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Mechanistic Investigation of DAXX-Dependent Nucleosome Assembly and Regulation of Endogenous Retroviruses

By
Aayushi Jain

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CHAPTER 6

Chapter for the Public: Chaperoning your way to the world of parasitic jumping genes and their tamers

5.1 Intention for writing this chapter

As a young teenage girl in a small town in central India, I remember the thrill of discovering the name of Dr. Hargobind Khorana (one of the three scientists who cracked the genetic code, here at UW-Madison!) in my class 7th biology textbook. His name, so relatable, stood out among the unfamiliar, foreign-sounding names of other scientists. It was a revelation. Here was proof that someone like me, from a place like mine, could contribute to the grand tapestry of scientific discovery. The excitement of solving nature's puzzles, pushing the boundaries of human knowledge, ignited a passion within me. I wanted to pursue STEM.

CHAPTER 6

MOLECULAR BASIS OF INHERITANCE

6.6 Genetic Code

During replication and transcription a nucleic acid was copied to form another nucleic acid. Hence, these processes are easy to conceptualise on the basis of complementarity. The process of translation requires transfer of genetic information from a polymer of nucleotides to a polymer of amino acids. Neither does any complementarity exist between nucleotides and amino acids, nor could any be drawn theoretically. There existed ample evidences, though, to support the notion that change in nucleic acids (genetic material) were responsible for change in amino acids in proteins. This led to the proposition of a genetic code that could direct the sequence of amino acids during synthesis of proteins.

If determining the biochemical nature of genetic material and the structure of DNA was very exciting, the proposition and deciphering of genetic code were most challenging. In a very true sense, it required involvement of scientists from several disciplines – physicists, organic chemists, biochemists and geneticists. It was George Gamow, a physicist, who argued that since there are only 4 bases and if they have to code for 20 amino acids, the code should constitute a combination of bases. He suggested that in order to code for all the 20 amino acids, the code should be made up of three nucleotides. This was a very bold proposition, because a permutation combination of 4^3 (4 × 4 × 4) would generate 64 codons; generating many more codons than required.

Providing proof that the codon was a triplet, was a more daunting task. The chemical method developed by Har Gobind Khorana was

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instrumental in synthesising RNA molecules with defined combinations of bases (homopolymers and copolymers). Marshall Nirenberg's cell-free system for protein synthesis finally helped the code to be deciphered.

Figure 6.1: Screenshot from my biology textbook which mentions Dr. Khorana in the chapter on molecular basis of inheritance. NCERT India (National Council of Educational Research and Training). [1]

With this chapter, I aim to empower others, especially those who might feel excluded from the world of science. I want to show that science isn't just for a select few; it's for anyone with curiosity and a desire to understand. I also believe that by making scientific knowledge accessible to all, we can break down barriers, foster a scientific mindset, and cultivate a deeper appreciation for the incredible complexity and beauty of the natural world.

Imagine the thrill of unraveling the mysteries of life, from the intricate workings of a single cell to the complex interactions of entire ecosystems. Picture the satisfaction of developing groundbreaking technologies that improve lives. The world needs more scientists to address pressing global challenges like climate change, diseases, and poverty.

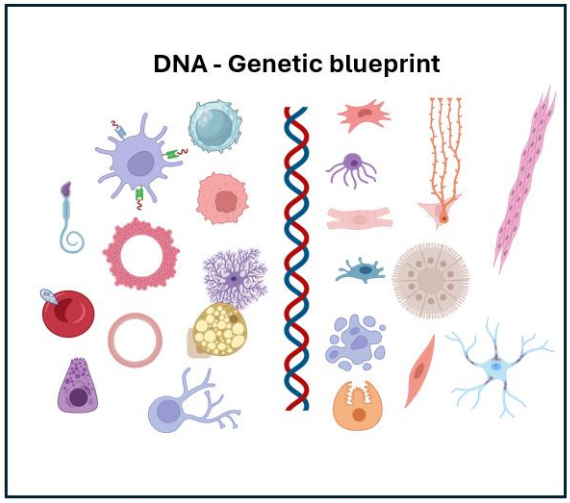
So, whether you're a curious child, a motivated student, or an adult looking for a new direction, I encourage you to explore the world of science. It's a journey filled with wonder, discovery, and the opportunity to make a real difference. Together, we can build a brighter future for ourselves and generations to come.

5.2 Inspiration for studying chromatin and associated protein machineries

5.2.1 A remarkable instruction manual – the human genome

Our bodies are intricate cities composed of trillions of tiny architects: cells. These architects, despite sharing the same blueprints, construct vastly different structures, each with a unique purpose [2]. The blueprint is the human genome, which is the complete set of genetic instructions for building and maintaining a human being.

The human genome has remarkable adaptability, which allows it to produce over 200 diverse cell types from a common genetic code [3]. Can you imagine a single instruction manual capable of guiding the assembly of every machine that you can find in a modern home? From microwaves to lamps, ovens to air conditioners, each device would be made following the same fundamental blueprint, yet each would be tailored to perform specific tasks. Our genome is akin to this universal manual. Every cell in our body - skin, eye, liver - carries the same genetic information, yet each develops into a distinct type, fulfilling its unique role.



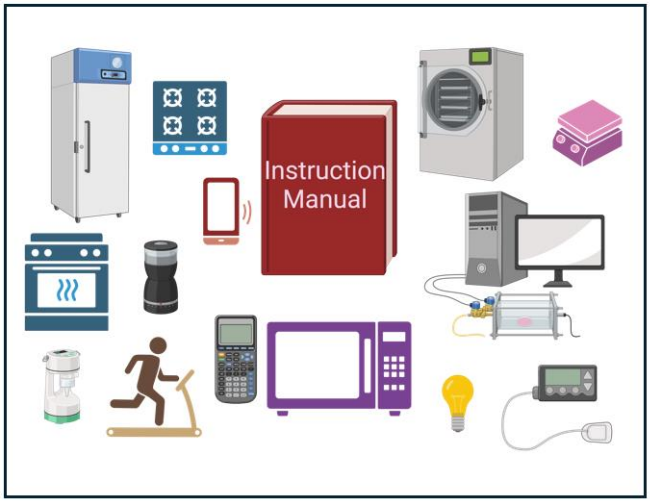


Figure 6.2: A remarkable instruction manual – the human genome. Same genetic information contained in over 200 types of cells in a human body (left). In comparison, imagine if there existed an instruction manual that had the same information, just read differently to make over 200 types of machines (right). [4]

So, how do cells, despite possessing identical DNA, manifest into such diverse types? The answer lies in the field of epigenetics. Epigenetics allows the same genetic information to be interpreted differently [5, 6]. But, before we understand what epigenetics is, let's understand what genes are.

