wellcome sanger institute

TECHNOLOGIES

NANOSEQ: NANORATE SEQUENCING, ULTRA-ACCURATE DETECTION OF SOMATIC MUTATIONS

ADVANTAGES

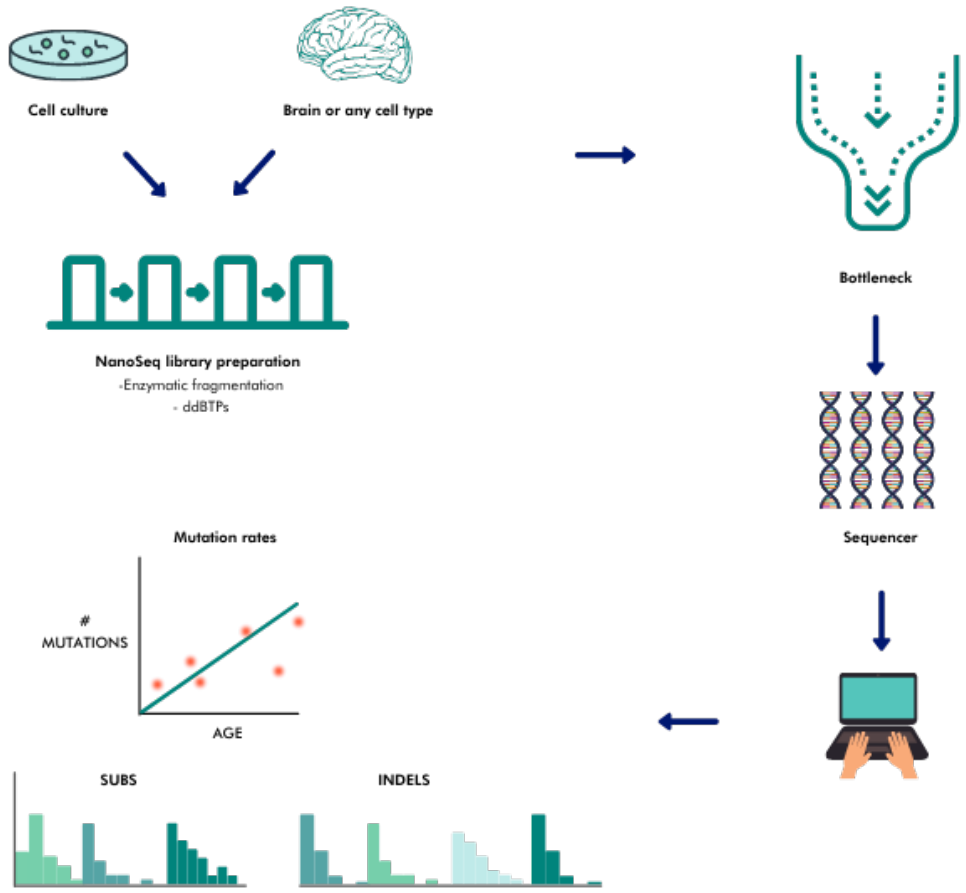
- **UNDERSTAND** somatic mutation rates in any cell type, including non-dividing cells.
- **ACCURATE** measurement of mutation rates and signatures in mutagenesis screens.
- **ABILITY** to detect mutations in blood or non-invasive biopsies.

TECHNOLOGY

Nanorate sequencing (Nanoseq), is a method developed by scientists at the Sanger Institute that reduces error rates to less than 5 errors per billion calls, much lower than typical somatic mutation rates. This is achieved by limiting errors during the preparation of DNA libraries, avoiding extension of internal nicks and error-prone end-repair.

Nanoseq uses blunt-end restriction enzymes to fragment DNA and dideoxy bases (ddBTPs) to avoid nick extension. A mathematically modelled dilution step is used to optimize the efficiency and yield of the method. The bioinformatic pipeline incorporates a set of carefully calibrated methods to filter unreliably mapped reads and detect contamination.

How it works: Nanoseq can take relatively small DNA input prior to using blunt cutting enzymes, in combination with BTPs, during library preparation to keep error rate low. A carefully calibrated dilution step dilutes the sample appropriately prior to sequencing.



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BACKGROUND

The ability to distinguish real mutations from experimental noise in somatic tissue is key for understanding the role of somatic mutation in cancer and ageing or how our bodies deal with environmental insults. We know that cells accumulate mutations as they age and these can drive disease states such as cancer. While detecting mutations in tumours is straightforward, detecting mutations in non-clonal cell populations (e.g. tissue biopsies or blood) is not possible with standard sequencing methods and has required special approaches.

APPLICATIONS

Highly specific detection and quantification of somatic mutations in any cell type. Quantitating the impact of environmental exposures on human tissues or studying known or new mutagens in vitro.

COMPARABLE TECHNOLOGIES

Existing highly error-corrected protocols, such as bottleneck and duplex sequencing, have error rates similar or above the rate of real somatic mutations in normal tissues. Hence, when applied to human samples a considerable number of technical errors is introduced, complicating the interpretation of results.

INTELLECTUAL PROPERTY

Priority patent application filed.

The Wellcome Sanger Institute is offering non-exclusive licenses to its IPR.

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