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Understanding a human pangenome map

What is genome sequencing and why is it important? Why is the reference genome map considered one of the most important scientific breakthroughs? What is the difference between a reference map and a pangenome map? How is India hoping to benefit from the latest genome map?

EXPLAINER

Binay Panda

The story so far:

A new study published in the May 10 issue of the *Nature* journal describes a pangenome reference map, built using genomes from 47 anonymous individuals (19 men and 28 women), mainly from Africa but also from the Caribbean, Americas, East Asia, and Europe.

What is a genome?

The genome is the blueprint of life, a collection of all the genes and the regions between the genes contained in our 23 pairs of chromosomes. Each chromosome is a contiguous stretch of DNA string. In other words, our genome consists of 23 different strings, each composed of millions of individual building blocks called nucleotides or bases. The four types of building blocks (A, T, G and C) are arranged and repeated millions of times in different combinations to make all of our 23 chromosomes. Genome sequencing is the method used to determine the precise order of the four letters and how they are arranged in chromosomes. Sequencing individual genomes helps us understand human diversity at the genetic level and how prone we are to certain diseases.

The genome is an identity card like Aadhaar. As each of our Aadhaar card is unique, so is our genome. As sequencing individual genomes of all humans is expensive, we do not yet have all our genome identity cards. To circumvent this, one can have a collective identity card. For example, we can have a single genome identity card for everyone living in a region.

What is a reference genome?

When genomes are newly sequenced, they are compared to a reference map called a reference genome. This helps us to understand the regions of differences between the newly sequenced genome



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and the reference genome. One of this century's scientific breakthroughs was the making of the first reference genome in 2001. It helped scientists discover thousands of genes linked to various diseases; better understand diseases like cancer at the genetic level; and design novel diagnostic tests. Although a remarkable feat, the reference genome of 2001 was 92% complete and contained many gaps and errors. Additionally, it was not representative of all human beings as it was built using mostly the genome of a single individual of mixed African and European ancestry. Since then, the reference genome map has been refined and improved to have complete end-to-end sequences of all the 23 human chromosomes.

Although complete and error-free, the finished reference genome map does not represent all of human diversity. The new study published in *Nature* changes this.

The main paper and the accompanying articles published in the same journal and *Nature Biotechnology* describe the making of the pangenome map, the genetic diversity among the 47 individuals, and the computational methods developed to build the map and represent differences in those genomes.

What is a pangenome map?

Unlike the earlier reference genome, which is a linear sequence, the pangenome is a graph. The graph of each chromosome is like a bamboo stem with nodes where a stretch of sequences of all 47 individuals converge (similar), and with internodes of varying lengths representing genetic variations among those individuals from different ancestries. To create complete and contiguous chromosome maps in the pangenome project, the researchers used long-read DNA sequencing technologies,

which produce strings of contiguous DNA strands of tens of thousands of nucleotides long. Using longer reads helps assemble the sequences with minimum errors and read through the repetitive regions of the chromosomes which are hard to sequence with short-read technologies used earlier.

Why is a pangenome map important?

Although any two humans are more than 99% similar in their DNA, there is still about a 0.4% difference between any two individuals. This may be a small percentage, but considering that the human genome consists of 3.2 billion individual nucleotides, the difference between any two individuals is a whopping 12.8 million nucleotides. A complete and error-free human pangenome map will help us understand those differences and explain human diversity better. It will also help us understand genetic variants in some populations, which result in underlying health conditions. The pangenome reference map has added nearly 119 million new letters to the existing genome map and has already aided the discovery of 150 new genes linked to autism.

Although the project is a leap forward, genomes from many populations are still not a part of it. For example, genomes from more people from Africa, the Indian sub-continent, indigenous groups in Asia and Oceania, and West Asian regions are not represented in the current version of the pangenome map.

Even though the current map does not contain genome sequences from Indians, it will help map Indian genomes better against the error-free and complete reference genomes known so far. Future pangenome maps that include high-quality genomes from Indians, including from many endogenous and isolated populations within the country, will shed light on disease prevalence, help discover new genes for rare diseases, design better diagnostic methods, and help discover novel drugs against those diseases.

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THE GIST

▼ A new study published in the May 10 issue of the *Nature* journal describes a pangenome reference map, built using genomes from 47 anonymous individuals.

▼ A complete and error-free human pangenome map will help us understand differences and explain human diversity better. It will also help us understand genetic variants in some populations which result in underlying health conditions.

▼ Future pangenome maps that include high-quality genomes from Indians, including many endogenous and isolated populations within the country, will shed light on disease prevalence.

Category:

- Prelims
- GS-3

What is a genome?