Genes are like the recipes in a cookbook, containing the instructions for building and maintaining cells. Only here, genes provide instructions for creating different proteins, which are the building blocks of cells and tissues. Just like some recipes are used frequently and others are kept secret and only used on special occasions, some genes are more commonly used and stay active (much like leaving open a frequently used cookbook), while others are inactive (akin to keeping an infrequently used cookbook closed). Epigenetics is like a meticulous chef who decides which recipes are to be used and when. The chef uses special tags and markers to label every page of the cookbook. These tags can be added, removed, or changed based on the needs of the cell or the environment. For example, if the cell orders a specific dish (protein), the chef will open the specific recipe in the cookbook, put a book opener (add a tag), and keep it open for as long as needed. If the recipe is no longer needed, the chef might close it by removing the tag. This system ensures that the right genes are turned on or off at the right time, helping the cell function properly.

“Identical twins have exactly the same genetic code as each other. They share the same womb, and usually they are brought up in very similar environments. When we consider this, it doesn't seem surprising that if one of the twins develops schizophrenia, the chance that his or her twin will also develop the illness is very high. In fact, we have to start wondering why it isn’t higher. Why isn’t the figure 100 percent?”

—Nessa Carey, *The Epigenetics Revolution*

5.2.2 A herculean topological problem

Imagine a thread so long that if stretched end to end, it would tower over you. That’s the DNA within a single human cell. Yet, despite its incredible length, it's neatly packed into a microscopic space. A human cell, though only a fraction of an inch (0.0002 inches) across, contains DNA that, if unraveled, would stretch nearly six feet (exactly a foot taller than I am!) [7], which basically means that the width of a human cell is roughly 360,000 times smaller than the length of genetic material it contains.

To top it all, there are trillions of cells in a human body. Now, you must be wondering - how is this amazing degree of compaction achieved? The answer lies in chromatin, a complex structure composed of DNA wrapped around proteins called histones. There are four core histones – H3, H4, H2A and H2B. Histones act like spools, winding the DNA into compact coils. Each single unit of DNA wrapped around eight histone proteins is called a nucleosome, the fundamental unit of chromatin. These coils are further organized into higher-order structures, ultimately forming the chromosomes we can see under a microscope [8]. The intricate dance of chromatin packaging allows our cells to store vast

amounts of genetic information in a remarkably small space, enabling the complex functions of life.

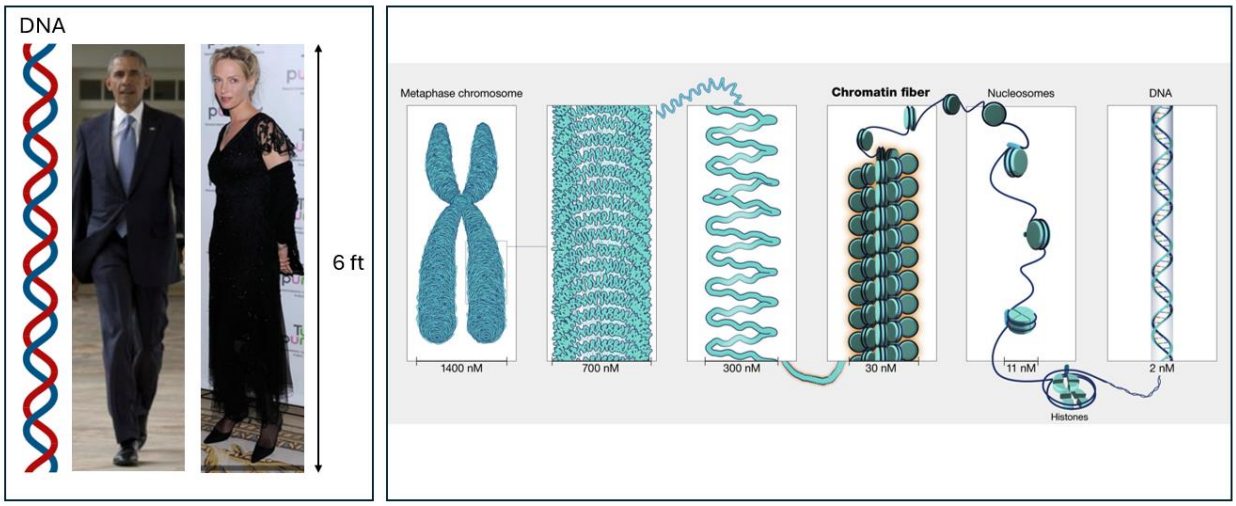


Figure 6.3: Topological challenge of DNA compaction is achieved through chromatin. On the left; A comparison: DNA from one human cell is extended end to end amounting to 6 ft, as tall as President Obama or the wonderful actor Uma Thurman. On the right, DNA is chromatinized, the nucleosome being the fundamental unit of chromatin, which gets condensed further (right to left). [9][25]

5.2.3 Histone H3.3 and its delivery systems

Think of nucleosomes as beads on a necklace. When a cell needs to read the information stored in DNA, the nucleosomes must unravel like a necklace. Once the cell is done reading, the nucleosomes must be reassembled. During DNA replication, the entire genome gets wrapped with a specific version of histone H3 called H3.1. But there's a twist!

