**The Y of Sex**

**Zareena, Mookayi and Mari**

Mari looked at her watch for the last time before getting into the auto for catching the train for attending the People’s Science Meeting. The auto driver Krishna was known to her and he asked her why she was looking flustered and if her mother Usha was not coming.

Mari told him in Tamil, “I am going to give a talk on the **Y chromosome** at the People’s Science meeting in Kerala. I am used to discussing my talk with my mother and so was hoping she would be able to travel with me. But my mother said, “Don’t wait for me. Take the auto and go to the train. If I don’t come, I will join you at the meeting. Don’t worry. Anyway your friends Zareena and Mookayi are also coming with you!”

Krishna said, “Oh good! Zar and Mooks are with you. Surely you will have a good journey. You can discuss your talk with them on the way. Let’s catch the train”.

He laughed and added, “On the way you can tell me in simple language why you are talking about Y”.

Mari smiled and said “Krishna Anna, have you heard about the human genome? The genome is the DNA in our cells that make us human beings”.

Krishna said, “Oh, that is why politicians talk about our DNA”.

Mari laughed and continued, “Their talk is nothing to do with reality. Our DNA is made of chemicals. It looks like a spiral staircase. Only it is not one long thread. It is made of pieces called **chromosomes**. You are a man, so you have two chromosomes called X and Y along with other chromosomes in your genome. I am a woman and I have two X chromosomes and not Y in my genome”.

“So XX is girl and XY is boy! That is simple” responded Krishna.

Mari said, “Yes. Recently they were able to determine the string of chemical letters in the human Y chromosome. Like the sentences in a book chapter, we now have all the letters that make up the Y chapter. We just need to understand what it means”.

Suddenly Krishna said, “Look at that man, how he is driving recklessly. Such guys should not exist!”

Mari amusedly said, “It will surprise you that the Y chromosome is getting shorter and in about 100 lakh years will disappear!”

“Thank goodness it is such a long time. But then what will happen to us men?” Krishna shouted above the traffic noise. Mari started to reply but by then they had reached the station.

Krishna said, “You come back and tell me the story. Now go and catch your train. Be safe”.

Mari thanked Krishna and said, “Yes, I will tell you more about the Y when I come back”.

When she reached the compartment she found Zar and Mooks already settled in it. They said almost together, “Finally, our lady has come. Where is Amma?” Mari put her backpack under the berth, sat down and told them what happened.

When Mari finished retelling her conversation with Krishna, Mooks said, “Good, you can tell us about your talk and whether men will disappear in the future”.

The three fell into an animated conversation. Mari went into what she was going to talk about in the People’s Science movement conference in Kerala. Just then the train started and they found there were three others in their part of the compartment. One was an old lady who had started reading a book. Another was a girl like them but looking outside the window. The third was a middle-aged woman who was looking at them. They smiled at her and continued. Soon they were interrupted by the ticket inspector who asked for their names, checked the list and moved on.

Mooks recalled, “Most people have 22 pairs of chromosomes plus two sex chromosomes – either a pair of X chromosomes or one X and one smaller Y chromosome. Is that correct?”

Zar put in, “Yes, if I remember right, having a Y chromosome usually – but not always – results in an embryo developing male characteristics”.

**BOX on Hormones versus Chromosomes**

A living cell contains DNA with chormosomes that determine the characteristics of that individual. Humans have 23 pairs of chromosomes, of which the 23rd pair determines the sex of the individual. Each chromosome contains hundreds or even thousands of genes. These genes *code* for certain characteristics. For instance, whether you will have black or brown (or green!) eyes, etc. Some genes are present on the chromosome but are not *expressed*. This means that the gene is not performing the function that it codes for. In simple language, you may have a gene that codes for green eyes, but if it is not activated or *expressed*, you will not have green eyes! Typically genes are activated by chemicals called hormones. You could say this acts as a switch to turn on the gene.

**End of BOX**

Mari agreed “True. The sperm from the male carrying the X and Y chromosome enters the egg cell of the female having the two X chromosomes. Then they divide and a bunch of cells are formed. This will have one X chromosome from the female and either an X or a Y chromosome from the male. By default they will develop as female.”

“Then how do we have males?” asked Zar.

“There is a gene called **SRY** on the Y chromosome. It is not enough for the daughter cell to have XY chromosome. Only if this gene on the Y chromosome gets *expressed* (see Box for explanation) will the cells form male sex organs like testes. There are other genes from other chromosomes as well. Along with other hormones for male development, they will take the process forward. Otherwise we will have an embryo carrying XY chromosomes but without the male organs. So also if the male hormones are not expressed properly then we will have an embryo carrying male organs but developing female characteristics.”