- Collection of all genes contained in the **23 pairs of chromosomes**. Each chromosome is made up of tightly packed **DNA** and DNAs are repeating units of **nucleotides or bases**. Each nucleotide is composed of one of four nitrogen-containing nucleobases (**cytosine [C], guanine [G], adenine [A] or thymine [T]**), a **sugar called deoxyribose, and a phosphate group**.
- Genome sequencing is a method to determine precisely the order of the four nucleobases in the DNA. This method helps us understand human diversity and how prone we are to certain diseases.

What is a pangenome?

- A human genome reference sequence is an accepted representation of the human genome sequence that is used by researchers as a standard for comparison to DNA sequences generated in their studies.
- The first reference genome was sequenced in **2001** which was **92%** complete.
- A pangenome map refers to the representation and analysis of the collective genetic information present in the genomes of a particular species or a group of related species.
- Unlike a reference genome, which represents a single individual or a consensus sequence, a pangenome map captures the genetic diversity and variation across multiple individuals or populations.
- Built using genomes from **47** anonymous individuals mainly from Africa, also from **Caribbean, Americas, Europe**.
- Although the project is a leap forward, genomes from more people from Africa, Indian sub-continent, indigenous groups in Oceania etc. are yet to be represented in the pangenome reference map.

Why is it necessary?

- It will help us understand human diversity better by knowing the differences of **nucleotides** between different individuals.
- Better understanding of genetic variations which result in health conditions.
 - For ex: This map has already aided discovery of **150 new genes** linked to **autism**.

Indian Govt. initiatives:

- IndiGen Genome Project
- Genome India.

India, U.S. to hike technology cooperation; co-production of jet engines on the table

Dinakar Peri
NEW DELHI

India and the U.S. are discussing possibilities of co-producing jet engines, long-range artillery and infantry vehicles under the Initiative on Critical and Emerging Technologies (iCET) announced earlier this year, and officials said some high-technology initiatives are expected to be announced during Prime Minister Narendra Modi's upcoming visit to the U.S. next month.

Ahead of the visit, the launch of INDUS-X under the iCET to promote partnerships between the two countries' defence innovation ecosystems is scheduled in Washington.

In the run-up to the visit, these issues were discussed at the 17th meeting of India-U.S. Defence Policy Group (DPG), chaired by Defence Secretary Giridhar Aramane from India and Under Secretary of Defence for Policy Colin Kahl last week.

"The two sides reviewed the progress made in furthering defence industrial cooperation and

If the U.S. agrees to transfer jet engine [technology] to India, it sends a very strong message to China

operationalising the India-U.S. Major Defence Partnership. Important aspects such as military-to-military cooperation, and cooperative activities in the Indian Ocean Region were discussed," the Defence Ministry said in a statement.

Enhancing cooperation
The Ministry further said that considerable focus was given on the ways and means to enhance defence industrial cooperation, including technology partnership, long-term research and development, and improving supply chain security.

Officials from both sides confirmed that the jet engine collaboration was discussed during DPG along with other collaboration mechanisms within co-production and co-development.

Among proposals being discussed is to jointly pro-

duce a jet engine for India's future indigenous jets for which General Electric is competing with Safran of France and Rolls-Royce of U.K.

Commenting on this, Mukesh Aghi, president and CEO of the U.S.-India Strategic Partnership Forum (USISPF), said only four countries make jet engines for planes, and India will be the fifth one if the deal is announced.

"So the jet engine deal will take India's capability in the aircraft industry to a new level. The deal also sends a message to the Chinese that the relationship between India and the U.S. is not just a surface relationship and is getting deeper," he told *The Hindu*.

If the U.S. agrees to transfer jet engine [technology] to India, which China doesn't at present have the capability for, it sends a very strong message, Mr. Aghi further said.

Earlier efforts at co-developing a jet engine has failed to take off owing to U.S. domestic legislation.

(With inputs from Suhasini Haidar)

Context:

- PM Modi's scheduled visit to the **USA in June 2023**.
- India and US discussing possibilities of co-producing jet engines, long range artillery and infantry vehicles under iCET.
- Only four countries until now produces jet engines for planes.
 - This deal therefore could take India's aircraft industry to a new level.

Initiative on critical and emerging technologies (iCET):

- Launched by **US President and Indian PM** on the sidelines of **Quad summit (in May 2022)**.
- Aimed at elevating and expanding Indo-U.S. strategic technology partnership and defense industrial cooperation.
- Under iCET, six focus areas of co-development and co-production have been identified:**
 - strengthening innovation ecosystems;
 - defense innovation and technology cooperation;
 - resilient semiconductor supply chains;
 - space;
 - STEM** (science, technology, engineering, and math) talent;
 - next-generation telecom;
- Launch of **INDUS-X** scheduled in advance of PM Modi's US visit (development under iCET).

