An Illustrative Display of Epigenetics: Explanation, Mechanisms, and Context

Stephanie O'Neil, BFA Art and Design, Minor Biology

Summary

Transforming scientific information into a contemporary, museum quality display that also has my own illustrative and whimsical style has been the goal of my 8-month Integrative Process project. In doing so, I have embarked on research and continual learning about the subject of Epigenetics, an exploration of 2D and 3D media to best represent the complexity and beauty of the subject in a visually interesting way, and design skills to create a comprehensive, user friendly display. Here I will explain my creative process, place my work within a larger context of creative and informative work, and summarize my research.

Creative Process

Before working on any final piece for the show, I made experimental forms and drawings that eventually lead to final versions. My approach to the project always existed between two media, 2D and 3d digital. Ultimately I ended up showing a digitally printed three-panel poster that acted more as an expressive mural than an illustration one would find in textbook or paper(Fig 1). I took elements of conventional scientific diagrams, using them as reference but then making my illustrative hand very evident by taking it into a stylistic realm bordering on the surreal. To make this happen I would pull multiple image references from internet searches, then draw my own version with pen and pencil by adding embellishments and decorative details of my own choosing (Fig 2-3). The pencil drawing was then traced over with a pen ink technique to make the line work bold, specific, and to give form and depth to each element (Fig 4). I then scanned the inked image, and used Photoshop to remove any background and clean the lines further. For adding color, I painted with watercolor and scanned the swatches and used those pixels to allow for not only With this technique I hoped to make the final digital print appear handcrafted (Fig 5). I also chose to use color as a coding system, I made all DNA purple, all proteins blue, RNA green, and epigenetic chemical elements red and orange. In terms of the overall layout of the image, I made multiple sketches to make the flow of information clear. Each of the three panels was a different topic: 1. Gene to Protein, 2. Packaging DNA, and 3. Epigenetic Changes. I wanted the overall impression to be that even through DNA directs every biologic outcome through the direct creation of proteins, with epigenetics this process can be stopped, increased, or changed. I decided to point out two of the most common epigenetic processes, DNA methylation and histone tail modifications.

My challenge in creating 3D printed models was both technical and contextual. Again, as in my 2D process, I began by translating the common symbols used to represent structures like histones, nucleosomes, and DNA into my own illustrative three dimensional forms instead of a less visually interesting realistic version which would resemble lumps of protein structure. Instead, I chose to utilize the media of 3D printing to make interesting and intricate pieces that could by themselves be art. The first structure that I was happy with as a final piece was the nucleosome (Fig 6-7). The process of printing these forms was interesting and challenging (Fig 8). Because of the intricacies of the structure and the printing process, there was a lot of excess plastic strings and imperfections that had to be filed down. I also had to make many subtle adjustments in files in order for them to even begin printing. I printed one large version, and six smaller ones. I used the big one to demonstrate how the 'tails' carry the epigenetic changes, and the small ones to demonstrate how the proximity of one nucleosome to another can affect the DNA's ability to be expressed (Fig 9).

The small ones I hung of up with fishing line, three that were tight tighter and three that were loose. I printed two fairly standard DNA sculptures, as well small forms to represent methyl groups and transcription factors, then chose to paint the methyl groups a light red and the transcription factors turquoise, in keeping with my color coded system (Fig 10). I put the methyl groups on one strand of DNA (using small magnets), as well as the tight strung nucleosomes, and the tail of the big nucleosome. I put the turquoise transcription factors on the other DNA with no methyl group and the loose nucleosomes to represent that these were active.

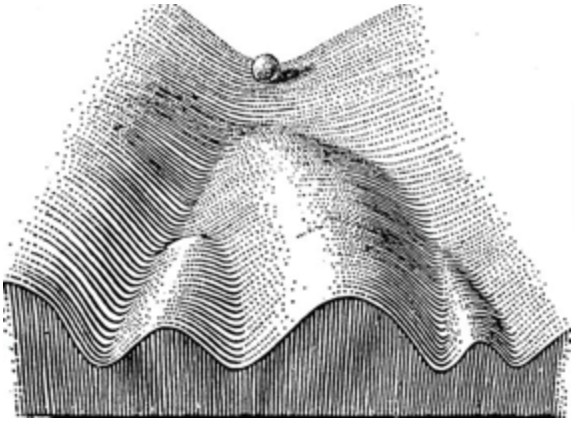
The last element of my project was the progression of cancer in tissue in the form of a 3D printed sculptureS (Fig 11). For this part of my project I pushed my abilities in structural modeling in Zbrush. At first, I made a test version with a blood vessel as a base and the tissue structure above (Fig 12-13). This part of the project is less designed and perhaps more conceptual; without the use of overt symbol and color in the other part. The idea that links the two is that epigenetic research and mechanisms can be used to change the outcome of cancers. It felt freeing to work organically in creating tissue and a vascular network, and building up textured cancer cells. For these complex pieces, I outsourced the printing, and was told it took several days to print each one, but it was clear the quality and resolution of the print was better than the ones I printed myself.

