（様式２）

令和４年度研究助成（参加費助成）研究成果報告書

2022 年 10 月 17 日

公益財団法人遺伝学普及会 代表理事 殿

貴財団より助成のありました研究の成果を下記のとおり報告します。

Dauyey Kaisar 氏名 印

出席学会等名称

開 催 場 所 The Lancet Summit: Sex and gender in rheumatology

開 催 期 間 2022 年 9 月 22 日 ～ 2022 年 9 月 23 日

研 究 成 果 の 概 要

The title of my poster presentation was “Polygenic prediction of rheumatic conditions using ancient DNA”. The conference was dedicated to recent discoveries in the field of rheumatology covering multidisciplinary approaches to complex diseases. Polygenic predictions form the basis of understanding genetic component of many rheumatic diseases. My presentation was among the few addressing such diseases as systemic lupus erythematosus (SLE), ankylosing spondylitis (AS) as well as Bechet’s disease.

I used genetic markers of rheumatic and bone diseases obtained from large-scale meta-analysis of genome-wide association studies to infer polygenic risks. The DNA sequence used for analysis belonged to an Funadomari Jomon individual (discovered in Hokkaido, Japan) having extremely high-quality genome sequence available (estimated age about 3,700 years BP with read peak depth 48X) as well as reference open-source dataset of 1000 Genomes Project.

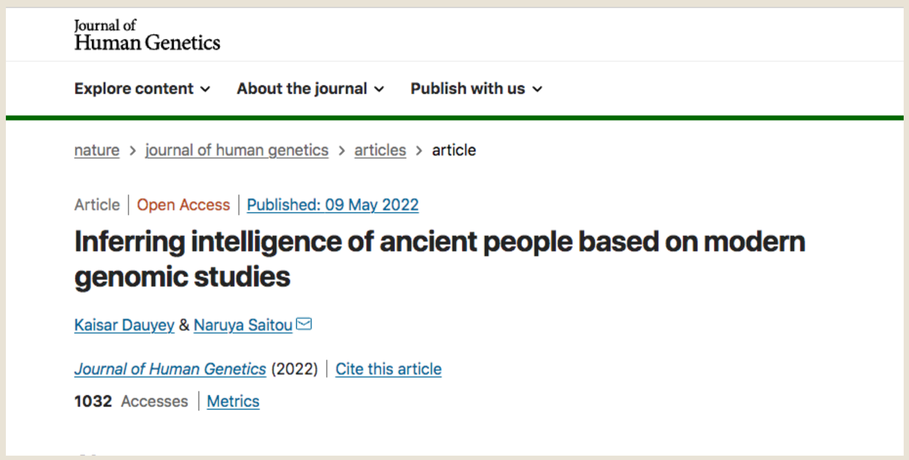
Funadomari Jomon SLE polygenic score fell 2.5 SD below population mean of 1000 Genomes Project, while AS polygenic risk score significantly above the mean suggesting low risk for developing SLE and high risk for AS. Archeological evidence confirmed that this ancient female individual was likely overweight and of short stature with some bone deformities. These results demonstrate that ancient DNA can be used for polygenic predictions and highlight the gender differences in developing rheumatic conditions in 3,700 years old individual. More detailed studies of Funadomari skeleton including high-resolution bone scanning as well as morphological examination are needed to confirm findings obtained from polygenic predictions.

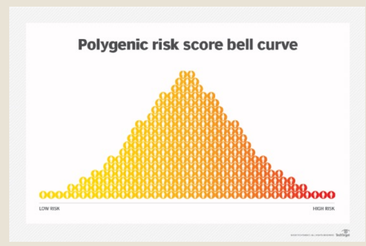
I attached the certificate of my presentation to this report.

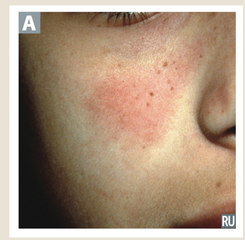
Polygenic prediction of rheumatic conditions using ancient DNA

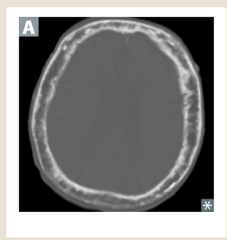
National Institute of Genetics, JAPAN
Kaisar Dauyey MD

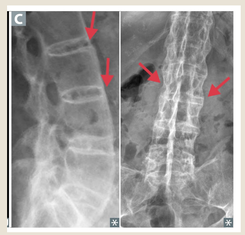
Figure 2. Photo of female 23 (F23), whose genomic DNA sequence was determined. Scale bar = 10 cm.











$$Score_{person} = SNP(1) * Effect(1) + \cdots + SNP(n) * Effect(n)$$

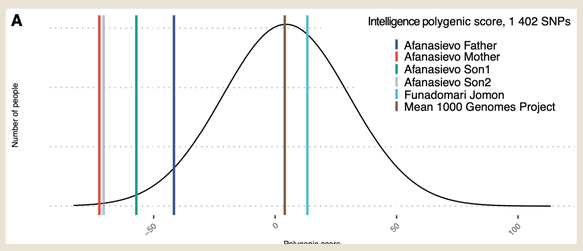
I utilized GWAS results to predict risks for developing rheumatic/bone conditions in an ancient human. Her scores were compared to same scores from 1000 Genomes subjects.