Category:

- GS-2
- GS-3

Use case:

- Indo-US relations.

What is the 'Open Network for Digital Commerce'?

How does the ONDC intend to achieve a level-playing field for online sellers? Why are major e-commerce players such as Amazon and Flipkart reluctant to join the ONDC?

Prashanth Perumal

The story so far:

The Union government is looking to formally launch the Open Network for Digital Commerce (ONDC) this year to “democratise e-commerce” and “to provide alternatives to proprietary e-commerce sites”. While it has urged companies to join the ONDC platform, major e-commerce players such as Amazon and Flipkart have been reluctant to get on board.

What is the ONDC?

The government wants to change the fundamental structure of the e-commerce market from the current “platform-centric model” to an open-network model”. The ONDC is modelled after the Unified Payments Interface (UPI) project that is seen as a success by many. The UPI project allows people to send or receive money

irrespective of the payments platforms on which they are registered. Similarly, the government wants to ensure that buyers and sellers of goods in the e-commerce market can transact regardless of the platforms on which they are registered. So under ONDC, a buyer registered on Amazon, for example, may directly purchase goods from a seller who sells on Flipkart. To make such transactions a reality, the government has ordered companies to list themselves on the ONDC. The pilot version of ONDC was launched last year in a few major cities and thousands of sellers have already been on-boarded onto the platform. Amazon and Flipkart, however, have not on-boarded their main shopping platforms onto the ONDC network yet.

Why is the Centre pushing for it?

The government believes that the ONDC will put an end to the domination of the e-commerce market by a few large platforms. It says that the e-commerce

market is currently broken into “silos” operated and dominated by private platforms. Amazon and Flipkart, for instance, have been accused of promoting certain seller entities in which they hold indirect stakes. Food delivery apps such as Swiggy and Zomato have also been accused of charging high commissions from sellers. With an open network like ONDC that connects buyers and sellers across platforms, the government hopes to level the playing field and make private platforms redundant.

What do critics say?

Critics argue that the purported benefits of an open network for digital commerce are far from certain at the moment. For one, sellers are already free to list their products across various e-commerce platforms even in today's platform-centric e-commerce model. Buyers also routinely shop across platforms. Then there are also services such as price-comparison that are offered by various private

websites that bridge the information gap and help buyers make better decisions. So, critics argue, the domination of the e-commerce market by platforms such as Amazon and Flipkart may not be due to any captive hold that these platforms have over buyers and sellers. Further, the supposed monopoly that platforms are said to enjoy may be no different from the limited monopoly that any business today has over its property.

What lies ahead?

The capacity of the government's technocrats to come up with an efficient alternative to e-commerce platforms that can work seamlessly will be tested as the government rolls out the ONDC. It remains to be seen if and how the government's open network will list products offered by various sellers. Competition generally pushes e-commerce platforms to prominently list products that are most likely to catch the fancy of buyers. Their on-boarding and listing of sellers is also heavily influenced by the ability of sellers to fulfil customer orders. In fact, platforms may invest money to build exclusive on-boarding and listing processes. If the open network's rules prevent platforms from benefiting from such investments, they may cease to make them anymore. This will eventually affect the quality of services available to consumers. Building an efficient marketplace for the sale of goods and services may turn out to be the key challenge for ONDC.

THE GIST

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▼ The government believes that the ONDC will put an end to the domination of the e-commerce market by a few large platforms.

▼ Building an efficient marketplace for the sale of goods and services may turn out to be the key challenge for ONDC.

Category:

- Prelims
- GS-2

What is ONDC?