Inspiration in Context

To get to this point I have gone through a variety of experiments in 2d media (Fig 14-15) and digital 3d space (Fig 16). The reason for the choice in incorporating both media is that they represent both the traditional scientific illustration and the contemporary trends. Pen and ink illustration has a long-standing tradition with scientific and medical illustration because of its ability to capture form, dimension, and texture and because it is easily copied and mass printed. Today, digitally modeled and rendered images have taken over traditional media because in three dimensions, organic forms are better represented. A huge amount of my process has been narrowing down and truly understanding the topic I'm working with which has involved countless internet searches, reading articles, books, incorporating classroom knowledge and speaking with professors. I've looked at a variety of artists, illustrators and designers for inspiration. In terms of turning a broad concepts into a single show I was inspired by the work "Post Natural History" by the French artist Vincent Fournier (Fig 17) in which he displayed his artwork as a natural history museum but with fictional futuristic species. In terms of illustration style I am influenced by the work of contemporary illustrator Katie Scott because of her incorporation of organic line work and soft colors(Fig 18-19). I also looked to graphic artist Anuj Shrestha's handle on line and his surreal representation growth and the progression of time (Fig 20-21). Digital artist Markos R. Kay renders scientific based imagery, his work was particularly inspirational in the process of visualizing abstract concepts (Fig 22). For the sculptures, I am inspired by the potential of the 3D printing medium itself to replicate complex organic structures, specifically the design collaborative Nervous System creates functional and sculptural 3D printed objects based on organic forms and mathematical models (Fig 23). I see this as giving life to an invisible world.

Research in Context

Epigenetics is a growing field with a wide variety of interpretations and definitions. It is a field that is touted for having immense potential in the future of medicine and public health. Because of the complexity of the subject and the variety of biological processes it encompasses, there was an inherent challenge in communicating this topic to a public audience. So what is Epigenetics? The root "epi" mean above, so it could be defined as whatever is "above" genetics. One could interpret this as environmental differences between genetically identical organisms, the old "nature versus nurture" discussion. However, it has been discovered through a variety of experiments over time that even identical organisms raised in highly controlled environments can show very different phenotypes (Carey). On the cellular level, scientists have long been aware that even though every cell in the body has the exact same DNA, a variety of cell types exist. In 1957, the British developmental biologist Conrad Hal Waddington introduced the idea of the "Epigenetic Landscape" (Fig.24).



If the "ball" at the top of the hill is an undifferentiated cell, it can roll down into a variety of valleys, or cell types. To do so it must undergo different molecular and chemical changes, this idea gave rise to our current understanding of epigenetics as the mechanisms that modify how genetic material is expressed, that do not change the underlying DNA sequence, and can be inherited from cell to cell (mitotically) or from parent to offspring (meiotically). Another common analogy is that epigenetic mechanisms are "switches" that turn on, off, or dim genes (active regions that code for protein on DNA).

Fig. 24

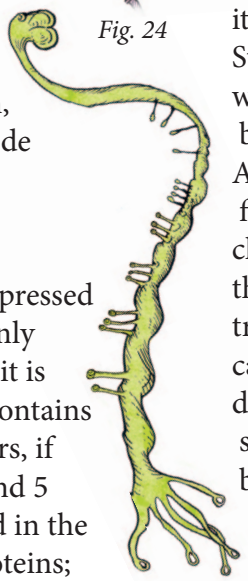


Fig. 25

The Importance of Structure

A large component of how genes are expressed is down to the physical structure, not only within the famed double helix but how it is "packaged" within each cell. Each cell contains DNA (Fig 24) around 3 billion base pairs, if stretched out the length would be around 5 feet. Within the cell, the DNA is housed in the nucleus and is bound to a variety of proteins; together the DNA and proteins it is associated with are called chromatin. How this chromatin is arranged in physical space allows the genes to be "read" by RNA(Fig 25), which turns the messages into the proteins that build and control our living body. When being transcribed, the chromatin is loosely arranged in the nucleus (Fig 26), and could be compared to tangled strands, though recent experiments have shown that even in this decondensed state the chromatin is arranged into areas called chromosome territories.

