

It's Written in your DNA – Or is it?

Popular belief holds that we have a gene for this and a gene for that, but a single gene is seldom responsible for a single trait. Rather, traits are much more complex, with many genes and hundreds if not thousands of interactions involved, with many small cumulative changes on genes affecting health outcomes. The ultimate aim at the forefront of genetics research is to eradicate disease, lift people out of poverty and ease suffering.¹ The main areas of investigation include: understanding variation in the human genome (code), understanding the biology of the genome (structure and function of DNA) and understanding the biology of disease.²

The biology of the genome and epigenome are relatively new fields. In these, the significance of three-dimensional structure on chromosomal regions is considered and the effects these have on changing the expression of the protein coding genes. Chemical modification of molecules in the epigenome control the compact nature of the DNA strand, but a full reading of the genome remains as much a mystery as the Rosetta Stone was for almost a century in the 1800s. The task ahead is to unlock the syntax and discover the role genetics and epigenetics³ play in our health and wellbeing.^{4 5}

THE NEW LANDSCAPE OF DNA

Julia Horsfield's research area is the protein complex known as cohesin.⁶ Her research group looks at the components of DNA strands ("noodles" in the nuclear soup) at a molecular level through the lens of biochemical experiments using proximity ligation. The lab captures molecular data to reveal information about the chromosome's contours and topological behaviour at the instant of fixation for investigation – noting of course that chromosome are fluid and dynamic, flexing and changing as they constantly transition between different states (work/ gene expression/protein manufacture and cell division). Research into the cohesin complex reveals that it controls DNA packaging within the "noodle soup"⁷ of the cell nucleus. The way DNA strands fold control which bits of a chromosome are *active*, in *communication* with each other *and* neighbouring strands, and which bits are not.⁸ Thus cohesin acts as a regulator to control which loops are working in concert, or otherwise, with the RNA gene expression machinery and other chromatin modifiers to determine the spatial and temporal organization within the cell. Cohesin is also important at the time of cell or DNA replication.

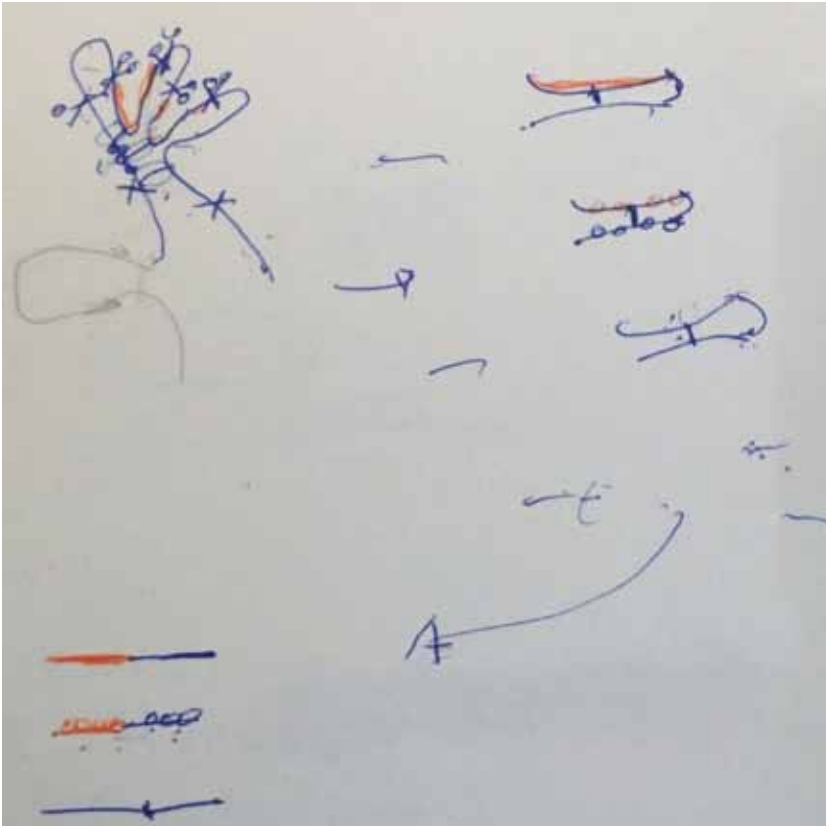


Figure 1. Diagram of proximity ligation from sketchbook – conversation Julia Horsfield and Pam McKinlay.

