mtDNAprofiler

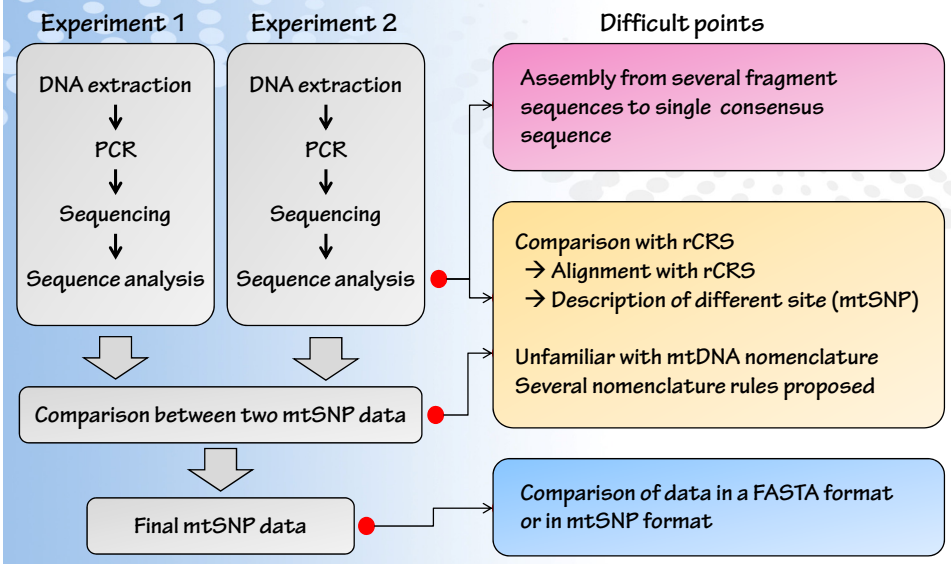
A web based Program for Nomenclature and Comparison of mtDNA Sequences

In Seok Yang
Dept. of Forensic Medicine
Yonsei University College of Medicine

Human mitochondrial DNA (mtDNA)

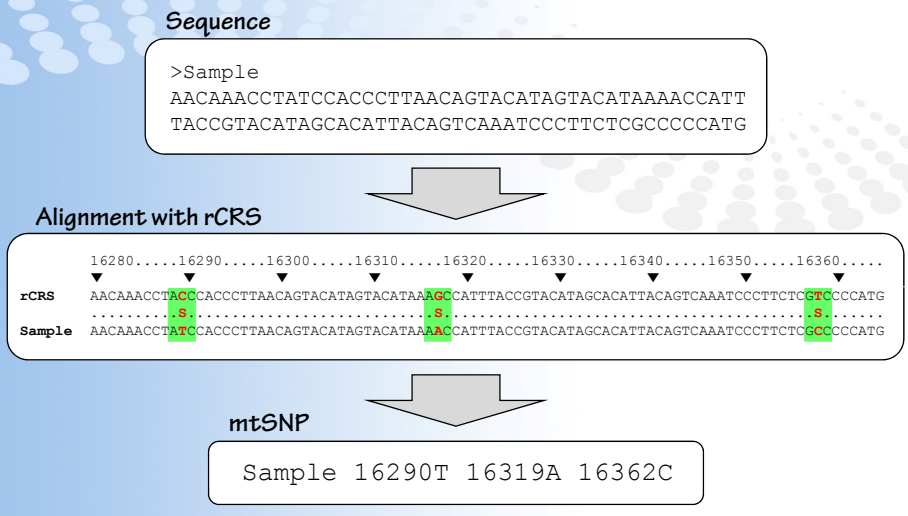
- Characteristics
  - 16,569 base pair, circular DNA
  - Maternal inheritance, high mutation rate, high copy number, lack of recombination
  - Certain mutations in mtDNA → diseases or clinical phenotypes
- Applications
  - Population genetics → genetic difference among populations
  - Medical genetics → diseases related with mtDNA variations
  - forensic genetics → personal identification

Human mtDNA analysis from samples



Page ▪ 3

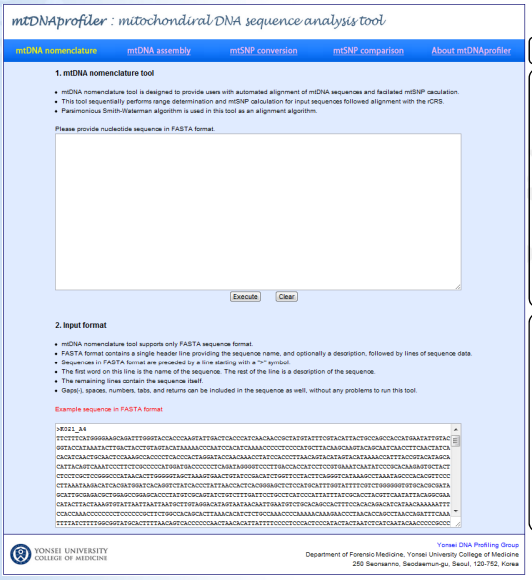
Nomenclature : mtDNA seq → mtSNP



Page ▪ 4

mtDNAprofiler (http://mtprofiler.yonsei.ac.kr)