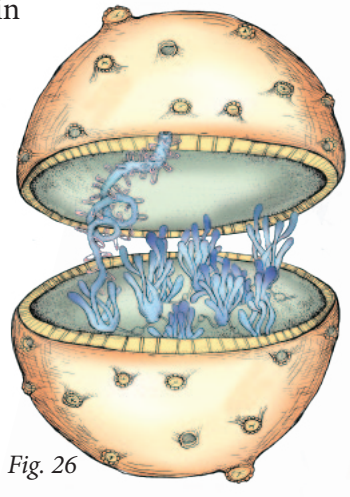


Fig. 26

the known structural hierarchy because epigenetic modification can alter this structure at its various levels. When it comes times for a cell to divide, all DNA is copied along with the protein and chemical markers associated with it. The chromatin gets wound up into chromosomes (Fig 27), and the dance of division knows as mitosis occurs. Specific proteins called histones are essential to regulate structure, they have "tails" that can bind to chemicals and proteins and change the ability of nearby genes to be transcribed. Eight histones cluster together in a ball and are wrapped twice with a DNA strand to create a structure called a nucleosome. (Fig 28)Repeated nucleosomes with linker DNA in the middle create the 10 nm fiber, which looks like beads on a string. This fiber can coil upon itself to create a 30 nm fiber (Fig 29). Structures between this level and the whole chromosome are less understood but an active area of research. A popular model is that the 30 nm fiber gets looped around a chromosome scaffold, and that long loose loops can be transcribed and tighter loops cannot. It is important to describe the known structural hierarchy because epigenetic modification can alter this structure at its various levels.

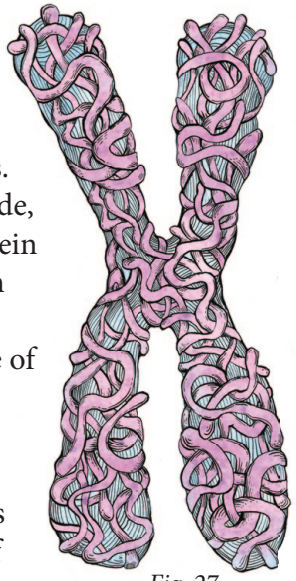


Fig. 27

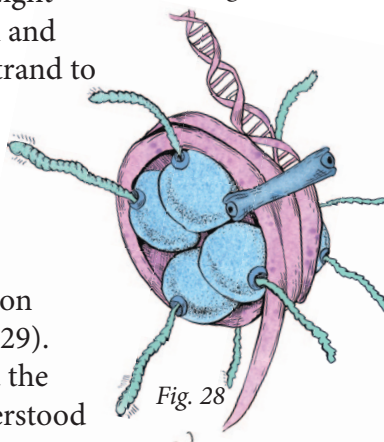


Fig. 28

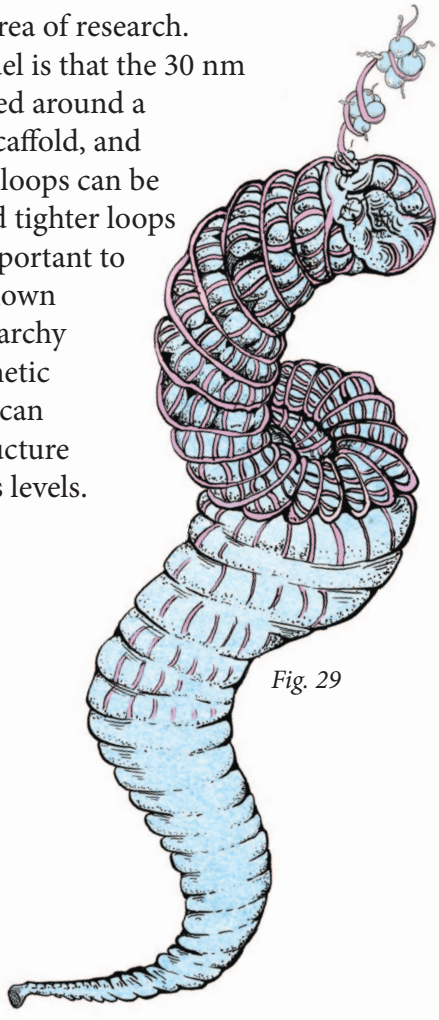


Fig. 29

Chemical and Molecular Mechanisms of Epigenetics

Specific epigenetic modifications are continually being discovered. Generally, these modification fall into DNA Modification, Histone Modifications, Histone Variants, and non coding RNAs. The only accepted DNA modification is the attachment of a methyl group to cytosine on DNA, this turns off any gene containing a methylated cytosine(Fig 30). The disruption of this mechanism has been found to be associated with cancer. There are many different types of histone modifications. The more common types are methylation (adding a methyl group to the histone tail), acetylation, and phosphorylation. Histone Variants are modifications that involve one of the core histones in the nucleosome being swapped out by a different version. These mechanisms have a variety of affects including regulating nucleosome assembly, transcription, DNA repair, and chromosome condensation.