In certain processes that require unwinding DNA, a different type of histone H3, called H3.3 is used instead. H3.1 and H3.3 are almost identical – they differ by only 3%! Yet, this tiny difference makes all the difference [10]. Different protein machines recognize H3.3 and deposit it in specific locations throughout the genome and these specific deposition patterns are remembered over time. These proteins, which escort histones to where they are required in the genome, are called histone chaperones. If the genome is a vast, sprawling city, H3.3 is a special type of building material that needs to be delivered to specific construction sites within the city, and chaperones are specialized delivery trucks.

- Specific Delivery: Just as FedEx or USPS can't deliver packages to any address, chaperones can only deliver H3.3 to specific locations in the genome.
- Specialized Trucks: Different chaperones are like different types of delivery trucks, each equipped with unique tools and abilities to handle H3.3 and deliver it to the correct construction site. For example, some chaperones might be better at navigating crowded areas of the genome, while others might be skilled at working in more open spaces in the genome.

So, while the genome is a vast and complex city, the chaperones ensure that H3.3 is delivered precisely where it's needed, much like a specialized delivery service ensuring packages reach their intended destinations [10].

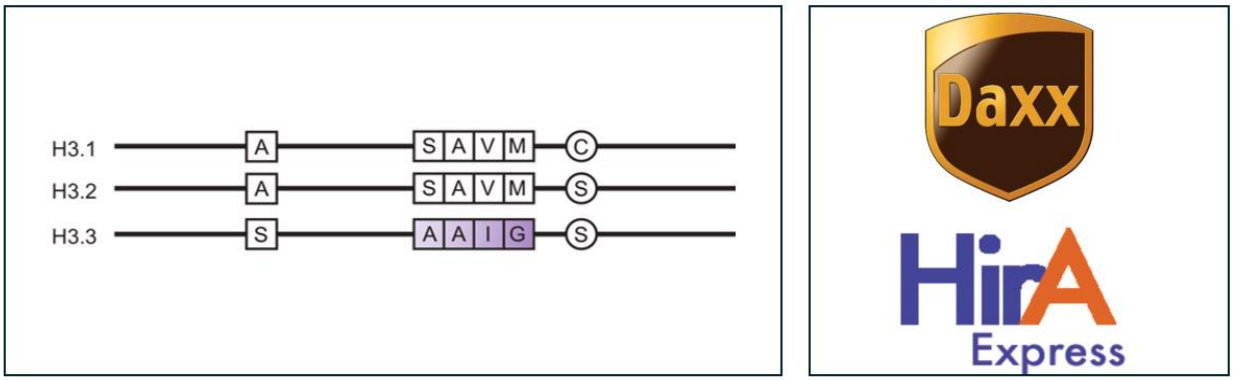


Figure 6.4: H3.3 vs H3.1/H3.2 differ at only 4-5 amino acids (left) [10]. HIRA and DAXX are H3.3-specific chaperones that deposit H3.3 at select locations in the genome. Adapted from [10][26].

5.2.4 Our genomes are part human, part virus

The human genome is a massive book of instructions, written in a code of just four letters: A, T, C, and G [1]. If we printed the entire genome in a standard-sized font, the book would be over 1.5 million pages long! That's almost 2,000 times the size of the entire Lord of the Rings trilogy. Strangely, only a small part of our massive genome contains instructions for building proteins (genes). If the genome were a road stretching across the Indian ocean, the genes would be like a few small islands scattered along the way. These islands would be so small compared to the vast ocean that they would barely be noticeable.

The vast majority—a surprising 98%—is made up of non-coding DNA [11]. This non-coding DNA can be found between genes (intergenic DNA) or within genes (introns). The non-coding DNA doesn’t directly code for proteins, but it plays important roles in regulating gene activity. It is often called junk DNA or dark matter of the genome, since our understanding of its functional significance is limited.

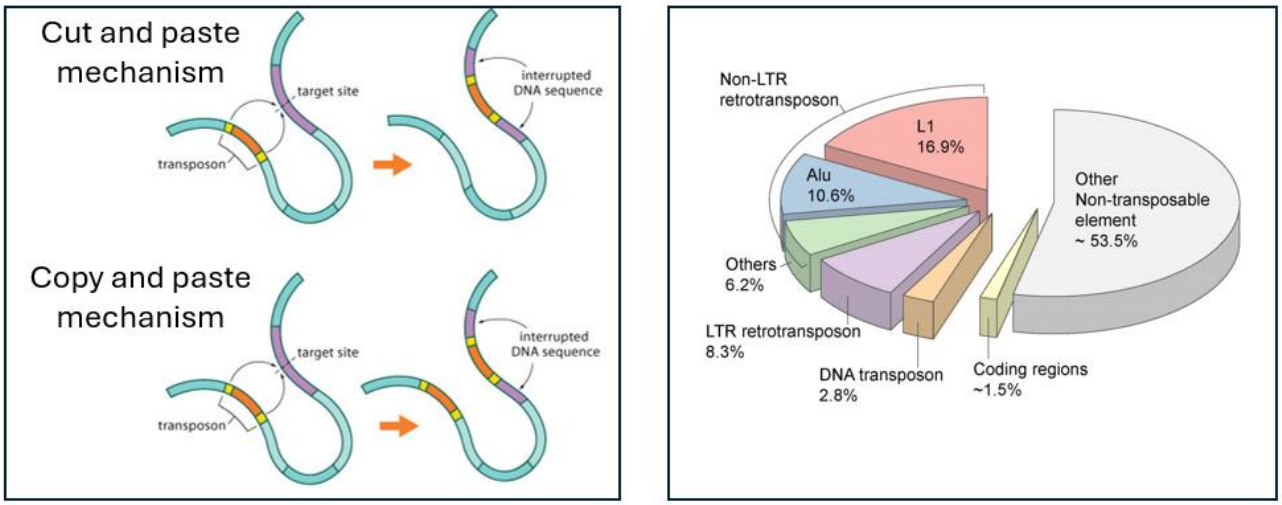


Figure 6.5: Transposable elements propagate in the genome primarily through two mechanisms; copy and paste and cut and paste (left) [12]. Mobile elements are abundant in our DNA. Pie chart shows the proportion of the human genome that is composed of various types of transposable elements (right) [13].

