4 DNA and genomics advances recognized in R&D 100 Awards in 2024

By R&D Editors | November 24, 2024

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DNA analysis has undergone a quiet revolution in recent years thanks to next-generation sequencing (NGS) advances. In addition to its potential in medicine, NGS is taking off in forensic science. This technology allows for more detailed and accurate genetic analysis, improving the resolution of criminal cases and helping solve cold cases that have remained unsolved for years. DNA technologies were also one of the focus areas of this year's R&D 100 Awards, with winners showcasing advances in forensic analysis, synthetic DNA production, and sequencing accuracy.

The following article recaps five DNA and genomics advances recognized in the R&D 100 Awards in 2024. Among them is a forensic technology from MIT Lincoln Laboratory that can separate mixed DNA profiles from crime scenes. In addition, Elegen's ENFINIA DNA technology can achieve 20x higher accuracy in synthetic DNA production. At the same time, PacBio's Onso system delivers a 15-fold improvement in sequencing accuracy — finally, Oak Ridge's innovative approach to engineering multiple genes in plants simultaneously.

1. Elegen's cell-free platform synthesizes linear dsDNA with 99.999% accuracy

ENFINIA DNA
Elegen Corp.

ENFINIA DNA is a synthetic DNA manufacturing technology developed by Elegen that produces linear double-stranded DNA (dsDNA) fragments between 1–7 kilobases in length. The cell-free synthesis process achieves a reported per-base accuracy of 99.999% (error rate ~1:70,000 bp), verified through next-generation sequencing (NGS) validation. The cell-free synthetic DNA manufacturing technology can be delivered within 6-8 business days for standard sequences and ten business days for high-complexity sequences. The technology can handle challenging sequences, including inverted terminal repeats (ITRs), hairpins up to 100 bp, homopolymers (A/T up to 30 bp, G/C up to 15 bp), short tandem repeats up to 60 bp, and long repeats up to 150 bp. Each DNA sequence is NGS-verified for accuracy and can be produced in yields up to 60 µg. The cell-free production process eliminates traditional cloning workflows in applications, including mRNA vaccines, cell and gene therapies, engineered crops, and synthetic biology products.