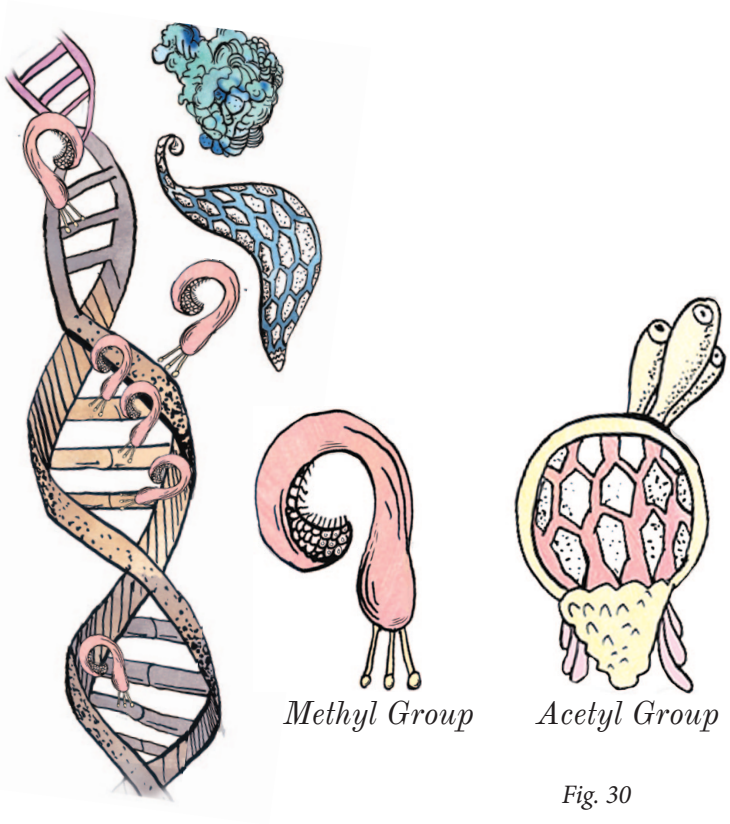


Fig. 30

Therapeutic Potential

Understanding the mechanism, and location within the complex structure of DNA compaction gives us the ability to moderate gene expression without tampering with the DNA itself. Epigenetic therapy is the use of drugs or other epigenome-influencing techniques to treat medical conditions (Dawson). Cancer is the uncontrolled growth of cells. This growth can be caused by the epigenome not working properly, such as the the methyl groups that re supposed to stop transcription as certain areas are lost, cancer can result (Li).

Conclusion

The topic of Epigenetics is a challenge to visualize yet provides a rich amount of details to inspire creative exploration. By breaking it down into pieces, and by using multiple mediums it can be explained to a public audience that can learn some level of information about biological systems in their own body as well. With my work I hope to inspire curiosity about the interesting complexity of the natural world.

References

Carey, Nessie. The Epigenetics Revolution: How Modern Biology Is Rewriting Our Understanding of Genetics, Disease, and Inheritance. 2013.

Dawson, Mark A., and Tony Kouzarides. "Cancer Epigenetics: From Mechanism to Therapy." Cell: 12-27. Print.

"Katie Scott Is a Freelance Illustrator Based in London." Katie Scott. Web. 25 Apr. 2015. <http://katie-scott.com/>.

Li, Keqin K., Fangcheng Li, Qiushi S. Li, Kun Yang, and Bilian Jin. "DNA Methylation as a Target of Epigenetic Therapeutics in Cancer." Anti-cancer Agents in Medicinal Chemistry(2013): 242-47. Print.

"MRK : MRKism : MRKfolio." MRK : MRKism : MRKfolio. Web. 25 Apr. 2015. <http://www.mrkism.com/>.

"Nervous System." Nervous System. Web. 25 Apr. 2015. <http://n-e-r-v-o-u-s.com/>.