The bulk of this dark matter of the genome is composed of mobile DNA, or transposons. Mobile DNA, as the name suggests, refers to DNA sequences which are capable of propagating within the genome. Mobile DNA is found in nearly all organisms. Dr. Barbara McClintock made a groundbreaking discovery in 1948 while studying maize [14]. She noticed that a specific chromosome in maize was breaking and rearranging during development. This unusual behavior was caused by mobile DNA elements, which she called "transposons." When McClintock presented her findings at a scientific conference in 1951, her ideas were met with disbelief and skepticism. Some scientists believed that transposons were a rare and unusual phenomenon only found in maize. However,

McClintock was convinced that this discovery was crucial to understanding the development of plants and other organisms.

“They thought I was crazy, absolutely mad.”

- Barbara McClintock *in response to the National Academy of Sciences to her theory that proposed that genes could transition/jump to new locations on a chromosome.*

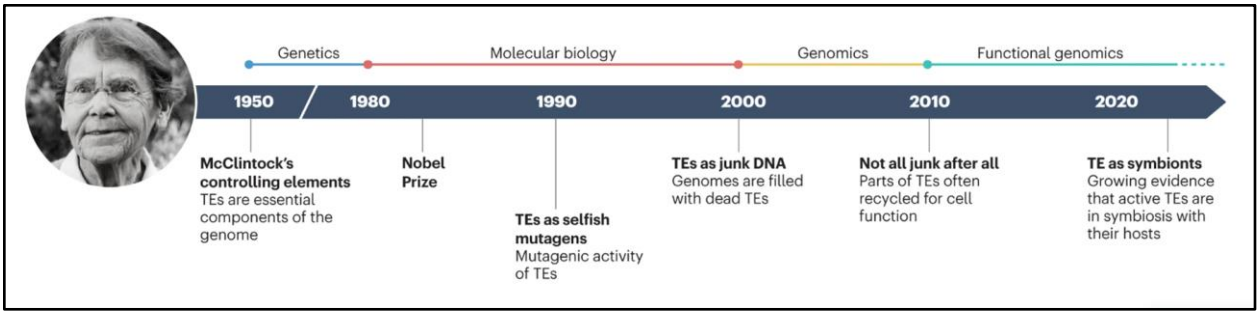


Figure 6.6: Paradigm shift in our understanding and perception of transposable elements. [15]

Indeed, in the early 2000s, the human genome project concluded that roughly half of the human genome is repeatable and mobile elements. Transposons and their remnants make up at least 40% of our genome. Endogenous retroviruses account for another 8% [11].

What are the endogenous retroviruses that compose 8% of our genomes? Endogenous retroviruses are relics of ancient viral infections that got integrated in our genomes during viral infections that happened to our ancestors millions of years ago, and they are now passed from parents to offspring just like the rest of the DNA. It is unsettling that half of our own genetic material is derived from genetic parasites. But fear not, most of the mobile DNA sequences in the human genome are actually no longer capable of moving around.

They have now become permanent fixtures in our genome. Even though greater than 99.9% of human transposable elements are fixed in the population – that still leaves plenty still jumping around, and thousands that are not shared across individuals. Amazingly, in our own genome, we can count more genes derived from viruses than those encoding cellular proteins (i.e. proteins known to have cellular functions). However, most of these viral sequences are crippled with mutations and are clearly no longer capable of encoding intact viral components (in fact nobody has ever found one fully capable of encoding an infectious virus).

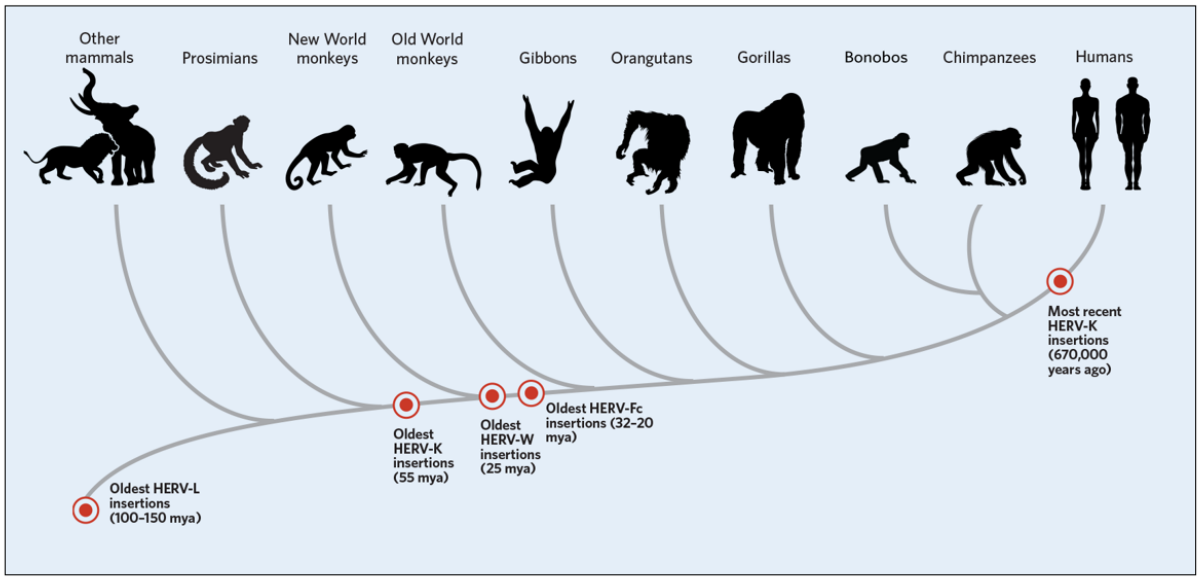


Figure 6.7: Endogenous retroviruses are remnants of ancient viral infections that got integrated in our genomes throughout our evolution. [16]

Transposons provide us with a glimpse into our pasts, they constitute history encrusted into our genomes quite literally. This debris of the past is a record of all the ancient battles that were fought on the ground that is our genome against the viral invaders. While these scars highlight the inherent vulnerability of our genetic material, they also serve as a

reminder of our ancestors' incredible resilience. We get to see all the strategizing that ensued in the face of continuous viral onslaught [17]. By studying these relics, we get to witness the adaptability and ingenuity that is baked into our genomes. These battles that our predecessor genomes participated in are testament to the intense collective will to survive and thrive that is ingrained into our DNA.