ENFINIA DNA

2. Onso short-read sequencing system

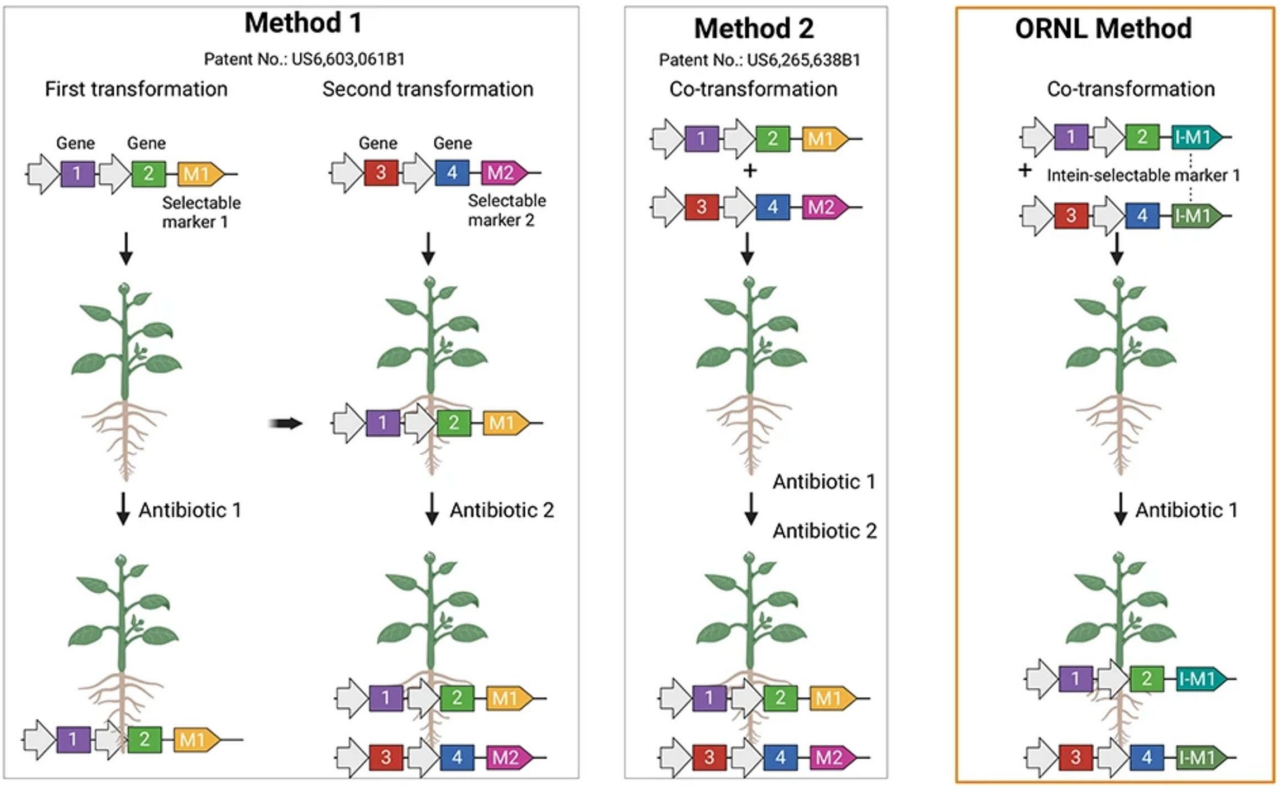
PacBio

The Onso benchtop short-read DNA sequencing system from PacBio uses a unique sequencing-by-binding (SBB) chemistry to achieve Q40+ specification (1 error in 10,000 bases sequenced), representing a reportedly 15-fold improvement in accuracy. The platform delivers 400 to 500 million reads during a 48-hour sequencing cycle, with options for 200 and 300-cycle kit configurations for paired- and single-end reads. The system's low error rates enable the detection of rare variants in liquid biopsy research, requiring lower sequencing depth than traditional sequencing-by-synthesis (SBS) approaches. Researchers at McGill University are currently using the SBB technology to explore new diagnostic approaches for endometrial and ovarian cancers, typically identified at advanced stages in 75% of cases. The technology's applications extend to resolving low-complexity regions like homopolymer repeats for reference genome work and analyzing complex heterogeneous samples in metagenomics, CRISPR-based editing, and wastewater surveillance.

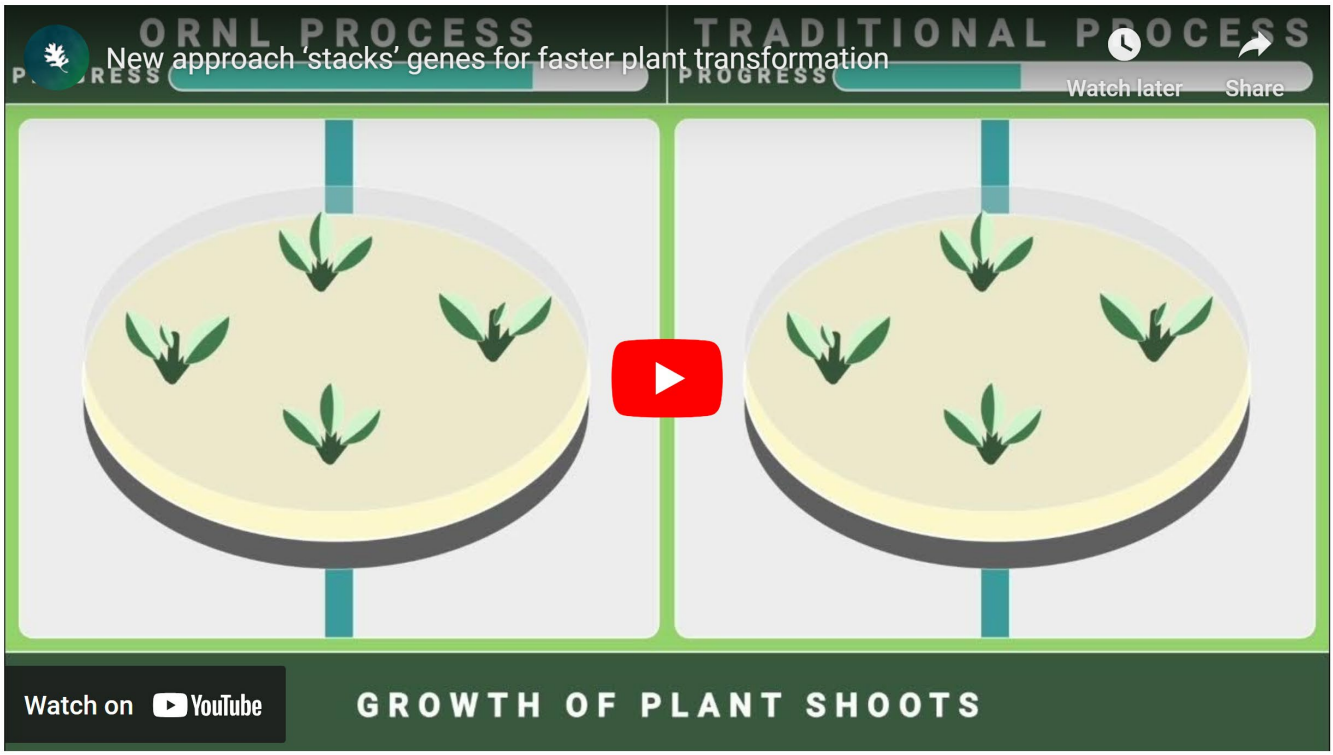
3. Plant multigene engineering system

Oak Ridge National Laboratory (ORNL)