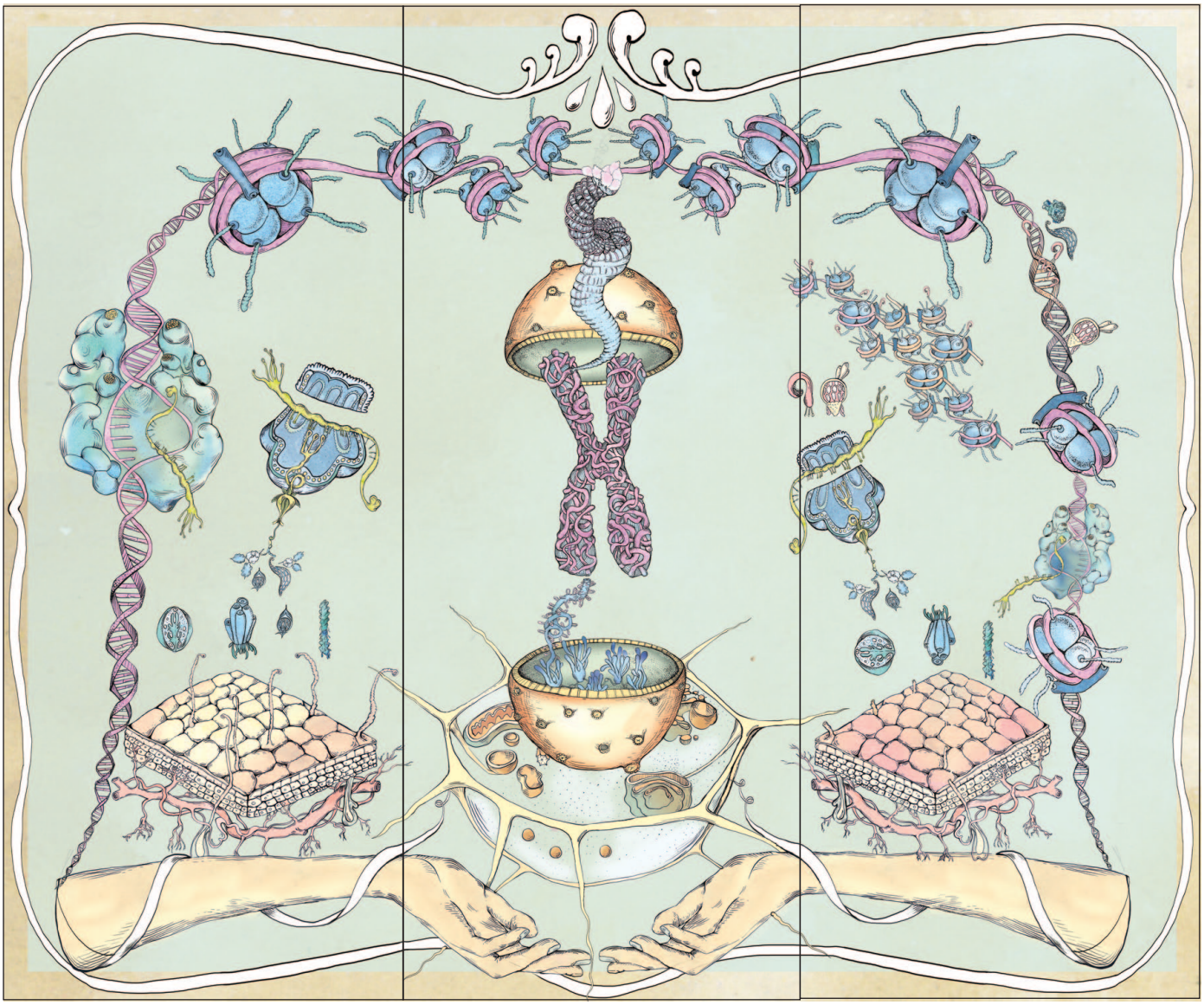


Figure 1

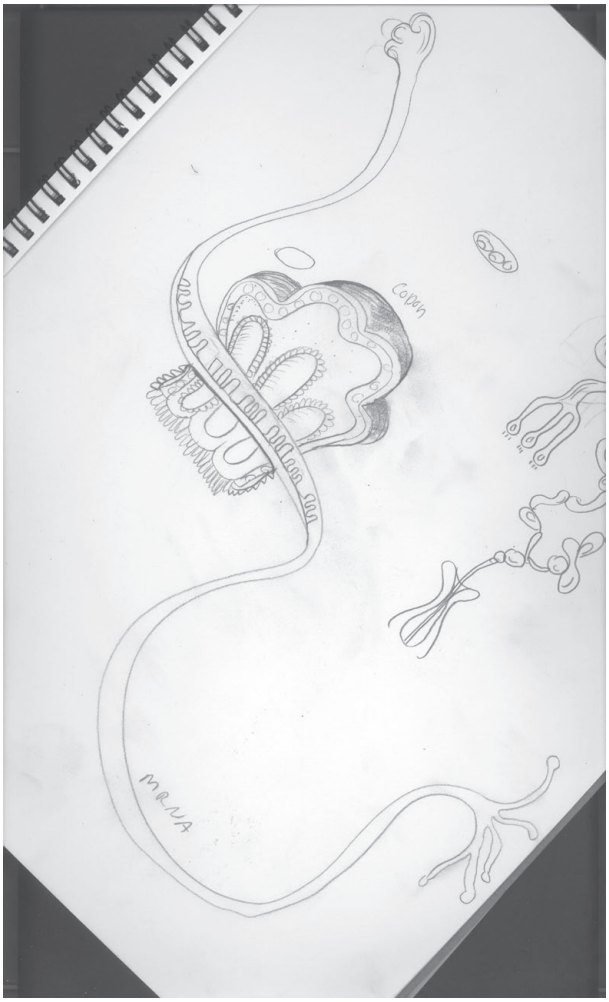


Figure 2