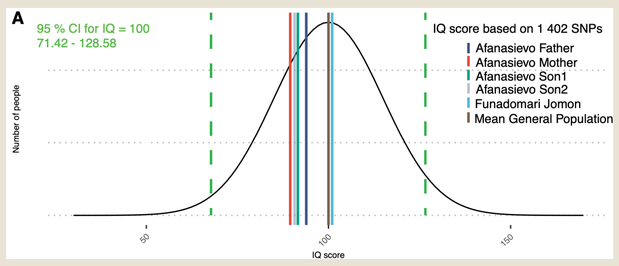
Studies used for PGS derivation:

Systemic lupus erythematosus (PMID 28714469) Zscore -2.485

Paget's disease (PMID 21623375) Z-score 1.983

Ankylosing spondylitis (PMID 23749187) Z-score 1.658





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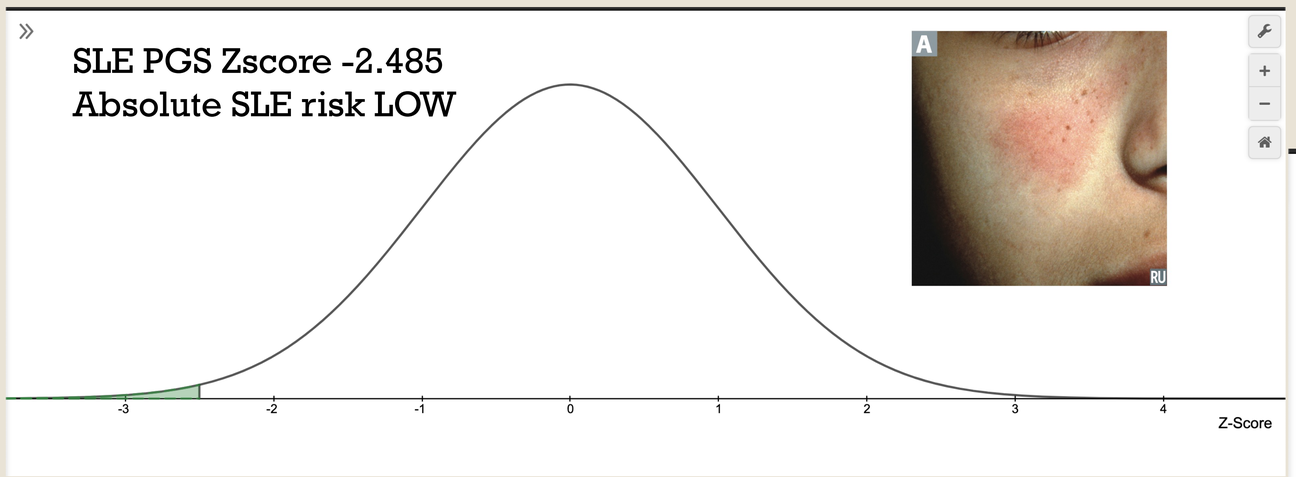
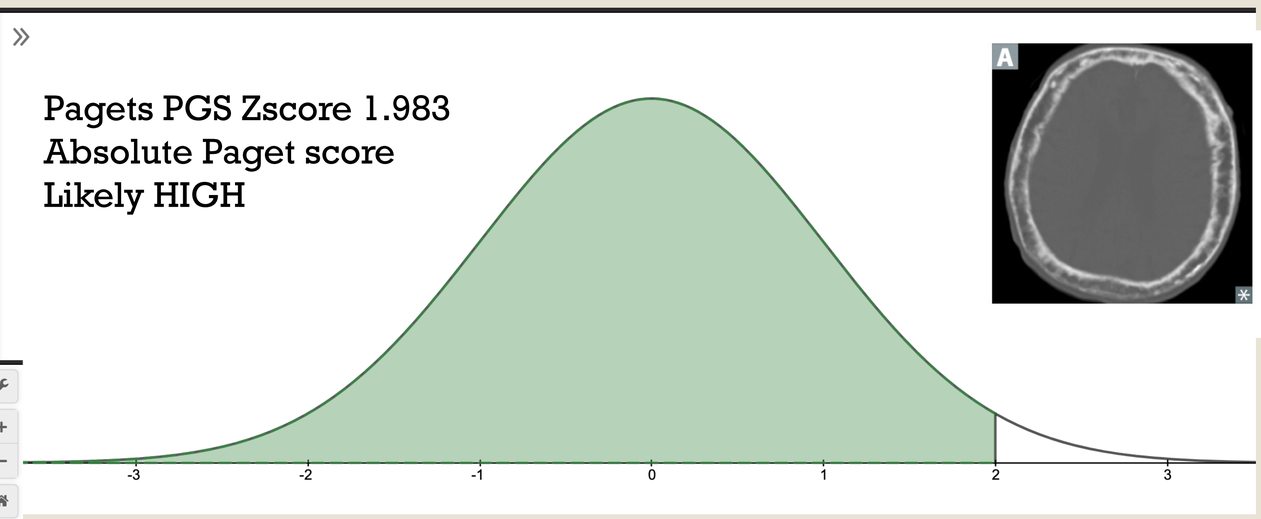
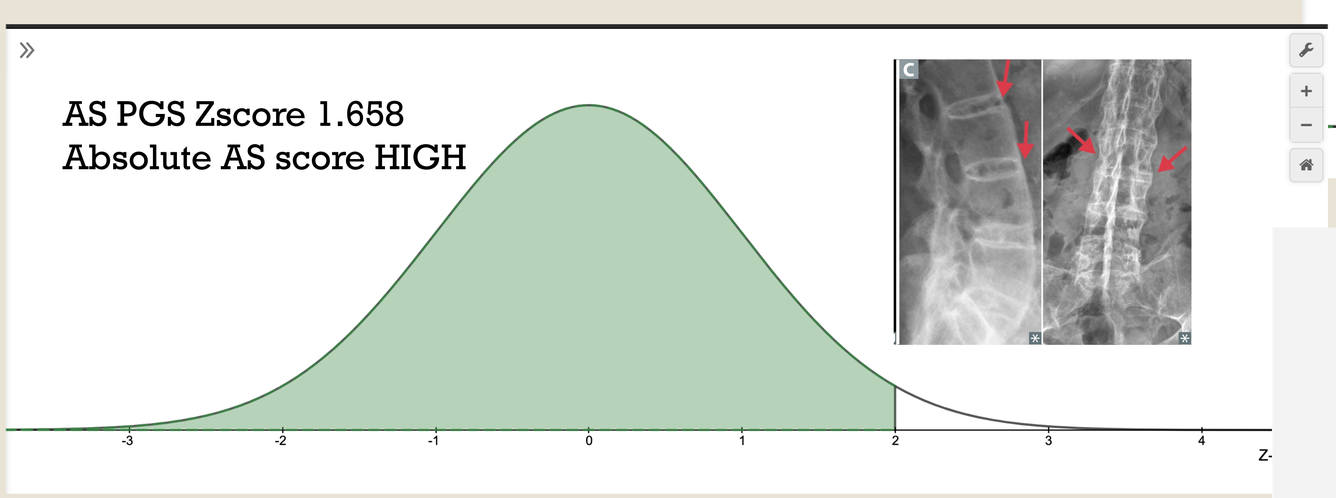
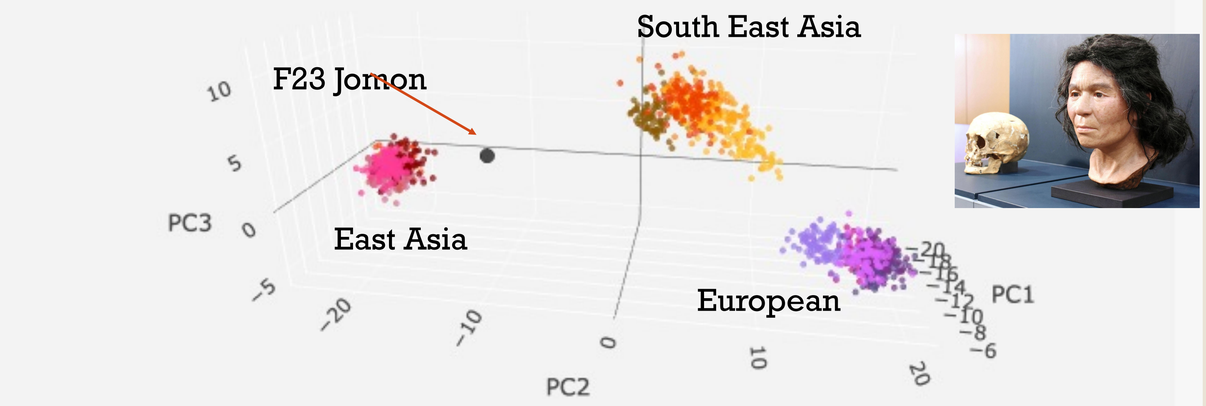