Mooks said, “So all cells with XX chromosomes will develop into females?”

Mari said, “Not always. We can even have XX chromosomes but if the gene **SOX9** on the human chromosome 17 gets *duplicated* or *expressed* then it can cause male organs such as testes to develop. *Intersexuality* or hermaphroditism can happen when there are mutations in SOX9. Or even if some of the associated genes that work with it are not present”.

Mooks let out an understanding sigh. “Oh, that is why we have this *gender spectrum* people talk of!”

The old lady who was in the compartment broke into the conversation. “Girls, good that you are talking about this. I am a **sociologist**. I am also going to the conference to which you are going. You should highlight this in your talk so people realise that the male is responsible for the male child being born! Because only *he* can contribute a Y chromosome. Even nowadays, women in marriages undergo so much violence because they don’t give birth to a son, although it is no fault of theirs”.

Mari replied, “Ma’am, yes, I will put that in my talk. Glad to meet you. I am Mari and these are my friends Zareena and Mookayi”.

The lady exclaimed “Are you Usha’s daughter Mari?” Mari was surprised and asked, “How do you know my mother?” The lady burst out laughing “I am Seema Jharia Minz. Your mother and I worked with the tribals in Jharkhand for many years before she got married and moved to Madras. I know her from our student days. Is she still the firebrand she was?”

Zar and Mooks giggled and Mari glared at them. “Seema ma’am, my mother will be so happy when she meets you at the conference”. Seema smiled and said, “Drop the madam nonsense. Just call me Seema. Glad that Usha is coming. We can catch up on what happened to us”. Seema was lost in thought.

**BOX on The Human Genome Project**

The Human Genome Project (HGP) is one of the greatest scientific feats in history. An international group of researchers got together to study all of the DNA (collectively known as a **genome**) of a select set of organisms. It was started in October 1990 and completed more than 10 years later in April 2003. For the very first time, the entire sequence of the human genome was generated. This provided fundamental information about the human blueprint. The resulting understanding of various functions at the genetic level has helped generate new kinds of treatment for various diseases.

**End of BOX**

Mari continued talking. “Remember around 2003 the Human Genome Project was declared completed (see Box). At that time the Y chromosome had still not been fully sequenced (along with mostly the end difficult parts of other chromosomes). Recently, using better technology, two groups have independently fully *sequenced* the Y chromosome. One group completed characterising the Y chromosome obtained from a person of European descent. The other team sequenced the Y chromosomes of 43 diverse men, including 21 of African origin. As with scientific efforts nowadays, the two groups did not collaborate. Not only is the Y chromosome the smallest, but it’s also the most complex chromosome, so this was a feat indeed. As men age, sometimes the Y chromosome gets altered (mutates) or degerates or even disappears altogether, especially in cells like blood cells. This shows that proper Y chromosome gene function is incredibly important for the overall health of men. The study also found 41 more genes than the earlier sequence, bringing the total number on Y chromosome to be 106. So, overall, the Y chromosome is now known to have 624.60029 lakh base pairs! This is about 300 lakh base pairs longer than the earlier known sequence. But it is still smaller than the X chromosome that has 1,543 lakhs base pairs in size and has around 800 genes.”

**BOX on The Y Chromosome and its genes**

The Y chromosome was particularly hard to dequence because it is unusually repetitive, with stretches of DNA that are repeated many, many times. Sometimes they have unique sequences in-between. The Y chromosome also contains palindromes — sequences of letters that are the same backward and forward, like the word “radar”. But many of these are copies of a single gene called **TSPY** which is present only in testicular tissue (tissue of the testes). For instance, the number of copies of the TSPY gene ranges between 23 and 39 in the 43 men who were studieore importantly, it was found that the region on the Y chromosome that can pair and recombine with X chromosome is smaller than known previously.

There are special types of repeated sequences on a Y chromosome. One kind is a **tandem repeat**, where the sequence repeats again and again, one after another, with no other sequence in between. Another is an **inverted repeat**, where the ordering in a portion of the chromosome is inverted. The scientists involved in the study found many inverted and tandem repeated sequences. This complexity and repetition may be the reason for the high mutation rate and degeneration seen in the Y chromosome.”