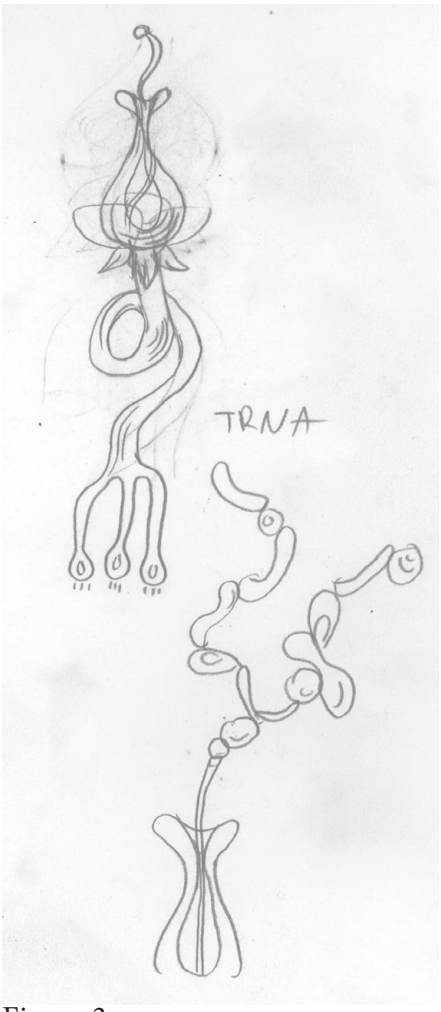


Figure 3

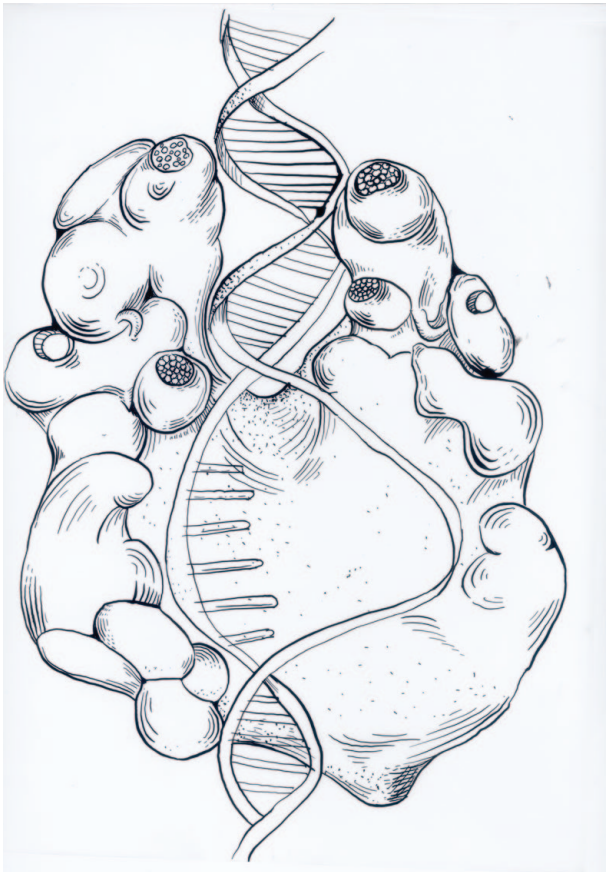


Figure 4

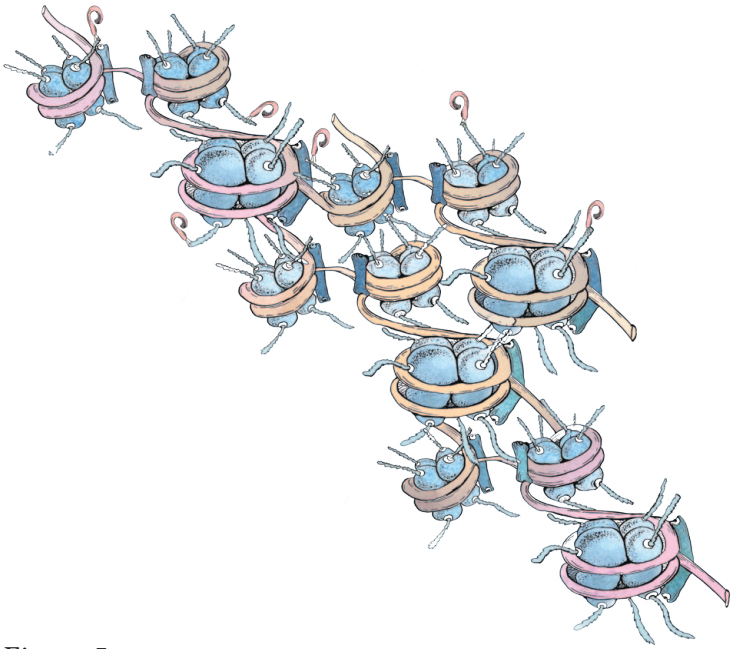


