B111 Eye, Hair, and Skin Color Prediction Using the HIrisPlex-S (HPS) System and Massively Parallel Sequencing (MPS)

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Learning Overview: After attending this presentation, attendees will understand the field of Next Generation Sequencing (NGS) technologies by exploring the capabilities of the integration of the HIrisPlex-S (HPS) System and Massive Parallel Sequencing (MPS).

Impact on the Forensic Science Community: This presentation will impact the forensic science community by outlining the advantages of Next Generation Sequencing technologies and illustrate how they can be used successfully in DNA phenotyping to help as investigative leads in forensic casework, anthropological cases, and missing persons cases.

Forensic DNA Phenotyping acts as a "biological eyewitness." It can predict externally visible characteristics from a small sample of DNA, and provide investigative leads in anthropological cases, missing person cases, and forensic casework. Fundamental genetics research has led to a better understanding of the specific variants responsible for physical appearance characteristics, particularly eye, hair, and skin color. With this knowledge, the prediction model system termed 'HIrisPlex-S' with model parameters generated from thousands of individuals combines the categorical prediction of these three pigmentation traits in one using only 41 variants of DNA. Currently, average prediction accuracies are approximately 95% for blue or brown eye color, 83% for red, blond, brown, or black hair color and 86% for very-pale, pale, intermediate, dark or dark-to-black skin color. The most probable pigmentation profile can be obtained once these variants are uploaded to the freely accessible online prediction tool found at https://hirisplex.erasmusmc.nl.

At present, these 41 variants can be generated from two developmentally validated capillary electrophoresis assays to generate the required input genotypes.[1,2] However, due to next generation sequencing technologies and the use of Massive Parallel Sequencing (MPS) in assay design, here the authors describe a validated MPS assay for use on both the Ion Torrent and MiSeq systems that is capable of producing fragments that incorporate all HIrisPlex-S variants in one sensitive assay. By integrating the HIrisPlex-S system with a fully automated sequencing pipeline, high throughput data can be generated and uploaded to the on-line tool for an easier workflow at a lower cost. In addition, due to the nature of sequencing and the generation of data surrounding the required prediction variant, it allows the capacity to better deconvolute mixtures. It is also one step closer to adding all known physical appearance prediction markers, beyond pigmentation, into a single library preparation for Massive Parallel Sequencing, creating a true biological sketch. The HPS-MPS assay now overcomes a large hurdle in forensic DNA phenotyping as physical appearance predictions can now be possible with mixtures in addition to single source DNA profiles.

Reference(s):
1. Walsh et al., *Developmental validation of the HIrisPlex system: DNA-based eye and hair color prediction for forensic and anthropological usage.* Forensic Science International Genetics 9: 2013.
2. Chaitanya et al., *The HIrisPlex-S system for eye, hair and skin color prediction from DNA: Introduction and forensic developmental validation.* Forensic Science International Genetics 35: 2018.

Phenotype, Prediction, Sequencing