Viral elements originating from human ancestors are systematically activated in the early development of embryos

June 24 2015

Credit: AI-generated image (disclaimer)

Viruses incorporated into the human genome millions of years ago may now play a role in the early stages of human embryo development, according to researchers at A*STAR.

Certain types of viruses make use of early embryonic cell development to integrate their own DNA into the human genome, allowing the virus to be passed down through generations. Elements of ancient viruses that infected our ancestors long ago are still found in the human genome today, and are known as endogenous retroviruses (ERVs). Most of these elements have lost their ability to generate active viruses. However, Jonathan Göke and co-workers at the A*STAR Genome Institute of Singapore have shown that groups of ERVs may still play an active role in human embryonic development.

"In our previous work, we found that one class of ERVs, called HERV-H, is activated in human embryonic stem cells," describes Göke. "Although these stem cells are used as a model of the human embryo, there are many differences between them. We wanted to clarify if ERV families are also expressed in human embryos, and what pattern this expression follows."

The team analyzed publicly available data to establish the amount of RNA related to each gene containing ERV elements. However, the elements they were searching for were highly repetitive, occurring in almost identical copies several thousand times in the human genome. To get around this, Göke and his team exploited the fact that every ERV hosts unique mutations, and only analyzed the regions containing these mutations to trace the activated ERVs.

To their surprise, the team found that each specific ERV group was activated according to the developmental stage of the embryo. The number of activated ERVs was highest in the early stages, from one-cell (oocytes) and two-cell (zygotes) embryos to four-cell embryos. The later cell stages also exhibited considerable ERV expression. ERVs were systematically activated, and highly cell-type specific, particularly in the later stages.

"We didn't expect ERVs to contribute so prominently, or so methodically, to the process," states Göke. "It means the ERVs can be used to identify subpopulations of cells. We have already demonstrated this approach by identifying a stem cell state that is closer in terms of gene expression to the human embryo than current embryonic stem cells ."

Göke and his team aim to conduct further investigations into ERV expression to understand the nature of embryonic cells and how they mature, as well as to clarify if ERVs have specific functions within human cells.

More information: "Dynamic transcription of distinct classes of endogenous retroviral elements marks specific populations of early human embryonic cells." *Cell Stem Cell* 16, 135–141 (2015). dx.doi.org/10.1016/j.stem.2015.01.005

Provided by Agency for Science, Technology and Research (A*STAR), Singapore