Figure 5

Figure 6

Figure 7

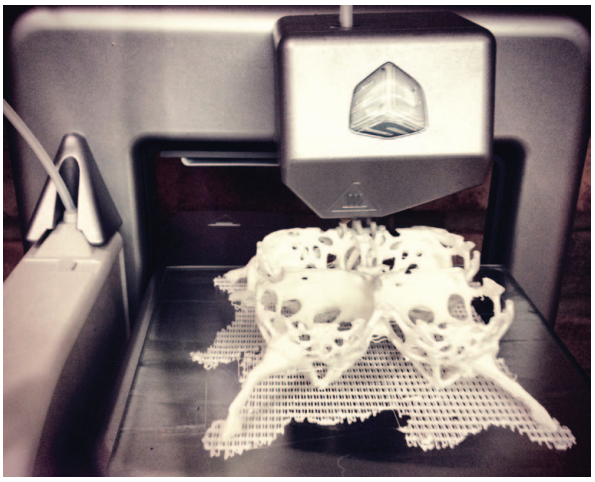
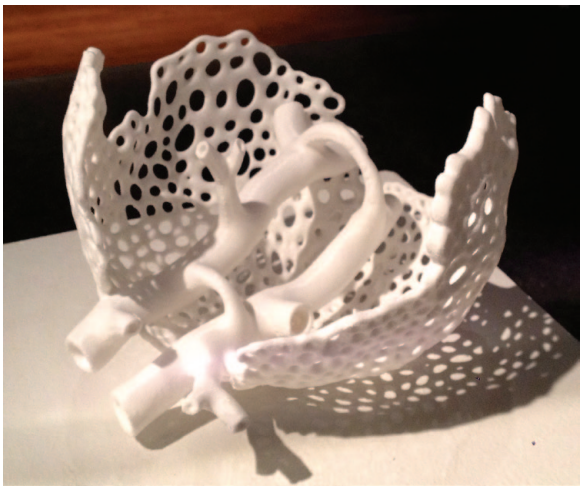