- **Four tools**
  1. mtDNA nomenclature
  2. mtDNA assembly
  3. mtSNP conversion
  4. mtSNP comparison
- **Development**
  1. Web environment
  2. Language : PHP
  3. Operating system : Linux
  4. Web-service program : Apache HTTP server



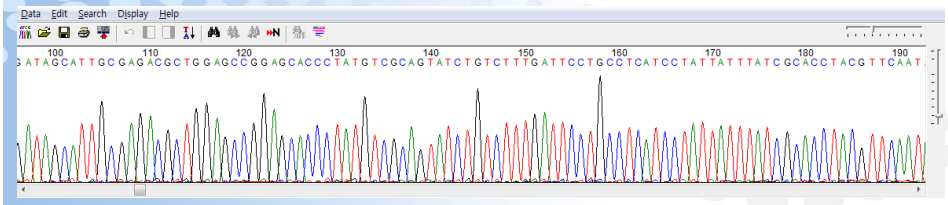
Main menus

Each tool

Input format

Sample sequences → FASTA format

Electropherogram profile




```
>PK-028-F3144
AGAACCCTAACACCAGCCTAACCAGATTTCAAATTTTATCTTTTGGCGGTATGCACTTTTAACAGTCACCCCCCAACTAACACATTATTTTCCCCTCCCACTCCCATACTACTAATCTCATCAATACAACCCCCGCCCATCCTA
>PK-028-F16524
GATGGATCACAGGTCTATCACCCTATTAACCACTCACGGGAGCTCTCCATGCATTTGGTATTTTCGTCTGGGGGGTGTGCACGCGATAGCATTGCGAGACGCTGGAGCCGGAGCACCCTATGTCGCAGTATCTGTCTTTGATTC
>PK-028-R0424
TCGTGATGTCTTATTTAAGGGGAACGTGTGGGCTATTTAGGCTTTATGACCCTGAAGTAGGAACCAGATGTCGGATACAGTTCACTTTAGCTACCCCCAAGTGTTATGGGCCCGGAGCGAGGAGAGTAGCACTCTTGTGCGGGA
>PK-028-R6354
AGGAGGTAGCTACATAAACTGTGGGGGGTGTCTTTGGGGTTTGGTTGGTTCGGGGTATGGGGTTAGCAGCGGTGTGTGTGTGTGNTGGGTAGGATGGGCGGGGGTTGTATTGATGAGATTAGTAGTATGGGAGTGGGAGGGC
>PK-028-R6354
GAGGAGGTAGCTACATAAACTGTGGGGGGTGTCTTTGGGGTTTGGTTGGTTCGGGGTATGGGGTTAGCAGCGGTGTGTGTGTGTGNTGGGTAGGATGGGCGGGGGTTGTATTGATGAGATTAGTAGTATGGGAGTGGGAGGC
```

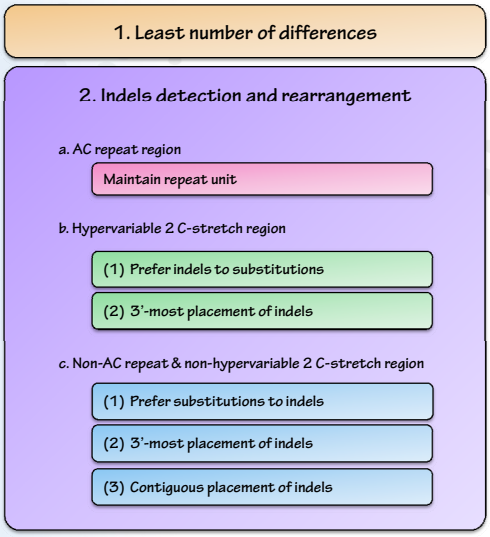
Sample sequences in FASTA format

mtDNA nomenclature protocol

1. Alignment in mtDNAprofiler basically uses parsimonious Smith-Waterman algorithm and follows alignment rules which is selected by scientific working group on DNA analysis methods (SWGDAM).