Not only did our ancestral genomes emerge victorious against viral invasions, but they domesticated and repurposed some of the invader DNA for our own benefit, a perfect example of when life gives you lemons, make lemonade! Co-opting viral DNA for our benefit has allowed us to establish sophisticated gene networks, with a relatively fewer number of genes than several other organisms [19]. We have really done remarkably with the cards that we were dealt!

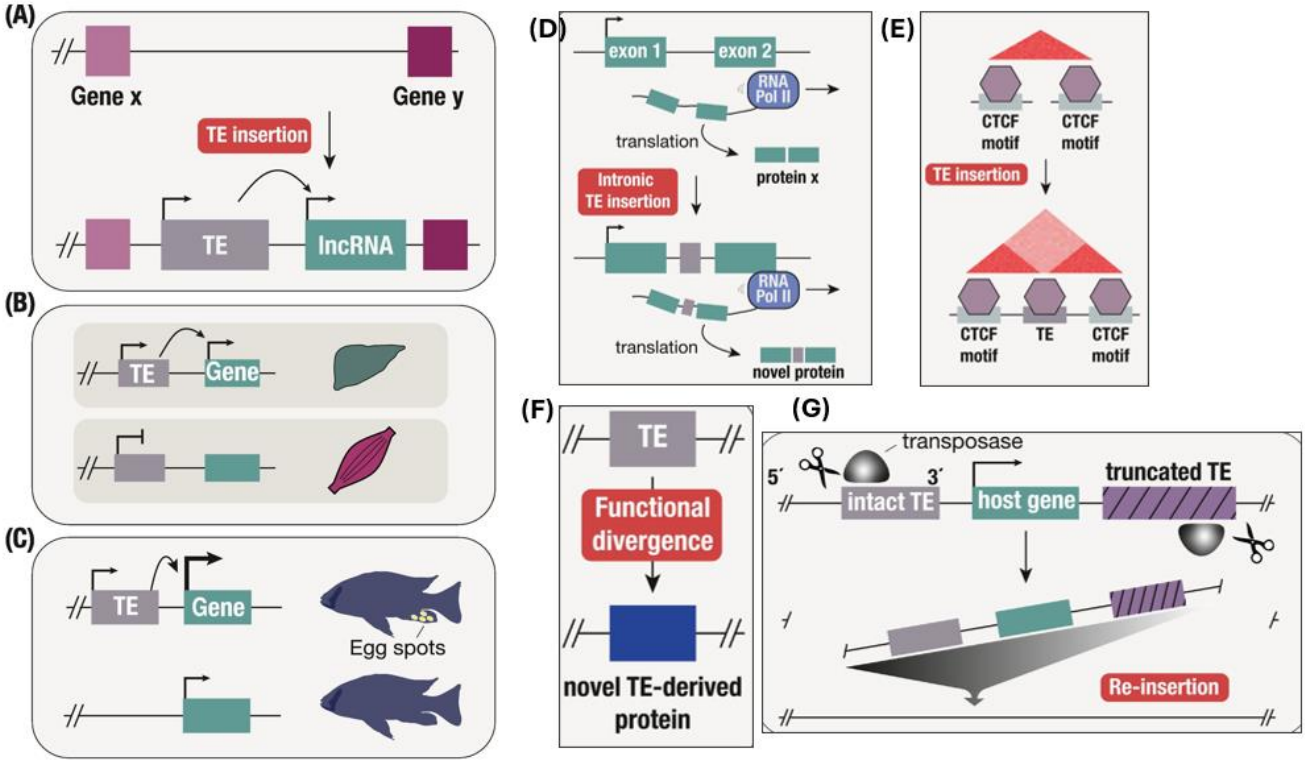


Figure 6.8: Modes of domestication of Transposable elements (TEs) A. Creating new genes: TEs can activate nearby genes that were previously silent, leading to the creation of new genes. Tissue-specific regulation: TEs can be turned on or off in specific tissues, influencing the activity of nearby genes and potentially leading to tissue-specific functions. C. Altering gene expression: TEs can act as enhancers, boosting the activity of nearby genes. This can lead to the development of new traits, like the presence or absence of egg spots in cichlid fish. D. Adding new protein domains: TEs can be incorporated into genes, adding new protein domains that can give the gene new functions. E. Regulating genome topology: TEs can be bound by proteins that help organize the genome in 3D, influencing gene activity. G. Capturing and moving genes: TEs can capture and move entire genes, which can contribute to genome evolution. Abbreviations: RNA Pol II, RNA polymerase II; TE, transposable element. [19]

Not only can transposons be harmful, since they can cause diseases like hemophilia, neurodegenerative disorders and cancers, but they also play a crucial role in shaping the evolution of species [20]. I find transposable elements and the mechanisms that our cells have developed to regulate them quite a fascinating and worthy field of study. My work revolves around understanding some of the tamers of endogenous retroviruses, which I will be discussing in the next section.

5.3 Outstanding questions in the field and our discoveries

5.3.1 Introduction to my work

I work on an evolutionarily conserved protein called DAXX. DAXX participates in many cellular processes and among the many hats that DAXX wears, one is that of a histone chaperone, specific for histone H3.3.

Histone H3 is one of the four histones that make the fundamental unit of chromatin. Chromatin is like a spool of thread. It's made up of DNA, which is the genetic material that contains our instructions for building and running our bodies, and proteins called histones. These proteins help package the DNA into a compact form, like winding thread around a spool, so that it can fit inside our cells.