In the first part of proximity ligation, formaldehyde fixes the loops in stasis. They are cut up by “molecular scissors” and the ends of the segments are joined together by ligase. When the newly joined sections are compared against a standard linear chromosome, it is found that the counterpart sequences appear far apart; the ligation means that they must have been adjacent or closer to each other when folded or contracted in three-dimensional nuclear space. The conceptual model used to explain this is that the chromatin strand forms loops held in place by cohesin, which acts like a climbing carabiner. It guides how the chromosome folds into a compact space, but still has the ability to freely move when needed. The frequency of these loop proximities are proportional to the number of times a particular DNA segment appears in the experimental read-out, and show which segments of DNA interact the most frequently.⁹ The frequency of interactions can be visualised in a “heat map”, and reveal Topological Associated Domains (TADs), which are zones of high 3D connectivity.¹⁰ The analysis of the diagram reveals which loops were in communication with each other at the time of fixation and which bits were isolated. Active linked regions are shown in hotter colours, e.g., red. This was an area of research explored in the Art and Genetics project.

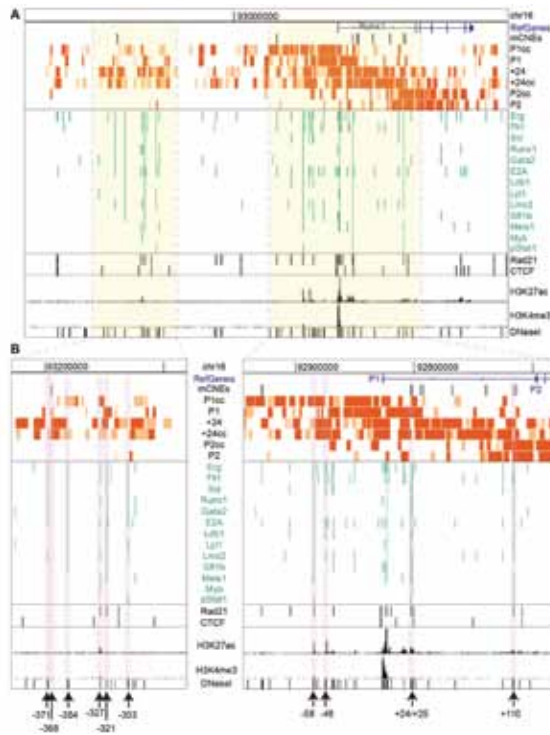


Figure 2. Heat map from Julia Horsfield's research.

WOVEN IN OUR DNA

Genetics is the study of heritability. We talk about DNA as the thread of life and of traits as being woven in our DNA. The project with weavers Keller and McKinlay naturally lent itself to a textile expression. We inherit our genes when we are born, and baby blankets are also an item passed down the generations as an heirloom. In the finished piece, Christine wove a DNA baby blanket.

The idea was to use a dye process to mimic what happens to individual chromosomes in the cell. The technique of ikat weaving is when the threads woven (warp or weft) are tied and dyed before weaving. The technique has appeared in various places on the planet, but historically evolved to mastership in Indonesia, Japan and parts of Africa. While in Indonesia the ikat motifs are more often figurative, the Japanese style is more geometric, nonfigurative and lineal. The colour choice in Japanese ikats is minimal and our choice of only one colour aligns more with the Japanese tradition. In our project, we did not tie the warp threads before dyeing, as in resist dyeing techniques. Jun and Josiko Tomita describe in their book *Japanese Ikat Weaving*¹¹ a variation called *fukiyose ikat*, a technique in which the material is dip-dyed. This is similar to the process of dyeing for the warps in *Heirloom*.

Twentythree individual warps (our 23 pairs of chromosomes) were carefully laid out and measured on Christine's footpath before looping. The intersections of the loops were then marked with red dye in the dye bath. The warps were folded onto the loom in pairs, creating 46 sections. The areas



Figure 3. Composite image of dyeing process. Our cohesin loop-model experiment used red dye to mark the areas of contact where the cohesin molecule complex would be. When laid flat, the relationship on the lineal warp to the compacted or folded state of the chromosome was revealed.

of red marks spaced along the straightened warps now revealed the interactions which had been occurring between the sequences amongst the neighbouring loops, as previously packaged in the dye bath (our noodle wool soup/cell nucleus). The final woven piece mimicked both the appearance of a “heat map” and the ikat form of weaving.

The colour red is one we found often used when researching the active linked regions of the heat maps. As Christine is from Hamburg and red and white are the colours of that city, that gave us another reason to choose this colour. Christine writes about her weaving process:

It was a great joy to work with the theoretical framework and set of numbers provided to me by the science, and then see what would happen. When folding the warps on the loom, I assigned the number "1" to the pair in the middle of the loom and "23" to the two edges. While weaving I realized that chromosome number nine was too narrow. I had made a mistake and therefore caused a mutation in chromosome nine. Also as threads in the chromosome sixteen broke. I needed to do some genetic editing there. I chose to use fresh genetic material – an option I had just learnt about on Radio National. The selvedge on the blanket did not work out as smooth as a weaver wishes for, and that meant to me that the person related to the blanket might have some gender issues – interesting ... For presentation of the piece, I needed to find the solution for the different length of the warp ends and made them into wild long tassels. I googled that changes on chromosome number sixteen could cause thalassemia,¹² an inherited blood disease, and for me it was clear what they meant – tasslemania. I surely have it!