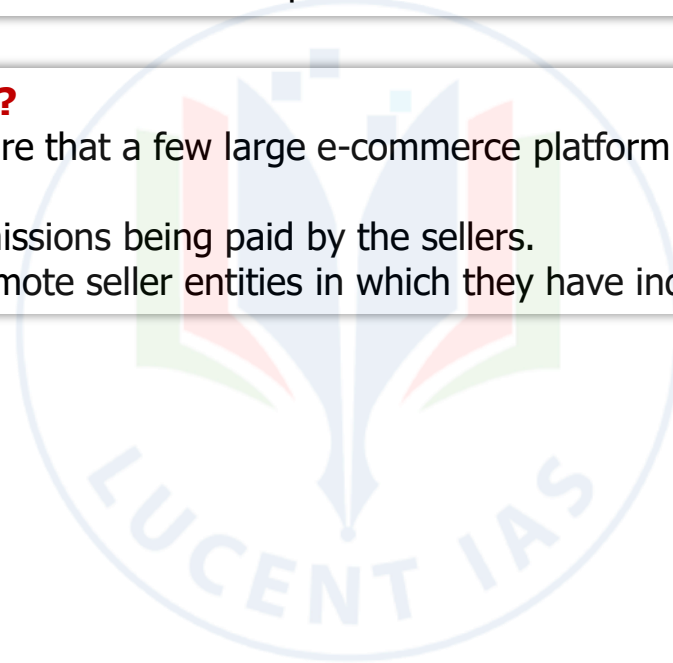
- ONDC is modelled after the **Unified Payments Interface (UPI)** with an idea to change the fundamental structure of e-commerce market from platform centric model to an open-network model.
- Initiated by the **Government of India**.
- Through ONDC, Govt wants to ensure sellers and buyers can transact regardless of the platforms.
- For this to be achieved, companies need to list themselves on ONDC.

Challenges with the proposed scheme:

- Uncertainty with the benefits to be accrued.
- Most sellers are registered already across platforms. Also price comparisons across platforms make the e-commerce market very competitive.
- Most platforms invest to build exclusive on-boarding and listing processes. ONDC may cease them to benefit from such investment also affecting the quality.
- To provide for an efficient and better place for such transactions.

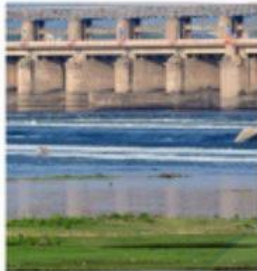
Why is it necessary?

- Govt. wants to ensure that a few large e-commerce platform do not dominate the market.
- To avoid high commissions being paid by the sellers.
- Many platforms promote seller entities in which they have indirect stakes.



Stalemate over sharing of Krishna water to continue

B. Chandrashekhara
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Surplus water being discharged from Prakasam Barrage across Krishna river in Vijayawada. FILE PHOTO: G.N. RAO

With no resolution in sight over sharing of the Krishna river water between Telangana and Andhra Pradesh after the bifurcation, the stalemate is set to continue in the next water year, beginning June 1.

Telangana has made its stand clear at the recent meeting of the Krishna River Management Board (KRMB) that it would, under no circumstances, agree for the 34:66 (Telangana :Andhra Pradesh) ratio 'forced' upon it since the bifurcation for one more year. It highlighted the fact that judicious sharing of river water was one of the main planks of the Statehood movement.

"Telangana is entitled for 70% share in 811 tmc ft allocated to combined Andhra Pradesh by the KWDT-I Award as per the basin parameters, but the erstwhile A.P. had apportioned it in 512:299 tmc ft (A.P.:Telangana) ratio without protecting the in-basin requirements in the fluoro-ride and drought-affected areas of Telangana," Special Chief Secretary (Irrigation) of Telangana Rajat Kumar said.

Another senior official in the Irrigation Department stated that Andhra Pradesh is diverting about 300 tmc ft water out of 512 tmc ft to the areas outside the Krishna Basin, treating it as its right, forgetting the fact it is gross violation of KWDT-I Award.

KWDT-I had made it clear that in-basin needs be given preference over the needs of areas outside the basin while taking up new projects too.

After Telangana made it clear that it would not be a party to the orders issued by the board, without its consent for continuation of the existing arrangement, the board chairman has said that the matter would now be referred to the Ministry of Jal Shakti.

Category:

- Prelims
- GS-2

Context:

- Dispute between **Telangana and Andhra Pradesh** over the waters of **Krishna River**.
- Constitutional provision relating to such **water disputes** covered under **Article 262**.
- **Article 262 empowers the Parliament entirely** to legislate for adjudication of such matters.
- **Inter-State River Water Dispute Act 1956** was legislated under the provisions of said article.
- The act provides for creation of tribunals when necessary to settle cases.
- Major Inter-State River Disputes:
 - **Ravi and Beas:** Punjab, Haryana, Rajasthan
 - **Narmada:** Madhya Pradesh, Gujarat, Maharashtra, Rajasthan
 - **Krishna:** Maharashtra, Andhra Pradesh, Karnataka, Telangana
 - **Vamsadhara:** Andhra Pradesh & Odisha
 - **Cauvery:** Kerala, Karnataka, Tamil Nadu and Puducherry
 - **Godavari:** Maharashtra, Andhra Pradesh, Karnataka, Madhya Pradesh, Odisha
 - **Mahanadi:** Chhattisgarh, Odisha
 - **Mahadayi:** Goa, Maharashtra, Karnataka
 - **Periyar:** Tamil Nadu, Kerala