Recipe for iPSCs

Induced pluripotent stem cells (or iPSCs) are the result of a bio-technological intervention named cellular reprogramming which involves converting adult somatic cells into undifferentiated cells with acquired pluripotency. In other words, this process involves taking a mature specialized cell from adult human tissue (a skin cell, liver cell, heart cell, etc.) and transforming it into a cell that resembles those which are present during the early stages of embryonic development. Such cells effectively have the potential to develop into any type of cell in the body.

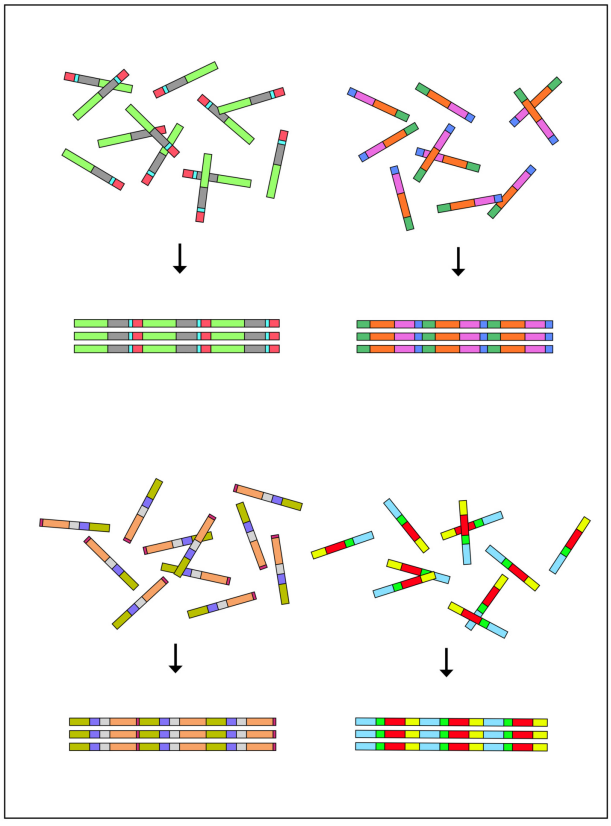
In 2012, medical biologist Shinya Yamanaka was awarded the Nobel Prize for Physiology or Medicine for his pioneering work on iPSCs. Yamanaka's breakthrough involved identifying 4 specific transcription factors (proteins which modulate the rate at which DNA in the genome is transcribed into messenger RNA), and facilitating their over-expression in mature cells to induce a pluripotent state. These factors, which are now often referred to as "Yamanaka factors," are named Sox2, Oct3/4, Klf4 and c-Myc.

iPSCs enable possibilities for novel research opportunities and clinical applications. For instance, iPSCs are used to grow organoids (miniature versions of animal tissues) by subjecting them to in vitro culturing environments which stimulate cellular specialization and structural self-organization. Researchers use these organoids to model disease, study function, or test cell therapies and drugs. iPSCs can also be used in longevity research to study the epigenetics of aging. Since epigenetic mechanisms are fundamental to both cell specialization and the aging process, researchers can use iPSCs to better understand how the accumulation of deleterious epigenetic alterations effect the ability for cells to function effectively over the organismal lifespan. iPSCs have also been used to recapitulate mammalian gametogenesis (the process by which sex cells are produced in an organism) in vitro. These researchers use mouse iPSCs to grow gametes in order to study meiosis, gamete development, infertility and other reproductive-related disorders. Some researchers have used these somatic cell-derived gametes to create embryos, which have gone on to develop into healthy, reproductively viable mouse offspring. Researchers are now working on achieving a similar process in human subjects.

While there is now more than one effective method for achieving cellular pluripotency, it is my understanding that Yamanaka's original work took something like the following approach:

Gene Synthesis

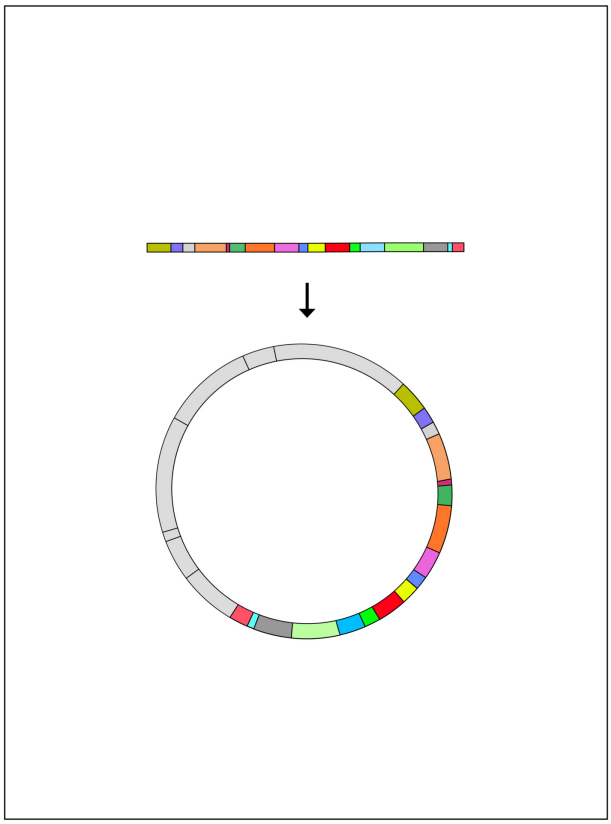
① Synthesizing a genetic sequence associated with the expression of the four Yamanaka factors.