Crop plants are significant sources of food, bioenergy, and biomaterials, with their traits typically controlled by multiple genes. The Plant Multigene Engineering System from Oak Ridge National Laboratory (ORNL) features a novel split selectable marker system that enables the co-transformation of two vectors, each containing a set of genes to be engineered into a single plant species. This system's co-transformation approach differs from traditional methods in that it uses an intein-based split marker system.



ORNL notes that the system offers several advantages over competing technologies: it provides higher efficiency and flexibility in selective agent usage while reducing time and cost requirements. A key feature is the ability to quickly identify transgenic events through two reporter genes visible on leaves under white and ultraviolet light, eliminating the need for expensive equipment or labor-intensive characterization. The technology has applications in plant biotechnology, including genetic engineering for climate change mitigation and improving crops for food, bio-based fuel, biomaterials, and pharmaceuticals. ORNL notes its "primary use is to improve the hardiness and yield of crops."



4. Mixture deconvolution pipeline for forensic investigative genetic genealogy

MIT Lincoln Laboratory

Forensic investigative genetic genealogy (FIGG) emerged as a new, rapidly growing field of forensic science after its use in identifying the Golden State Killer in 2018. FIGG converges familial genealogy with DNA technologies to enable investigative leads in unsolved cases by using direct-to-consumer genetic genealogy databases like 23andMe and Ancestry.com. The technology is in high demand across the international forensic community as it expands available forensic databases. Yet current FIGG searches are limited to single-source DNA profiles.

An estimated 50% of forensic casework samples contain low amounts of DNA, are partially degraded, or are mixtures, which can leave samples from unidentified human remains, violent crime, and matters of national security unresolved. The MIT Lincoln Laboratory's DNA mixture deconvolution software addresses this unmet need by enabling the deconvolution of mixed DNA profiles without requiring matching to reference profiles. The software is currently optimized for two-contributor mixtures but can be tuned for mixtures of up to six different contributors. Testing has succeeded with silico and natural experimental mixtures, achieving 3rd-degree familial matches for more than 61% (72% to 100% for significant contributors) and 4th-degree familial matches for 56% of major contributors.

MIT Lincoln Lab notes that the mixture deconvolution pipeline is "specific to two-person mixtures and commercially available FIGG kits (i.e., ForensSeq Kintelligence SNPs)." Still, it adds that it can be adapted to "enable more complex mixtures and evaluation of other kits."

Product Feature	Lincoln Laboratory Technology	Precision ID Identity Panel, ThermoFisher	ForenSeq Kintelligence Kit, Qiagen	STRMixNGS, STRmix	Competitive Advantage
Estimate the number of contributors in a DNA mixture using SNP DNA profiles	Yes	No, focuses on single-source samples only	No, focuses on single source samples only but provides a quality flag to detect DNA mixtures based on signal imbalance between alleles	No, utilizes short tandem repeats (STRs) only	Ability to estimate the number of contributors in a mixture is essential to enable accurate mixture deconvolution
Estimate concentration for each contributor in a DNA mixture using SNP DNA profiles	Yes	No, focuses on single-source samples only	No, focuses on single source samples only but provides a quality flag to detect DNA mixtures based on signal imbalance between alleles	No, utilizes STRs only	Ability to estimate the concentrations of contributors in a mixture is essential to enable accurate mixture deconvolution
Biological sex determination for each contributor in a DNA mixture using SNP DNA profiles	Yes	No, focuses on single-source samples only	No, focuses on single source samples only but provides a quality flag to detect DNA mixtures based on signal imbalance between alleles	No, utilizes STRs only	Identification of biological sex of each contributor enables investigative leads
Mixture analysis using SNP DNA profiles to identify contributors	Yes	No, focuses on single-source samples only	No, focuses on single-source samples only and can only provide a potential DNA mixture detection flag	No, utilizes STRs only	SNP analysis is required for pairing with FIGG techniques; other technologies focus on single source samples or STR analysis