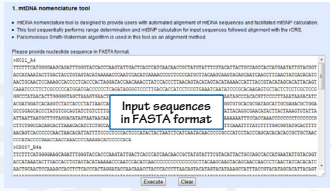
2. Its protocol is composed of two main rules as following: least number of differences and indels (insertions and deletions) detection and rearrangement.

3. Second rule is further divided into three sub-rules, which selects one rule according to the region.

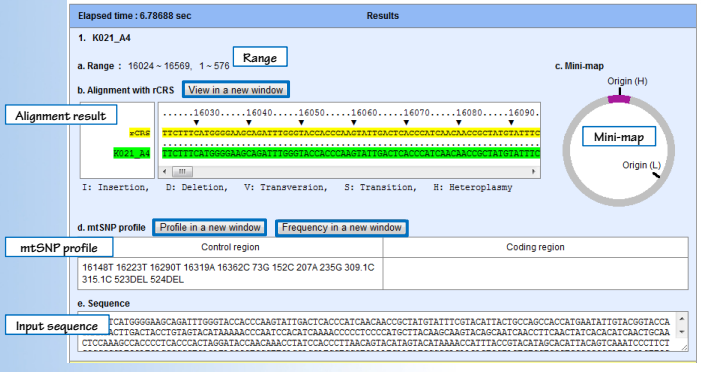


1. mtDNA nomenclature tool

mtDNA nomenclature tool is designed to provide users with mtSNP data through automated alignment of mtDNA sequences with rCRS.

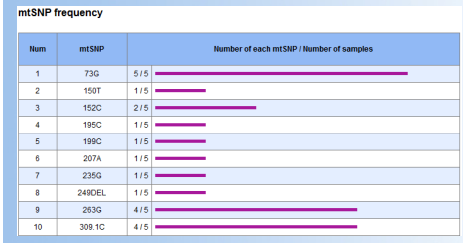


Start page

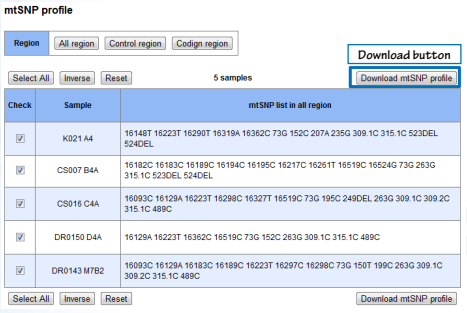


Result page

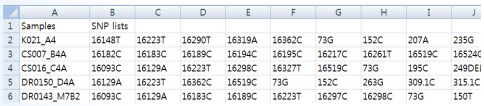
Alignment results in a new window



mtSNP frequency in a new window



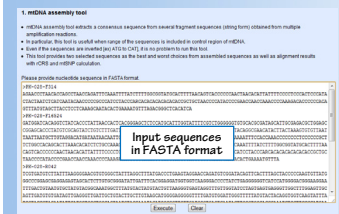
mtSNP profile in a new window



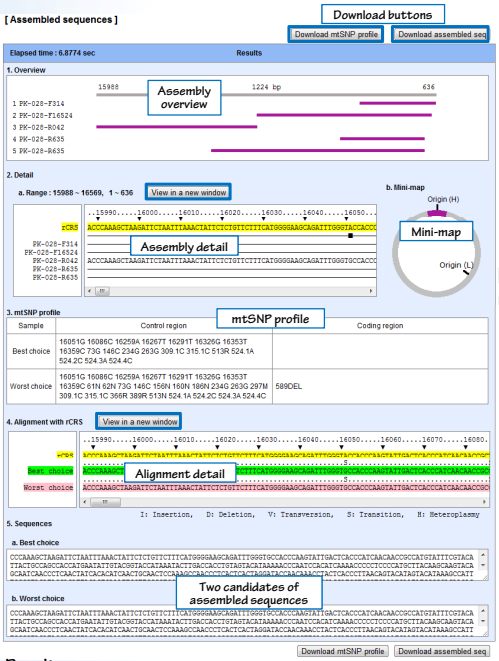
mtSNP profile in downloaded file

2. mtDNA assembly tool

The mtDNA assembly tool extracts a consensus sequence from several mtDNA fragment sequences obtained from multiple amplification reactions.



