**////Title: Genome Organisation and Centromeres and the Evolution of Cancerous Cell Lines**

**////Stand-first**:

There are over 3,600 established cell lines from 150 different species that can be used for scientific and medical research. In two recent studies, Dr Ruth MacKinnon and her team from St Vincent’s Hospital in Melbourne used multiple molecular methods to investigate changes in the way the genes are organised in two types of these cells. They demonstrated the importance of using multiple complementary methods and found that these cells can continue to evolve in the laboratory. They also uncovered evidence of a previously unreported process called ‘centromere capture’ which may be involved in the evolution of cancer cells.

**////Body text:**

The use of cell lines, which are populations of cells with the same genetic makeup, has revolutionised medical research. They are used in a huge range of ways including cancer research, vaccine development, and the scientific study of gene functions. Cell lines from cancer cells are particularly common in scientific research as they can often reproduce indefinitely in the laboratory environment and provide a good model to understand different cancers and treatment options without the ethical implications that come from using human tissues.

It is important to understand the background of the cells used in medical research and to know what underlies their ability to cause cancer. Cells can continue to evolve and change whilst in the laboratory, and this can lead to different research groups working on what they think is the same cell line. However, such changes have led to the cells behaving differently. Differences in the cells can be due to natural evolutionary changes or can be an artefact of the different methods used to screen for changes as part of the experimental approach.

Dr Ruth MacKinnon from St Vincent’s Hospital in Melbourne Australia leads research into understanding the role of chromosomes in the development of cancer, as well as investigating the impact of genetic changes in research cell lines.

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DNA in human cells is stored in structures called chromosomes, the classic X (and sometimes Y) shaped bodies. The karyotype is the complete set of chromosomes within a cell. Karyotyping is a way of looking at an individual or cells chromosomes, as well as showing the number of chromosomes present it also highlights structural changes such as deletions, duplications, and translocations or rearrangement of the chromosomes. These changes can lead to abnormalities, and complex genome reorganisation is known to be a feature of many cancerous cells. Unfortunately, these changes can be notoriously difficult to analyse.

Dr MacKinnon and her team have investigated the genome organisation of two cell lines commonly used in scientific research, U937 [U 9 3 7] and HEL [H E L]. U937 was established from a patient with histiocytic lymphoma and is commonly used to study the development of certain types of blood cells.

The HEL cell line was established from a patient with acute myeloid leukaemia and is used in the study of cell biology. The team used a broad range of molecular cytogenomic techniques to characterise the genomes of U937 and HEL – as well as defining the chromosomal arrangement of these cell lines, their work demonstrated the importance of using multiple complementary methods to understand genome changes in cancer cell lines.

Dr MacKinnon’s 2013 study investigated the genome organisation of HEL cells from different laboratories. This work showed that the HEL cell line has a highly rearranged genome, and in particular, the researchers found evidence to suggest that a specific type of chromosomal change called the ‘breakage-fusion-bridge cycle’ had led to increased numbers of cancer-causing genes within the cell line.

This study also provided the first evidence for a process called centromere capture which is involved in cancer evolution. The centromere is an area that links the two arms of a chromosome together, and when a cell divides the centromere helps distribute the divided chromosomes to the daughter cells. A telomere is the area at the end of a chromosome that protects the chromosome from damage.

Chromosomal rearrangement refers to when pieces of chromosomes are missing, duplicated or have moved location. If a broken chromosomal segment can acquire a centromere and telomeres, it is much more likely to survive which is important if this segment contains a cancer-causing gene. By looking at the gain, loss and change of parts of chromosomes this study also illustrated how the HEL cell line continues to evolve in the laboratory environment.

U937 was first described in 1976 but ten years on, the batches used by different research groups showed markedly different karyotypes. In a more recent study, Dr MacKinnon used a selection of molecular techniques to investigate these differences and compare them with previously published images and karyotypes to examine variation between U937 cell lines in different laboratories.

This study characterised the karyotype of U937 and highlighted how a combination of techniques can provide more detail and more accurate results than any technique used on simply its own. This work also helped demonstrate which differences are due to the evolution of the cell line and which are due to different methods of laboratory analysis. During this study, the research team again found evidence of centromere capture, suggesting it is very in common cancer cells.

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Dr MacKinnon and her team’s work has highlighted the importance of using multiple complementary methods to understand genome changes. They have also shown that these detailed and precise methods are useful in identifying the steps producing the genome changes which are common in both cancer and laboratory cell lines.

This work is hugely beneficial to the field of cell and cancer biology as it provides evidence that genome changes should be clearly kept in mind when using cell lines, as well as providing important evidence to support the use of appropriate experimental tools.

This SciPod is a summary of the papers ‘Genome organization and the role of centromeres in evolution of the erythroleukemia cell line HEL’ from Evolution, Medicine, and Public Health. DOI: [10.1093/emph/eot020](https://dx.doi.org/10.1093%2Femph%2Feot020), and ‘Detailed molecular cytogenetic characterisation of the myeloid cell line U937 reveals the fate of homologous chromosomes and shows that centromere capture is a feature of genome instability’ from Molecular Cytogenetics. DOI: <https://doi.org/10.1186/s13039-020-00517-y>

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