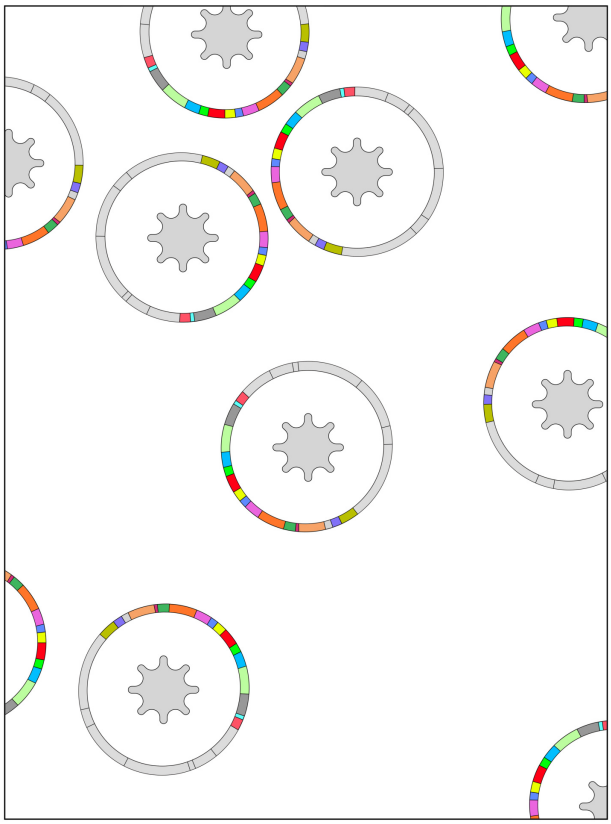
1

Integration+Replication

② Integrating the constructed plasmid into a retroviral vector and then ③ replicating it.



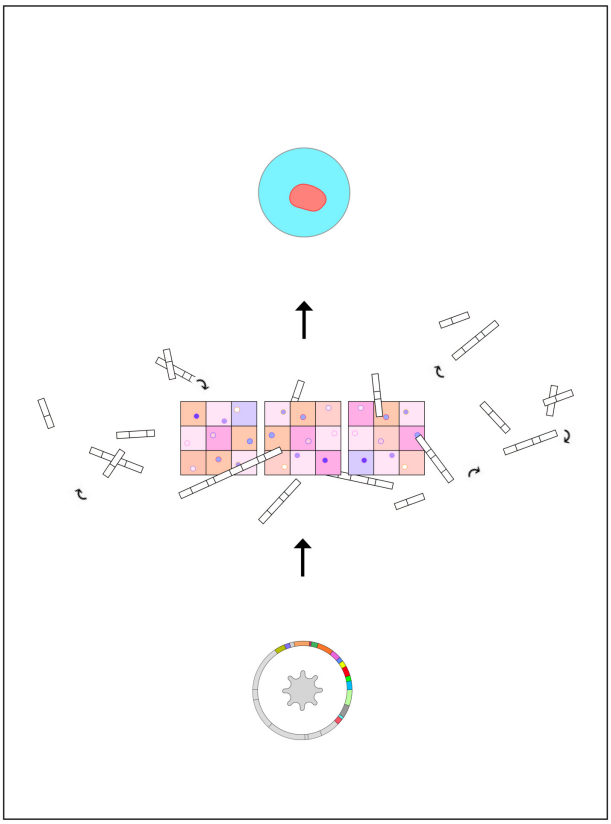
2



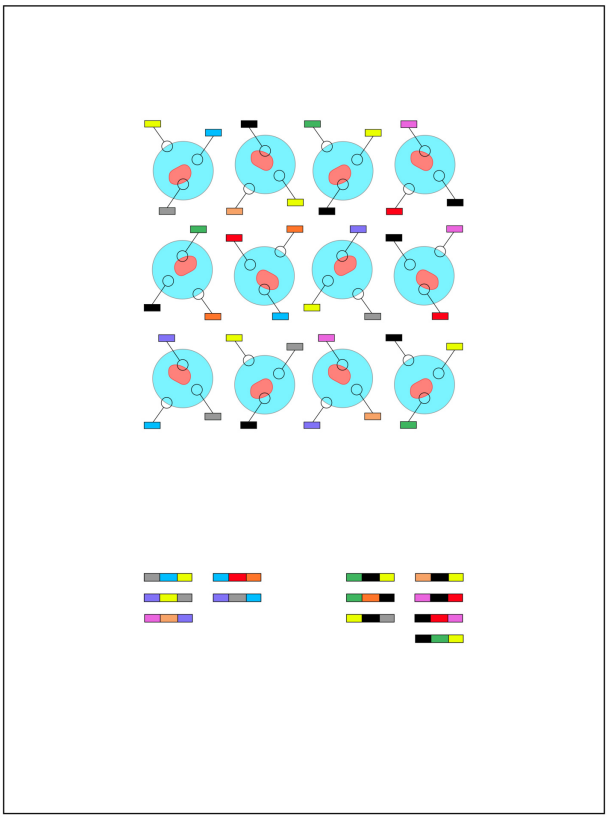
3

Transduction+Testing

④ Using the retrovirus' to deliver the transcription factors into adult cells in vitro (inserting the plasmid sequence into the cells' genomic activity) then ⑤ evaluating the cell samples to detect whether they exhibit common characteristics of pluripotency.



4



5