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# Human genetic history of New Guinea

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## CONTEXT

Recent studies have enlightened the complexity of the genetic landscape present in New Guinean populations. From the New Guinean genome, inherited from the Out-of-Africa dispersal 60 000 years ago, to the gene flows from Austronesian groups during the Holocene, and even to the high percentage of genetic introgression from an extinct Homo species named Denisova, the biological diversity of New Guineans is unique. It is a result of the various human migrations to the island but also within its territory, composed by a variety of different ecosystems. These processes created high genetic differentiations between New Guinean groups, a pattern that superficially mirrors the one drawn from the linguistic diversity, one of the highest in the world, with more than 900 languages. Despite these results, major issues remain unresolved regarding New Guinean genetic history. Since 2016, thanks to the French Ministry of Foreign Affairs and the University of Papua New Guinea, we have developed an international and interdisciplinary research project aiming:

- 1/ to reconstruct the demographic history of the island from the first settlement to the subsequent internal migrations
- 2/ to characterise the selective forces that influenced the New Guinean genome



Figure 1. Presentation of the project to a local community in New Guinean highlands (Waghi valley, Western Highlands, 2017).

### New sampling for the entire New Guinea Island

- Over 250 participants representing a large cultural diversity
- Anthropological questionnaires (ex: language, genealogy)
- Whole genome sequencing (30X) combined with large worldwide datasets
- Phenotypic data linked to environmental contexts (ex: pathogenic pressure, altitude)

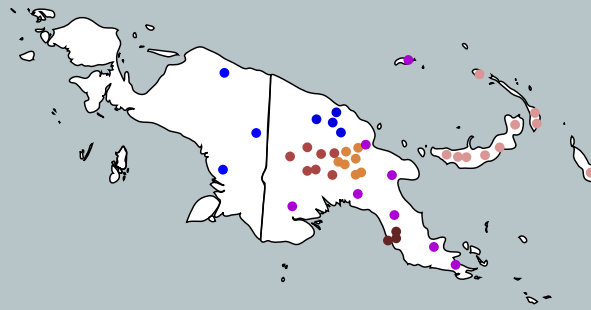


Figure 2. Locations of sampled individuals. Color scheme corresponds to the genetic clustering plotted on the tree branches of Figure 3.

### Biostatistical methods

- Demographic modeling (admixture processes, population divergence)
- Combined analysis of genetic and cultural data (ex: linguistic families, archaeological artifacts)
- Scan for signal of Selection in populations subjected to different environmental contexts
- Genome-wide association studies with phenotypes of interest

## RESULTS ON DEMOGRAPHY

Using a large dataset of 937 individuals including new whole genome data from Papua New Guinea and West Papua, and imputed data from available genotyping arrays, we decomposed the genetic diversity in New Guinea to identify relationships and gene flows (Figure 3).

New Guinean genomes can be described by six statistical clusters corresponding to large geographical areas, notably between New Guinea and surroundings islands, as well as within New Guinea between the highlands and the coasts, and even between western and eastern highlands.

Four genetic ancestries can be decomposed from the Papuan genetic diversity, along with a Southeast Asian component mostly present on the coasts. These genetic ancestries are present in different proportion across the island suggesting intense contacts between Papuan groups.

It reveals that the Papuan genetic patrimony is much more diverse than previously thought. We are currently exploring further the dynamics of gene flows between Papuan groups, notably by dating the migrations.

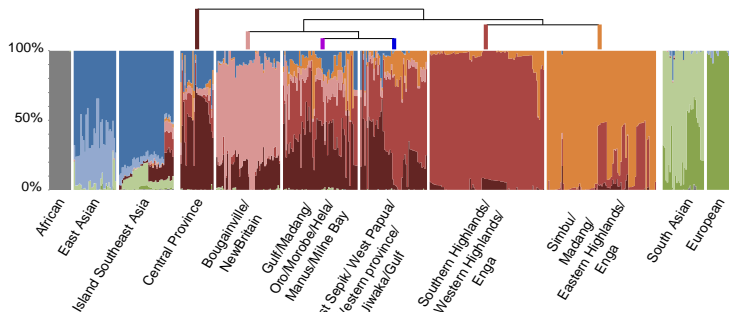


Figure 3. Genetic ancestries and structure in New Guinea. Genetic ancestries were decomposed with ADMIXTURE (K=9 showing the lowest cross-validation). Genetic structure were inferred with fineSTRUCTURE, identified as white bars and the tree for Papuan groups.

## RESULTS ON SELECTION

We analysed the Papuan genetic diversity to identify patterns of Selection in different environmental contexts using complementary approaches.

Coastal New Guinean genomes show significant signal of Selection in a network of genes involved in the immune response (Figure 4). It reveals a new Adaptive mechanism to the high pathogenic pressure existing on the coasts. Moreover many of the selected variants are of probable Denisova origin.



Figure 4. Average local ancestry plot on chromosome 1 of coastal Papuans. Local ancestry tracks were estimated with RFmix and PCAdmix. Papuan ancestry is in red and Asian ancestry in blue. Significant hit is represented by a star symbol (3S.D from the genome-wide mean).

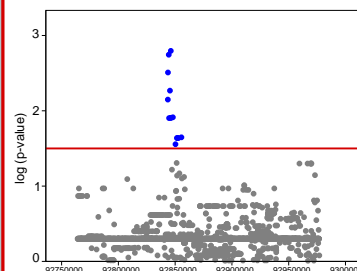


Figure 5. Genetic association test in SLC24A4 gene on melanin index. Significant SNPs are identified in blue ( $p > 0.05$ ). The red line indicate the threshold of significance.

New Guinean genetic variants are significantly associated with phenotypes related to skin protection to UV-light (Figure 5). While some of these genetic variants are located in genes known to be selected in human groups from across the globe, New Guinean genomes revealed new genes potentially under Selection in relation to the concentration of melanin in the skin.

Our analyses unveiled new Adaptive mechanisms specific to New Guinean groups. Ongoing analyses are performed to describe further these findings and new phenotypes will be gathered in relation to the biological fonction of interest,

## Our study shows an unexpected genetic diversity in New Guinea underlying new adaptive responses to the environment.

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