Figure 8

Figure 9

Figure 10

Figure 11



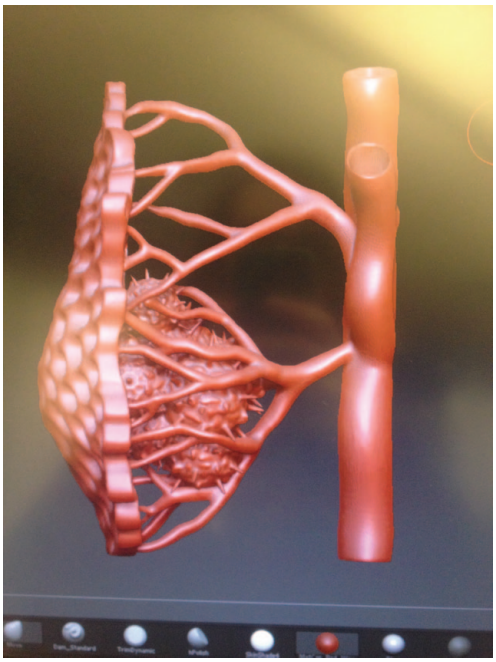


Figure 12

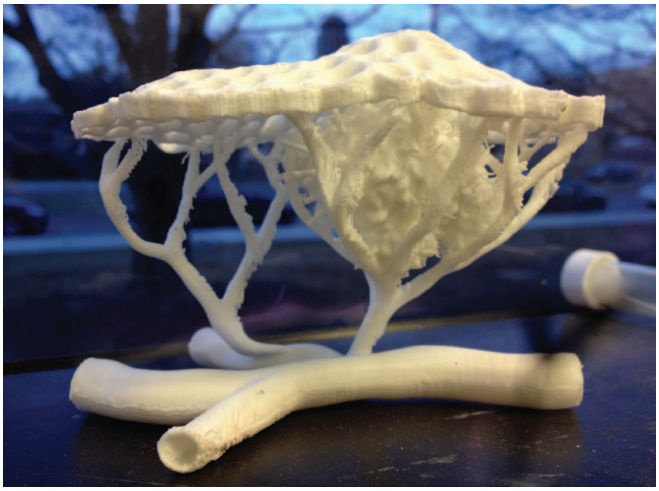


Figure 13

Figure 14

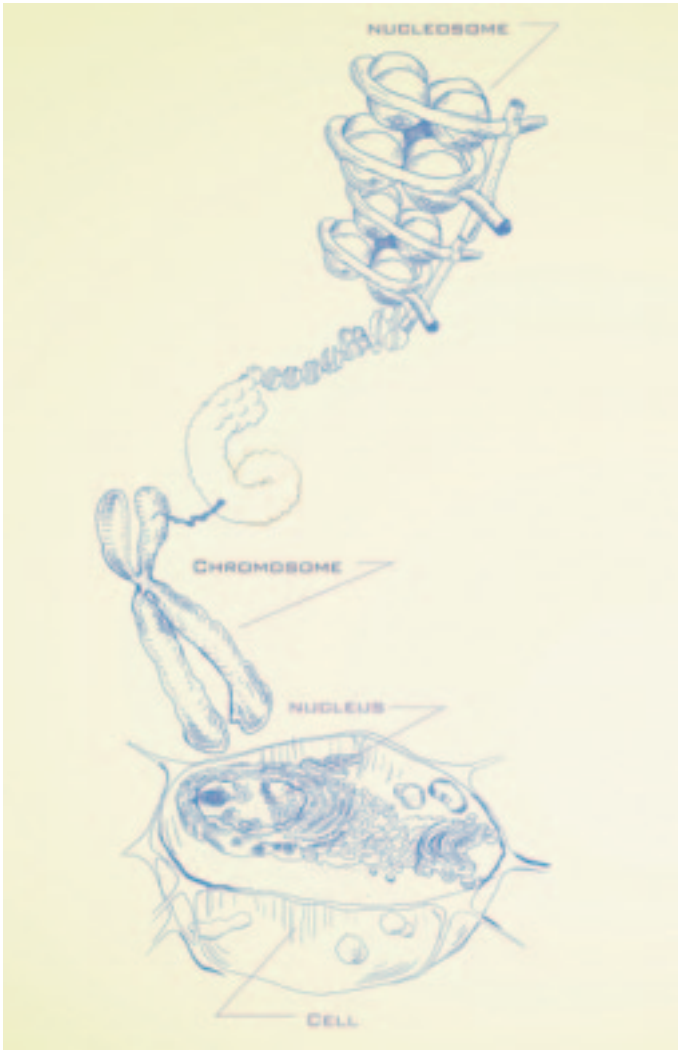


Figure 15

Figure 16

Figure 17- Vincent Fournier

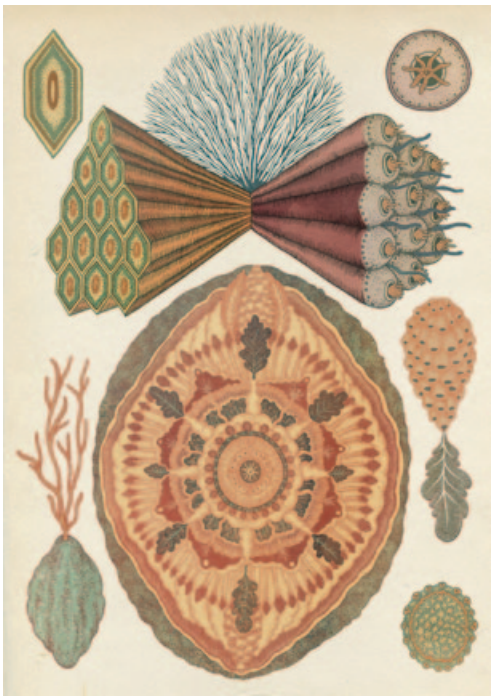


Figure 18- Katire Scott

Figure 19- Katie Scott

Figure 20- Anuj Shrestha'

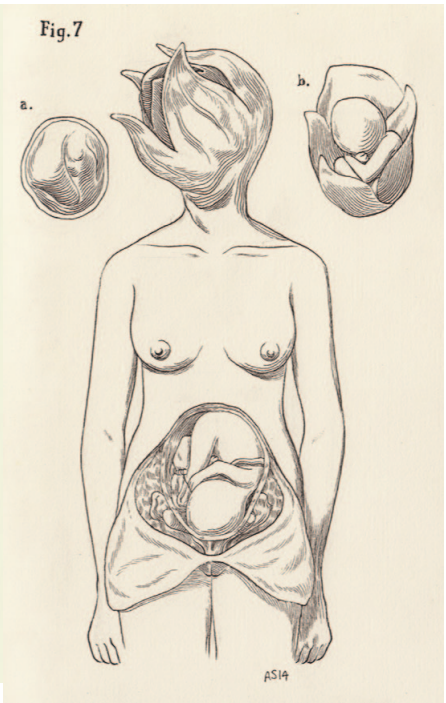


Figure 21- Anuj Shrestha'

Figure 22- Markos R. Kay

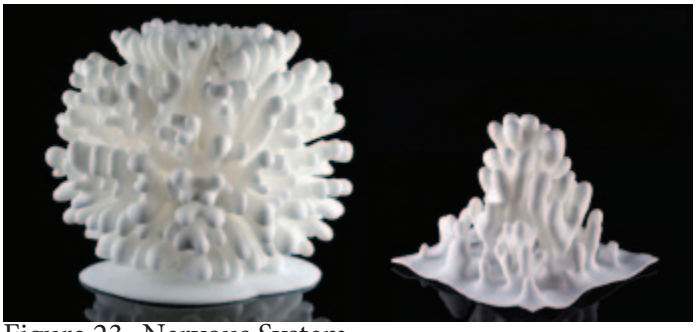


Figure 23- Nervous System