Histone H3.3 is a special type of histone H3, which is found at very specific places in our genomes. DAXX is one of the chaperones that escort H3.3 to these specific locations within the genome. Two major targets for H3.3 are structural repeats in the genome, such as chromosomal ends (called telomeres), and mobile elements, such as endogenous retroviruses. A peculiar thing common in these genomic regions is that they are very heterochromatic – meaning that they are highly condensed and compacted in space - making an inaccessible environment for the many protein machineries trying to work with the underlying DNA. Imagine a heterochromatin region as a dense, impenetrable forest. The DNA sequence is like a hidden path or clearing within the forest. Protein machineries are like explorers trying to navigate through the forest. The dense heterochromatin makes it difficult for the explorers to find and access the hidden path, representing the challenges

faced by cellular processes in accessing the genetic information within heterochromatic regions.

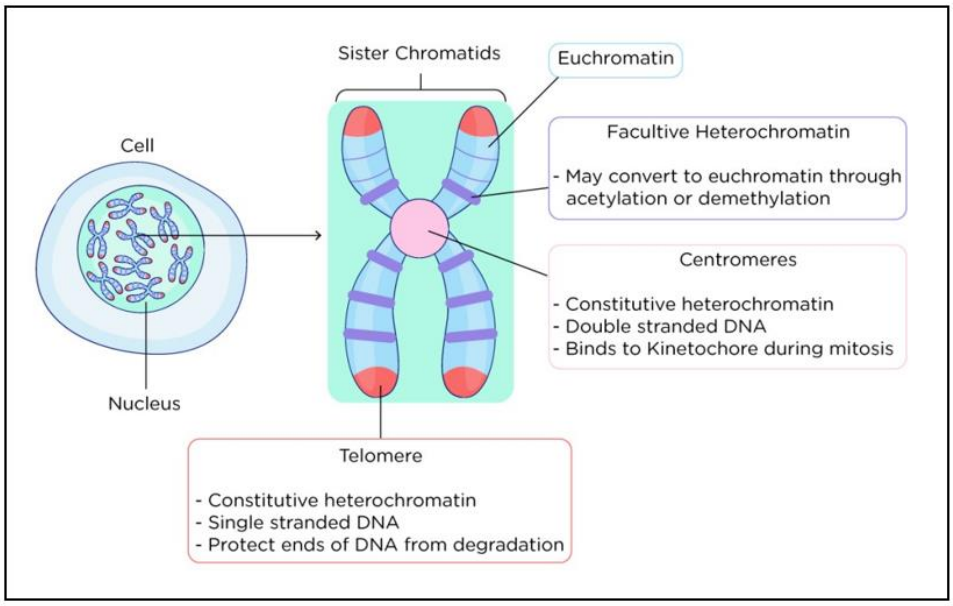


Figure 6.9: Representation of constitutive heterochromatin at telomeres and centromeres. [21]

Since DAXX and histone H3.3 are crucial for establishing chromatin at structurally important regions such as telomeres and mobile parasitic DNA, it is not surprising that mutations in such machinery lead to various diseases, including cancers. DAXX and H3.3 also play a critical role during mammalian development. For instance, if we prevent DAXX or H3.3 proteins from being made in mouse embryos, it leads to lethality [22] [23].

To give you a bird eyes' view of my work, I have used tools based in biochemistry and genomics in my attempt to understand the molecular mechanisms responsible for formation of chromatin by DAXX and how DAXX regulates the mobile elements.

Biochemistry and genomics are powerful tools in understanding the intricate mechanisms of life.

- **Protein-protein interactions:** Biochemistry helps us identify and characterize the proteins that interact with DAXX. These interactions are crucial for DAXX's function in chromatin formation and regulation of mobile elements.
- **In vitro experiments:** Biochemistry allows us to study the molecular mechanisms of DAXX in a controlled laboratory setting, often using purified proteins and substrates, such as DNA, on which nucleosomes can be assembled.
- **ChIP-seq:** This technique helps map the binding sites of DAXX and other proteins to DNA, revealing the regions of the genome they target.
- **RNA-seq:** By measuring RNA levels, we can understand the genes regulated by DAXX. This can help identify its downstream targets involved in chromatin formation or mobile element control.

The world is too complicated in all parts and interconnections to be due to chance alone. I am convinced that the existence of life with all its order in each of its organisms is simply too well put together. Each part of a living thing depends on all its other parts to function. How does each part know? How is each part specified at conception? The more one learns of biochemistry the more unbelievable it becomes unless there is some type of organizing principle-an architect.

- *Allan Sandage*

By combining biochemical and genomic approaches, we can gain a comprehensive understanding of the role of DAXX in chromatin formation and mobile element regulation.

Some of the potential areas where my discoveries could have implications are cancer research, developmental biology, chromatin biology, genomics and basic biochemistry. This knowledge can contribute to our understanding of fundamental biological processes and may have implications for human health and disease.

5.3.2 Scientific approach that I took

I used mouse embryonic stem cells as my model system to study DAXX. Although challenging to work with, I find stem cells to be fascinating. The versatility of stem cells is incredible; they have the potential to become almost any type of cell in the body. Studying stem cells has also taught me the importance of context and perspective. Everything matters—the timing, the environment, and the interactions between different factors. It's like a complex dance that ultimately shapes our individual cellular identities, which in turn defines who we are as a whole.

In order to study DAXX function, I systematically generated a range of DAXX mutants with deletions and modifications in its protein sequence. I introduced these mutant versions of DAXX into mouse embryonic stem cells that had been genetically engineered to not make DAXX protein originally. I then interrogated what parts of DAXX are important for its various roles. This process allowed me to pinpoint the roles of individual DAXX domains in the various functions that it performs. As a reminder, proteins are composed of amino acids, and the sequence of these amino acids determines the protein's structure. Specific regions of a protein may form domains which have more defined 3D structure, while others may be more flexible and disordered and not attain any specific 3D shape.