Figure 4. Composite image of Christine Keller weaving , work in progress.



Figure 5. *Heirloom*, installation view, rear view showing tassels.



Figure 6. *Heirloom* - installation view, front view showing "heat map".

Pam McKinlay has a Dip HSc (clothing/design and textile science) and a BA in art history from the University of Otago. She works predominantly in textiles , photography and sculptural installation.

Christine Keller MFA Concordia University, Montreal (2004), Masters equivalent in product design, Gesamthochschule Uni Kassel, Germany (1993). Head of textile section at the Dunedin School of Art (2005 – 2010). She founded Weaving on Hillingdon (2012) and Dunedin's LOOM ROOM (2015), where she now teaches weaving again.

Dr Julia Horsfield is a developmental geneticist based in the Department of Pathology at the University of Otago. Julia leads a research group investigating the role of chromosome structure in animal development and cancer. Her specific research interest lies in cohesin proteins.

Thanks also to Valerie Parkes of Honey Lane Studios for allowing us to weave on Rosalie Sommerville's loom.

1. Drew Berry, "Astonishing Molecular Machines," *TEDx Talks* (2011), <https://www.youtube.com/watch?v=DfB8vQokr0Q> (accessed 29 July, 2017).
2. Eric Green, "The Genomic Landscape," *National Human Genome Research Institute* (2014), https://www.youtube.com/watch?v=Lgm5dA1D_pc (accessed 29 July, 2018). For example, the search for a vaccine which would halt the suffering and mortality caused by the malaria parasite or new therapeutic means of fighting cancers.
3. Courtney Griffins, "Epigenetics and the Influence of Our Genes," *TEDxOU* (2012), <https://www.youtube.com/watch?v=JTBgGhqueuTg> (accessed 29 July 2017). Epigenetics is a set of instruction which sit on top of the DNA. The instructions are in the form of markers on the chromatin which tell the chromosome when and where to compact and affects how a cell reads the genes in the underlying DNA.
4. Jeffrey Alexander et al, "Nuclear Architecture as an Epigenetic Regulator of Neural Development and Function," *Neuroscience*, Vol. 264 (2014), 39-50 <http://www.sciencedirect.com/science/article/pii/S0306452214000657> (accessed 29 July 2017).
5. Courtney Griffins, 2012. New therapeutic approach possibilities in for example cancer – if we can use epigenetics to reverse the toxic abherent marks that have adverse effects eg. tumour suppressor gene in cancer – a reversal could keep this gene functioning to protect cells ie this way would be to restore cells to normal functioning nature – a radical departure from current conventional cancer therapy which is to kill cells.
6. Kim Nasmyth, "How is DNA Woven into Chromosomes?" *Israel Institute for Advanced Studies* (2016), <https://www.youtube.com/watch?v=uUv86Bu9cF8> (accessed 29 July 2017). The tri-partite ring of cohesin is an essential element in the protein structural biology model.
7. Kleinschidt "1961" in Nasmyth, "How is DNA Woven into Chromosomes?" *Israel Institute for Advanced Studies* (2016) 8:36-9:49, <https://www.youtube.com/watch?v=uUv86Bu9cF8> (accessed 29 July 2017).
8. Laura Elnitski, "Regulatory and Epigenetic Landscapes of Mammalian Genomes," *NHGRI Current Topics in Genome Analysis* (2014), https://www.genome.gov/pages/research/intramuralresearch/dircalendar/ctga2014/ctga2014_1ec05_color.pdf. (accessed 29 July, 2017). See diagrams and also how enhancer genes exploit the three-dimensional arrangement between neighbouring strands.
9. Stefanie Kaufmann et al, "Inter-Chromosomal Contact Networks Provide Insights into Mammalian Chromatin Organization," *PLoS Journal* (2015), <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0126125> (accessed 29 July 2017).
10. Kim Nasmyth, "How Does Cohesin Hold DNAs Together?" *Israel Institute for Advanced Studies* (2016), <https://www.youtube.com/watch?v=uUv86Bu9cF8> (accessed 29 July 2017). In the ring model cohesin holds sister chromatids in position – note this is a topological model, not a binding model. Think of cohesion as a freezer bag clip or climbing carabiner.
11. Jun and Noriko Tomita, *Japanese Ikat Weaving: The Techniques of Kasuri*, (London, Boston, Melbourne and Henley: Routledge & Kegan Paul, 1982), 9.
12. "How Do People Get Thalassemia?" *Information Centre for Sickle Cell and Thalassemic Disorders* (1998), http://sickle.bwh.harvard.edu/thal_inheritance.html (accessed 30 July 2017).