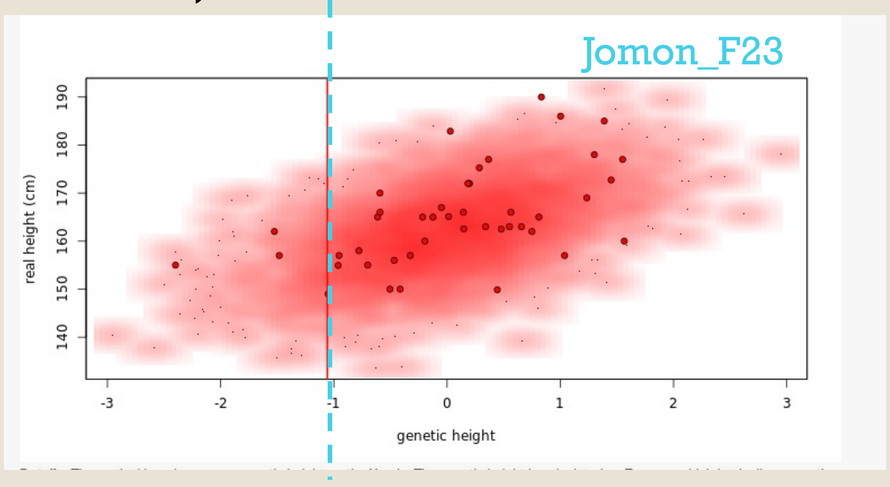




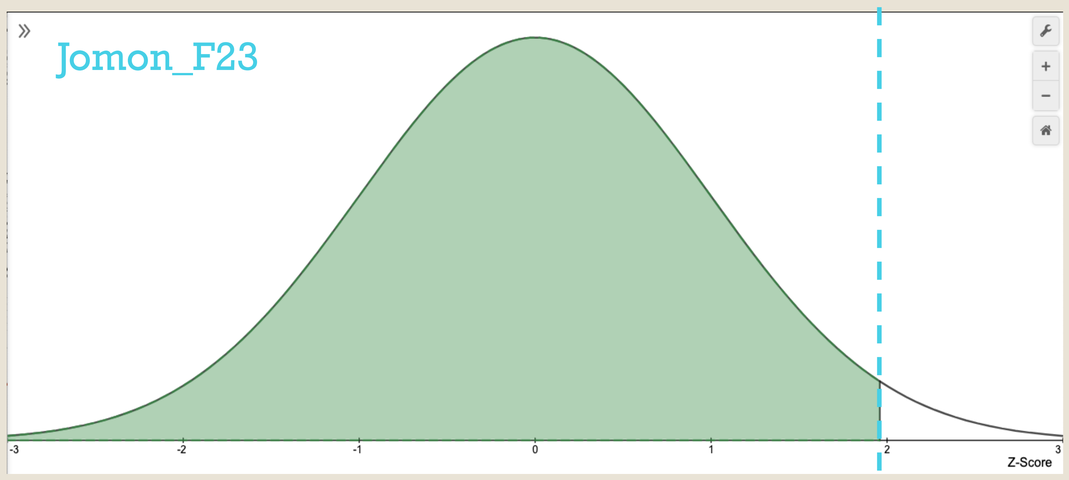
(Image: © The National Museum of Nature and Science, Tokyo)

- Funadomari Jomon Female
- Excavated in Northern Japan
- Estimated age ~ 3 700 years BP
- SNPs extracted across 22 chromosomes
- Total SNPs 1447035
- Biallelic, whole genome based
- 90% genotype call rat
- Submitted to IMPUTE.ME
- Absolute Risks converted from PGS

Polygenic score for height – 5000 SNPs Chung et al. 2019 (Z-score = -0.98) – short stature



Polygenic score for BMI – 751 SNPs Yengo et al. 2019 (Z-score = 1.96) – overweight



Reference:
1. Dauyey K & Saitou N. 2022 Inferring intelligence of ancient people based on modern genomic studies. Journal of Human Genetics; https://doi.org/10.1038/s10038-022-01039-8
2. Kanzawa-Kiriyama, Hideaki, et al. "Late Jomon male and female genome sequences from the Funadomari site in Hokkaido, Japan." *Anthropological Science* (2019): 190415.
3. Pain, O., Gillett, A.C., Austin, J.C., Folkersen, L. and Lewis, C.M., 2022. A tool for translating polygenic scores onto the absolute scale using summary statistics. European Journal of Human Genetics, 30(3)
4. Folkersen, Lasse, et al. "Impute. me: an open-source, non-profit tool for using data from direct-to-consumer genetic testing to calculate and interpret polygenic risk scores." Frontiers in Genetics 11 (2020).