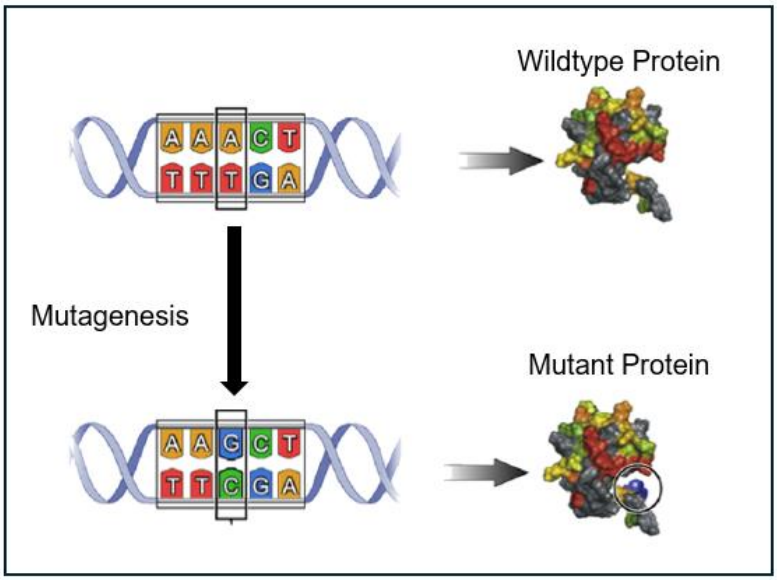


Figure 6.10: Mutagenesis is a technique used to introduce changes in the DNA sequence of a gene, which ultimately leads to changes in the structure and function of the protein encoded by that gene. By introducing mutations at specific amino acid residues, we can determine which residues are essential for the function of protein [24].

Some of the questions that I asked in my research are as follows:

1. Where does DAXX go within the genome of mouse embryonic stem cells?
2. Which parts of DAXX are important for recruitment of DAXX at those locations?
3. What parts of DAXX are important for regulating endogenous retroviruses?
4. What parts of DAXX are important for its interaction with other known proteins?
5. What parts of DAXX are important for depositing H3.3 at the places in the genome where it goes?

5.3.3 Some of the discoveries that I made through my experiments are as follows:

- I found that DAXX goes to very specific types of mobile elements, which make up less than 1.5% of all the repeats in the genome. Interestingly, these mobile elements enriched in DAXX are relatively new in evolutionary terms and still have the means to jump around within the mouse genome. This means that if these elements aren’t properly controlled, they can jump to other parts of the genome, potentially disrupting the genetic information in critical regions. Also, by breaking DAXX protein down into smaller domains, I figured out which parts of it are required to target DAXX to those transposable elements.
- I also found that DAXX prevents its target mobile elements from transcribing into RNA, a crucial step in their ability to move to new locations within the genome, hence solidifying its position in “the tamer of mobile elements club”. Essentially, DAXX plays a critical role in preventing its target mobile elements from jumping around the genome. For instance, certain mobile elements such as Hot L1 have been found to have jumped around in certain cancers, contributing to malignancy. In addition, I have identified what parts of DAXX protein are responsible for taming endogenous retroviruses and also host genes in the mouse genome.
- I have figured out parts of DAXX that are absolutely crucial for H3.3 deposition in the genome.
- Interestingly, I found that silencing of endogenous retroviruses by DAXX is independent of its ability to deposit H3.3. This means that DAXX's two primary functions — H3.3 deposition and silencing of transposons — are separated in cells. There's been debate among scientists about whether H3.3 deposition is essential

for silencing these mobile elements, especially since H3.3 is abundant in these regions. My research demonstrates that H3.3 deposition on mobile elements is not crucial for controlling them.

- By breaking DAXX protein down into various smaller pieces, I was also able to map its various parts to specific protein partners that DAXX engages with during its functional journey.
- Overall, through my experiments, I was able to place where DAXX fits in the cascade of silencers - proteins that play a vital role in silencing of the mobile elements - to understand the complex bigger picture as a whole.

* These discoveries that I have highlighted in this chapter are only part of one project. I am not discussing other projects in this chapter.

My findings, like the work of countless other scientists, are a small piece of the puzzle that is being assembled to unlock the secrets of life. As I continue my scientific journey, I remain inspired by the countless individuals who have paved the way before me and the endless possibilities that lie ahead.

5.4 Reflections on the PhD journey

The path of doing science is exciting and rewarding, but it is also challenging for many reasons. Couple technical difficulties with your own personal baggage, and the challenges can seem insurmountable. My journey was no different. It was hard and a bit unconventional in some sense. I want to highlight a few things that really helped me along the way. I want people to know that scientists do struggle, and that there are things that can help when you pursue harder things in life.

As cliche as it may sound, taking care of our mental health is vital. As an immigrant, who felt isolated away from home, I struggled with my mental health during graduate school and learned firsthand the importance of building a support system. When you have a lot going on, mental health is the easiest to overlook. Don't hesitate to seek help; there's no shame in it. It can provide the additional support you need to build on your resilience, learn advocacy skills, and prioritize rest. If it helps you to know and feel more seen, I should mention that I spend my Friday evenings in a psychotherapy session - giving myself that extra layer of much-needed support!

I also want to emphasize the importance of participating in diverse communities. It's easy to get caught up in the lab, but participating in communities like WINStep Forward and WiSolve was incredibly rewarding for me. These organizations offered opportunities to practice skills like teamwork and communication in a new setting beyond the lab. Interacting with scholars from different fields gave me a broader perspective of the scientific approach to solving problems that plague our world.

Taking up hobbies can be empowering. Exploring hobbies like art helped me slow down and feel more accomplished. I tried different styles of art, including mandala art, abstract, and geometric designs. It was rewarding to learn new skills and figure out how to create something unique outside of my comfort zone.