**END OF BOX**

Mooks sighed. “In the talk, you should spend more time on what you said and talk slowly! Too much detail. Anyway, forget all these details. More interesting: tell us how will men be there even if the Y chromosome disappears?”

Zar replied, “Because evolution will find a way to have two sexes. Don’t you remember what we learnt: that sex is important to provide a way for gene mixing and providing variation”.

Mari carried on. “Yes. In fact, the **Amami spiny rat** which is an endangered rodent found only on Amami Oshima, Japan, is one of just four mammals known to lack a Y chromosome, alongside its close relative the **Tokunoshima spiny rat**, as well as the **Transcaucasian mole vole** and the **Zaisan mole vole**. These are said to have the (X0/X0) system, the 0 standing for none. In the Amami spiny rat, the SRY gene is completely absent. But researchers recently solved this more than 30 year old puzzle. In the Amami spiny rat, there is a region **ENH14** that is duplicated. This is an *enhancer* of gene expression. The two copies of ENH14 act together (in concert) to increase the expression of **SOX9** gene on chromosome 3. This causes the cells to differentiate into testes and males to be formed. So you see as Zar said evolution finds a way”.

Mooks exclaimed, “Is it the same SOX9 gene you mentioned earlier in humans?”

Mari replied “Yes. The SOX9 gene is highly conserved across species, including mammals, birds, reptiles, and rodents. (“Conserved” means that you will find the same or similar gene sequence, with the same function, across many members of a species.) The SOX9 protein made from that gene is important for skeletal development and sex determination”.

Zar stated, “Evolution works in many ways to ensure reproduction and variation. Only then under different conditions, there will be some that survive and carry on life”.

“So true. While reading up all this for the talk, I learnt that in **platypus** the sex determination is strange. Males have 5X and 5Y chromosomes while the females have 10X chromosomes. Also, although the platypus is a mammal like us, its X chromosome is related to the chicken sex chromosome but not the mammalian one” said Mari.

Mooks asked, “Isn’t platypus the duck-billed, egg-laying, milk-secreting mammal from Australia and those regions? Is it related to birds?”

Zar said, “The platypus belongs to a group called **monotremes** with which mammals had a *common* *ancestor* 1,660 lakhs years ago. But with birds the common ancestor was 3,150 lakhs years ago. Mari, do you know how does the system works with birds?”

Mari answered, “Yes. I read about it. Birds, some reptiles and some insects have what is called the **ZW** sex discrimination system. The chromosomes are called Z and W. The females have two different kinds of chromosomes (ZW) while the males have two of the same kind of chromosomes (ZZ). But, as with evolution which likes variation, not all species depend upon the W for their sex. There are moths and butterflies that are ZW, but some have been found female with Z0, as well as female with ZZW. It has been recently found that some birds can decide the sex of their offspring based on nutrition availability!”

“No way,” said Mooks.

Mari smiled saying, “Somehow some female birds are able to manipulate whether the Z or W chromosome gets into an egg. Most bird species produce more males than females on average. Some birds, such as **kestrels**, produce different sex ratios at different times of the year and others respond to environmental conditions or the female’s body condition. For example, when times are tough for **zebra finches**, more females are produced. Some birds, such as the **kookaburra**, manage usually to hatch a male chick first, then a female one”.

Zari exclaimed, “Oh my...Look at the time. We should sleep and let others also sleep”.

Mooks concluded, “Mari, I understand sex is complicated but needed for survival. So why don’t you give an interesting title for your talk: ‘*The Y of Sex*’!”

**Further reading:**

1. https://www.newscientist.com/article/2388720-the-human-y-chromosome-has-been-fully-sequenced-for-the-first-time/

2. https://www.global.hokudai.ac.jp/blog/novel-sex-determination-mechanism-revealed-in-mammals/

3. https://uniavisen.dk/en/it-sweats-milk-and-has-glowing-fur-the-genome-of-the-platypus-has-been-sequenced/

4. https://en.wikipedia.org/wiki/Sex-determination\_system

5. https://www.nature.com/articles/s41586-023-06425-6

6. https://www.nature.com/articles/s41586-023-06457-y

7. Turnover of mammal sex chromosomes in the Sry-deficient Amami spiny rat is due to male-specific upregulation of Sox9 Proceedings of the National Academies of Sciences. November 28, 2022. DOI: 10.1073/pnas.2211574119

8. https://theconversation.com/how-birds-become-male-or-female-and-occasionally-both-112061

9. https://www.scientificamerican.com/podcast/episode/bird-controls-offsprings-gender-09-03-20/