing (NGS) technology capable of directly measuring mutagenesis in DNA molecules without the need for biological selection

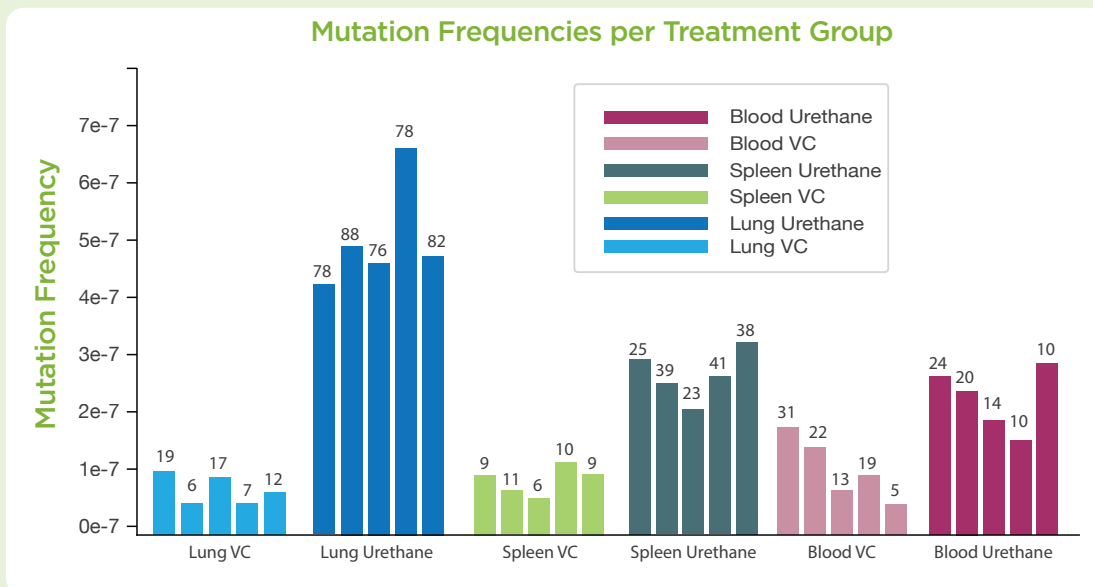
Accurately & reproducibly measures mutation loads on the order of 1/10,000,000

Equally applicable *in vitro* and to any tissue *in vivo*

Produces comprehensive mutation data, including frequency, simple spectrum and trinucleotide spectrum

Supports the diverse needs of academic, commercial, and regulatory users

Mutation Frequencies

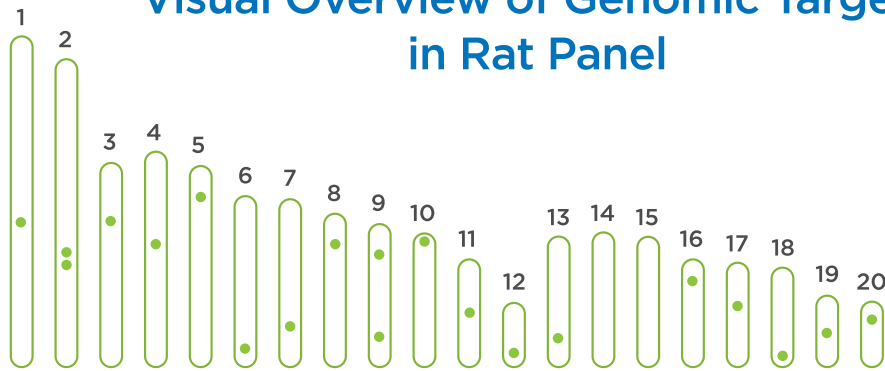


Urethane-induced mutagenesis detected by Duplex Sequencing in 3 mouse tissues. Mutation frequencies are highly reproducible across biological replicates (n=5/group), and statistically robust. The number of individual mutant nucleotides identified per sample among hundreds of millions screened is indicated above each bar. VC: vehicle control (untreated).

Mutagenesis Panel Overview



Visual Overview of Genomic Targets in Rat Panel

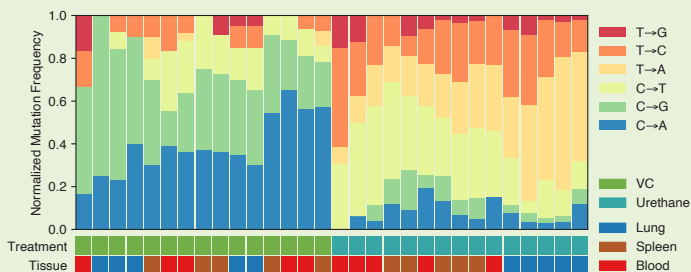


Location of genomic targets in the TwinStrand Duplex Sequencing™ Rat Mutagenesis panel. Mouse and human panels are similarly constructed.

The TwinStrand Duplex Sequencing mutagenesis kits use a 48kb panel targeting 20 arbitrary regions spread throughout the genome. The regions are balanced to provide an unbiased sampling of representative sequence contexts throughout the genome (GC content, genic/non-genic, coding/non-coding, etc). These sites have no known role in cancer and are unlikely to be significantly influenced by positive or negative selection. Currently available in human, mouse and rat formats.

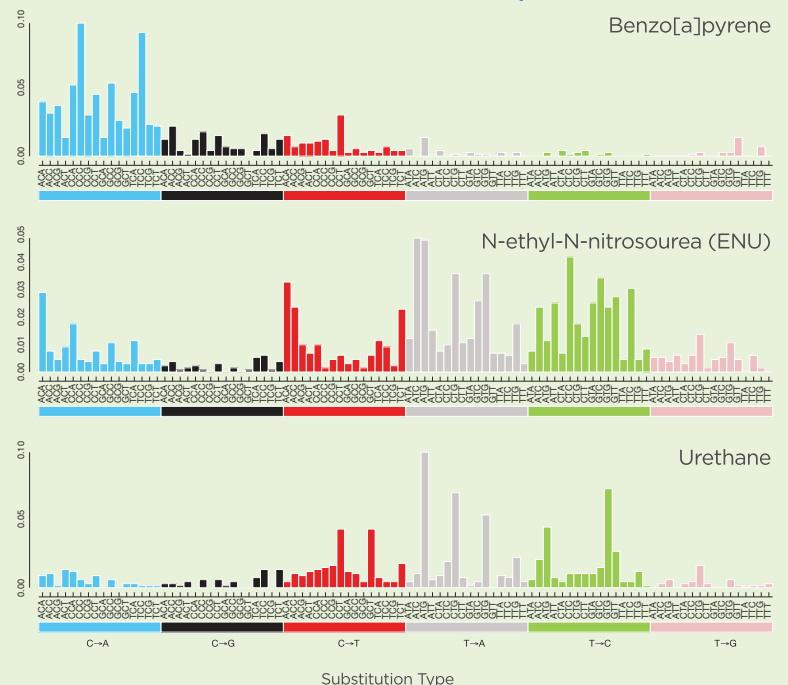
Duplex Sequencing Mutational Spectra

Simple Mutation Spectra



Simple mutation spectra detected by Duplex Sequencing of urethane-exposed mouse tissue. Unsupervised hierarchical clustering perfectly assigned all of the 30 tissues to the correct treatment groups (vehicle control on left, urethane on right).

Trinucleotide Mutation Spectra



Highly distinct trinucleotide signatures generated by Duplex Sequencing of normal (non-tumor) mouse tissues exposed to three mutagens: urethane, benzo[a]pyrene, and N-ethyl-N-nitrosourea. Figures generated using ultra-low frequency mutations present on the order of 1 in 1 million.