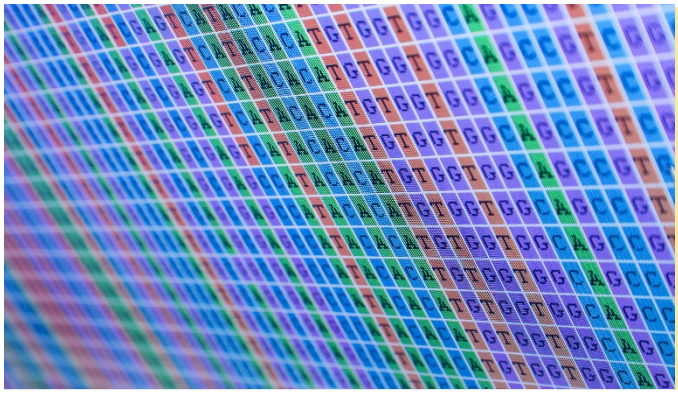
Moving Knowledge from Research to Impact

SUCCESS STORY

NIJ and the American Registry of Pathology

Maximizing the Use of Mitochondrial DNA in Identifying Remains and Aiding Missing Persons Casework



"The complete mtGenome reference data developed in this project serve as important milestones for the understanding of coding region heteroplasmy and the acceptance of full mtGenome sequencing in worldwide forensic genetics."

—Dr. Walther Parson,
Co-PI and Associate Professor, Institute of Legal Medicine, Innsbruck Medical University

Problem and Solution Synopses

Mitochondrial DNA (mtDNA) serves as an important tool in situations where traditional nuclear DNA analysis is unlikely to yield probative information. The high copy number of mtDNA in cells enables it to be recovered in biological evidence where nuclear DNA may be sparse or degraded, such as in aged bones, hair samples, or fingernails. With its basis of maternally inherited genetic information, mtDNA analysis is well suited for missing persons casework because even distant relatives can be used as references when no direct reference sample is available. mtDNA sequencing has traditionally focused on the control region, a small noncoding region of high variability which is used for identification purposes. The utility of the control region in individualization cases is limited because many unrelated individuals share these sequences. Complete sequencing of the mitochondrial genome (mtGenome), which includes coding regions of the molecule, has been shown to more effectively distinguish unrelated individuals[1,2].

The recent development of massively parallel sequencing (MPS) technologies has enabled complete mtGenome sequencing to be utilized for forensic casework. Although mtGenome sequence data have long been available in resources such as GenBank, they do not properly represent randomly sampled populations and do not meet the stringent data quality standards required for use in the forensic context. Datasets may have errors or lack important parameters for mtDNA analysis.

To address the gap in population data, the NIJ funded an award with Principle Investigators Drs. Jodi Irwin, Rebecca Just, and Walther Parson whom developed a forensic-quality mtGenome population database with more than 500 complete mtGenomes spanning three U.S. population groups. The work expanded the reference population database of the Armed Forces Medical Examiner System (AFMES), which has used mtDNA to identify the country's missing servicemen since 1991. The team also enhanced the existing European DNA Profiling (EDNAP) mitochondrial DNA population database project (EMPOP) with new tools and infrastructure to create a searchable database of full mtGenome data[1]. This database offers a foundation of forensically robust reference population data, with complete and accurate information which will ultimately improve discrimination between forensic samples with distinct maternal lineages.

Key Benefits

- Eases adoption of a technique that has demonstrated an enhanced ability to identify missing persons using mtDNA
- Provides accessibility to no-cost, forensic-quality mtGenome population data which improves discrimination between samples
- Improves the understanding of genetic mtDNA rarity between individuals
- Enables continuous improvement of the mtGenome population database
- Ensures incorporation of high quality population data, as EMPOP team evaluates quality of submission data

Published: April 2018

More Information

To learn more about the research presented in this success story, please contact:

Timothy McMahon, PhD
Chief of Forensic Services
Armed Forces DNA Identification Laboratory
timothy.p.mcmahon10.civ@mail.mil

To learn more about the FTCoE and the impact of NIJ research, please contact:

Jeri Ropero-Miller, PhD, F-ABFT
Director, FTCoE
RTI International
jerimiller@rti.org

Gerald LaPorte, MSFS
Director, Office of Investigative and Forensic Sciences
gerald.laporte@usdoj.gov

Research Support

The research presented in this success story was supported by NIJ award 2011-MU-MU-K402: Maximizing mtDNA Testing Potential with the Generation of High-Quality Genome Reference Data

Disclaimer

NIJ Research

Support from the National Institute of Justice (NIJ) enabled the investigators to expand mtDNA databasing efforts to include complete mtGenome through IRB-approved collaborations with the Armed Forces DNA Identification Laboratory (AFDIL) and European DNA Profiling (EDNAP) mtDNA Population Database (EMPOP) group. NIJ support played an instrumental role in development of a robust database infrastructure which currently enables submission and use of high quality datasets contributed by the forensic community.

Bringing Research to Practice

- More than 550 complete and forensically sound mtGenome profiles were sequenced across three U.S. population groups, helping to expand a unique reference population database that enables forensic use of the mtGenome.
- Reference population database has been used to build new tools within AFMES' existing LIMS system to enable analysis of mtGenome.
- Population data have been entered into the GenBank and EMPOP databases and published for public use[2].
- The EMPOP database is currently accepting mtGenome submissions to improve the tool. The team evaluates submitted population data to maintain the high quality of the database. Contributors can add to the database by direct submission to EMPOP through visiting https://empop.online/contribute.
- More than 50 presentations and 11 publications have been authored by the research team.

The Future

The complete mtGenome reference database will enable enhanced identification capabilities for laboratories that currently use mtNDA for identifying missing persons. The AFDIL has already validated an MPS-based mtGenome sequencing assay, and other operational laboratories in the U.S. are currently validating MPS protocols for complete mtGenome sequencing related to their missing persons casework.

The EMPOP team will continually improve the population database by adding more forensic-quality mtGenome data developed by collaborating laboratories around the world. The team anticipates rapid adoption of this high-quality database as MPS protocols for mtGenome sequencing are implemented in forensic casework.

[1]King JL, B.L. LaRue, N.M. Novroski, M. Stoljarova, S.B. Seo, X. Zeng, et al., High-quality and high-throughput massively parallel sequencing of the human mitochondrial genome using the Illumina MiSeq, Forensic Sci. Int. Genet. 12 (2014) 128–135.

[2]R.S. Just, M.K. Scheible, S.A. Fast, K. Sturk-Andreaggi, A.W. Röck, J.M. Bush, et al., Full mtGenome reference data: development and characterization of 588 forensic-quality haplotypes representing three U.S. populations, Forensic Sci. Int. Genet. 14 (2015) 141–155.

Image Credit (Page 1): taraki/Shutterstock.com