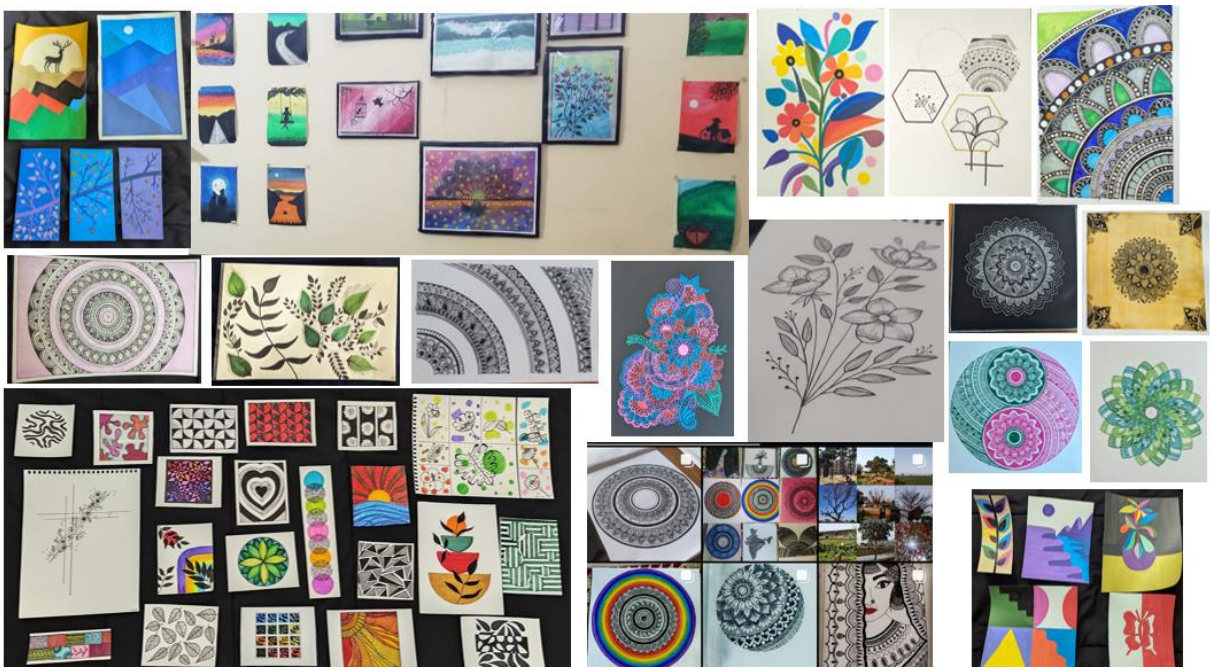


Figure 6.11: Images of some of my artwork

5.5 Acknowledgements

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5.6 References used in the chapter

1. NCERT Textbooks PDF (I-XII)
2. Bianconi, E., Piovesan, A., Facchin, F., Beraudi, A., Casadei, R., Frabetti, F., ... & Canaider, S. (2013). An estimation of the number of cells in the human body. *Annals of human biology*, *40*(6), 463-471.
3. From One Genome, Many Types of Cells. But How? - The New York Times
4. Image was created using BioRender.com
5. The Epigenetics Revolution: How Modern Biology Is Rewriting Our Understanding of Genetics, Disease, and Inheritance by Nessa Carey
6. Adapted from Hyun, J., & Jung, Y. (2020). DNA methylation in nonalcoholic fatty liver disease. *International journal of molecular sciences*, *21*(21), 8138.
7. How Long is Human DNA?
8. Chromatin structure and function by Alan Wolffe
9. Adapted from Chromatin
10. Szenker, E., Ray-Gallet, D., & Almouzni, G. (2011). The double face of the histone variant H3. 3. *Cell research*, *21*(3), 421-434.
11. Bourque, G., Burns, K. H., Gehring, M., Gorbunova, V., Seluanov, A., Hammell, M., ... & Feschotte, C. (2018). Ten things you should know about transposable elements. *Genome biology*, *19*, 1-12.
12. Adapted from transposition

13. Adapted from Cordaux, R., & Batzer, M. A. (2009). The impact of retrotransposons on human genome evolution. *Nature reviews genetics*, *10*(10), 691-703.
14. McClintock, B. (1950). The origin and behavior of mutable loci in maize. *Proceedings of the National Academy of Sciences*, *36*(6), 344-355.
15. Feschotte, C. (2023). Transposable elements: McClintock's legacy revisited. *Nature Reviews Genetics*, *24*(11), 797-800.
16. Infographic: Human Endogenous Retroviruses and Disease | The Scientist Magazine®
17. Emerson, R. O., & Thomas, J. H. (2009). Adaptive evolution in zinc finger transcription factors. *PLoS genetics*, *5*(1), e1000325.
18. Urrutia, R. (2003). KRAB-containing zinc-finger repressor proteins. *Genome biology*, *4*, 1-8.
19. Almeida, M. V., Vernaz, G., Putman, A. L., & Miska, E. A. (2022). Taming transposable elements in vertebrates: from epigenetic silencing to domestication. *Trends in Genetics*, *38*(6), 529-553.
20. Gale Hammell, M., & Rowe, H. M. (2020). Editorial Overview: Endogenous Retroviruses in Development and Disease. *Viruses*, *12*(12), 1446.
21. Adapted from heterochromatin at telomeres.
22. Michaelson, J. S., Bader, D., Kuo, F., Kozak, C., & Leder, P. (1999). Loss of Daxx, a promiscuously interacting protein, results in extensive apoptosis in early mouse development. *Genes & development*, *13*(15), 1918-1923.
23. Bush, K., Cervantes, V., Yee, J. Q., Klein, R. H., & Knoepfler, P. S. (2023). A knockout-first model of H3f3a gene targeting leads to developmental lethality. *genesis*, *61*(1-2), e23507.
24. Adapted from Camp, K. M., & Trujillo, E. (2014). Position of the Academy of Nutrition and Dietetics: nutritional genomics. *Journal of the Academy of Nutrition and Dietetics*, *114*(2), 299-312.

25. Images of President Obama and Ms Thurman were taken from the google image search.

26. Image was created using DALLE-2.