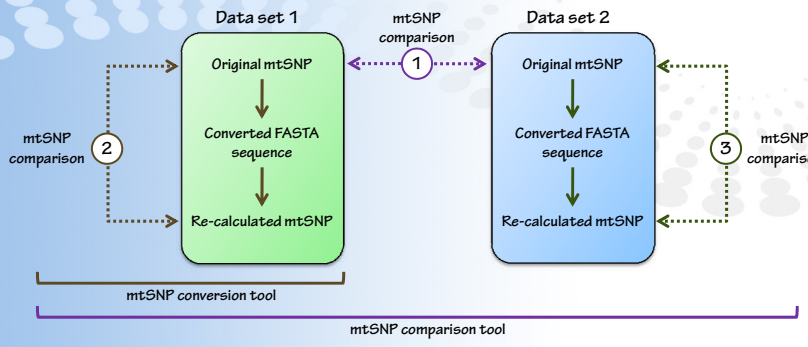
Start page



Result page

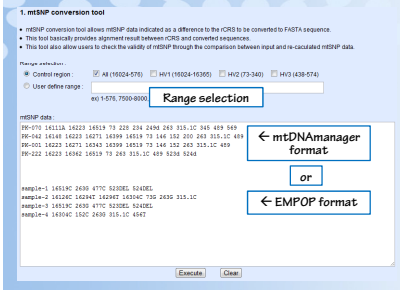
Protocols of two mtSNP tools

- mtSNP conversion and comparison tools

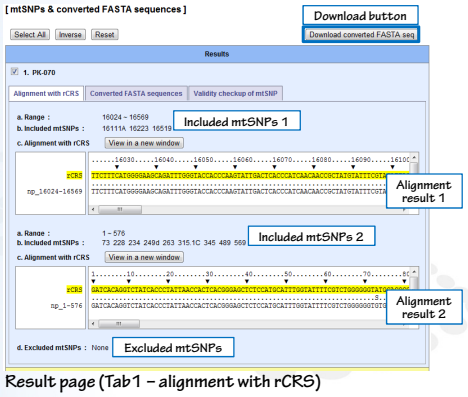


1. mtSNP conversion tool : mtSNP list → nucleotide sequence in FASTA format
2. mtSNP comparison tool : Comparison function between two mtSNP data gathered from independent two experments
3. Both tools have validity checkup function for the mtSNP in comparison with original input mtSNP and re-calculated mtSNP.

3. mtSNP conversion tool

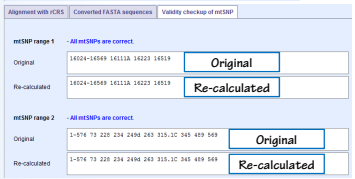


Start page – single data set input



Result page (Tab1 – alignment with rCRS)

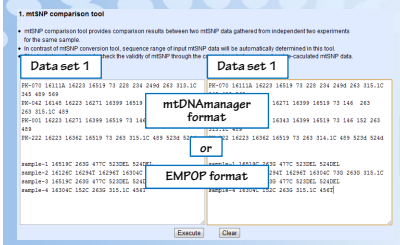
← Tab2 – Converted FASTA sequences



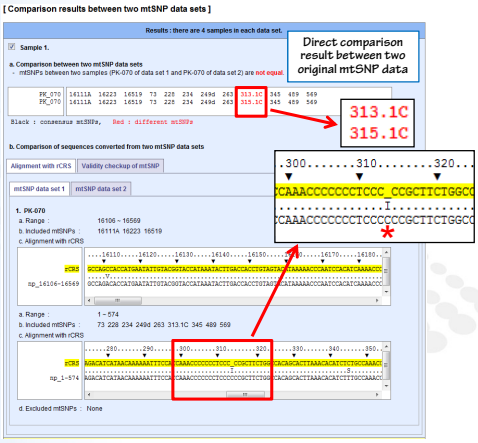
← Tab3 – Validity checkup of mtSNP

The mtDNA assembly tool extracts a consensus sequence from several mtDNA fragment sequences obtained from multiple amplification reactions.

4. mtSNP comparison tool

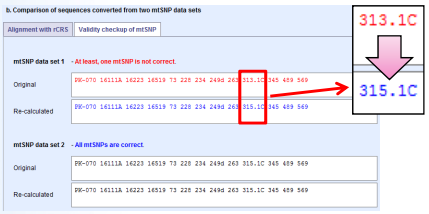


Start page – two data sets input



Result page (Tab1 – alignment with rCRS)

mtSNP comparison tool provides comparison results between two mtSNP data gathered from independent two experiments for the same sample.



Tab2 – Validity checkup of mtSNP

Conclusion

1. The description and analysis of mtDNA sequence variations compared to rCRS can be easily carried out using mtDNA nomenclature tool of mtDNAprofiler.

2. mtDNA assembly tool allows users to extract a consensus sequence from several fragment sequences of mtDNA.

3. mtSNP conversion and comparison tools help users to compare and manage the mtSNP data gathered by two independent experiments.

4. Therefore, mtDNAprofiler is a useful program to characterize and analyze mtDNA sequences for researcher dealing with mtDNA.


Thank you