Single chromosome sequencing with Haplomic Technologies

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Emily Warrender July 11, 2025

Explore single chromosome sequencing with Haplomic Technologies, starting with some background and corporate history

Haplomic Technologies Pty Ltd (HT) was established in 2004 by Dr Malcolm Simons (who sadly passed away in 2012) and Mr Geoff Swanson with the specific objective of developing intellectual property for the DNA sequencing of single chromosomes to determine the haplotypic phase. HT was granted over 20 international patents on haplotyping from 2004 to 2012.

The close professional working relationship between Dr Brian Tait and HT for many years generated volumes of laboratory data and technical substance on haplotyping, which contributed significantly to the development of HT's knowledge base and future commercial prospects.

However, at that stage, there were no reliable methods for routinely isolating single chromosomes from single cells for sequencing while the scientific world was reporting widely that haplotyping represented one of the greatest opportunities for understanding the genetics of many complex diseases!

In 2008, Geoff Swanson proposed the concept of using microfluidics to separate, isolate and collect single chromosomes from a single cell.

In early 2009, HT sought advice from CSIRO (Dr Philip Hendry, Genomics Research Program Leader, CSIRO Molecular & Health Technologies, North Ryde) regarding the merits of using microfluidics for single-chromosome isolation and collection. Further discussions were held with Dr Garry Hannan, Leader of the GWAS Study Group at CSIRO Molecular & Health Technologies, and Dr Yonggang Zhu, a CSIRO Senior Scientist, which resulted in CSIRO strongly endorsing HT's proposed microfluidics concept and offering a dollar-for-dollar joint venture (JV) development project with HT.

Unfortunately, HT was unable to raise equity funds, and the JV with CSIRO could not be realised. At this stage, HT continued to develop intellectual property and engage in widespread discussions with potential funders and partners.

A detailed search for expertise in scientific instrument R&D in Australia, particularly in microfluidics, led to the introduction of MiniFab (MF). HT successfully raised private investor funding and, in 2014, contracted MF to develop a prototype microfluidic test bed for isolating and collecting single chromosomes. MF was subsequently the subject of a takeover in 2019 and is now owned by the German company Schott.

Since commissioning the development program with MF, HT continues to provide technical support through its Technical Team and Consultants viz: Dr Brian Tait (CSO, HT) – Clinical Genomics, Mr Greg Allen (HT) – Cytogenetics, Geoff Swanson (HT) – Instrumentation, until his recent departure Filip Pajpach Dr Melinda Jasper (Consultant University of Adelaide) – Single Cell/Chromosome Sequencing, who has recently taken over Filip's work on labelling.

MF's R&D program is strongly complemented by expert engineering, design, and market intelligence from Planet Innovations Pty Ltd, a Melbourne-based engineering company, and Silverpond, which has developed AI software for the detection of a single metaphase cell suitable for lysis and chromosomes post-lysis.

Technology developed by HT

New groundbreaking technology for assigning phase to multiple mutations – a unique contribution to clinical medicine.

Background

Most human diseases have a genetic component which contributes to disease risk. This is detected at the population level in the form of mutations or changes in the DNA sequence of a gene or gene(s) in the patient cohort, which is statistically different in frequency from that seen in non-disease patients (control group).

These changes in the DNA sequence invariably reflect alterations in the functioning of the protein molecule coded for by the gene. If the mutations are in the regulatory region of the gene, the amount of protein produced can be increased or decreased. Alternatively, the mutations may result in changes in the part of the protein that is responsible for its function.

An increase in the amount of protein produced or an alteration in its function can result in a disease state depending on the gene involved and the network of gene functions which are disturbed.

Human cancers have multiple gene involvement, which makes for a complexity of susceptibility, which is difficult to interpret but is often best observed in the context of gene interactions in a network of processes which ultimately lead to disease.

In many human diseases, particularly human cancers, mutations in genes that lead to disease do not exist in isolation. They are often associated with other mutations in the same gene, and the "responsible" mutation is often defined as the one with the greatest statistical association. However, the entire gene is the unit of inheritance, and other mutations, which may not reach the same level of statistical association, can also play a role in disease susceptibility.

One approach to addressing this issue is to determine the phase of multiple mutations. In other words, determine whether observed mutations are inherited on the same chromosome or the other homologous chromosome. (one of each of the 23 pairs of chromosomes are inherited from each parent).

The combination of gene(s) mutations on one chromosome is referred to as a haplotype, a term first coined by Ruggero Ceppellini at the third Histocompatibility in Torino, Italy, to explain the co-occurrence of HLA alleles on one chromosome.

It is imperative to consider haplotypes in the interpretation of disease risk. For example, let us consider the simple hypothetical case where there are two gene mutations that impact the function of the product of that gene to the extent that it renders it non-functional.

If the mutations are on the same chromosome, then one protein product will be non-functional while the other chromosome will code for a normal product, i.e. 50% overall function. If one of the mutations occurs on one chromosome while the other is on the homologous chromosome, then both protein products will be affected, and function may or may not be affected. This simple example illustrates why it is critical to determine haplotypes or phase to accurately assess disease risk and to fully appreciate how particular genes function to confer disease.

Defining phase

The conventional method for establishing phase (haplotypes) is by family segregation studies. Providing an individual proband's parents are different for the gene sequences under study; then phase can be established, which can be two single nucleotide polymorphisms on one allele or for alleles at neighbouring genes.

In the absence of family studies, the assignment of haplotypes becomes an exercise in probability, based on linkage disequilibrium.

Technical synopsis

In the absence of reliable, definitive techniques for assigning haplotypes outside of family studies, we at HT believe the only method for assigning haplotypes over megabases of DNA with certainty and without relying on statistical probability involves the separation of the two homologous chromosomes from the 23 pairs of chromosomes within a single cell. To achieve that aim, we have developed a nanotechnologically designed cartridge which traps and then lyses a single metaphase cell, which releases the 46 (23 pairs) of chromosomes as singular entities, two of which are labelled (chromosomes of interest).

By selecting appropriate polymerase reaction (PCR) primers, the gene of interest can be haplotyped by sequencing. By definition, there is no limit to the length of haplotypes that can be defined by this method. This has not been achieved before, and such a technique would be applicable to any gene(s) and any disease; therefore, it is of profound

importance in the era of molecular and personalised medicine. We believe our technology will revolutionise both the research and treatment of a range of human diseases, including cancers.

One immediate application is in the field of bone marrow transplantation. This is an area of clinical medicine where haplotype matching has been shown to have a distinct effect in terms of patient survival using unrelated donors. The haplotypes which are matched are called HLA and are found on a 3-megabase stretch of DNA on human chromosome 6. Those donor/ recipient pairs who are haplotype matched have been shown to have significantly lower life-threatening graft versus host disease (GVHD) than those pairs which are matched at individual HLA loci, but not haplotype matched.

Our customer market surveys indicate a keen interest in this technology amongst both clinicians and scientists involved in bone marrow transplantation.

Multiple other medical disciplines will come online and benefit from our technology when information concerning HT technology becomes more widespread.

Primary Contributor

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