STEM CELLS

The survival of the fittest

An analysis of over 100 human embryonic stem cell lines reveals a genetic change that might confer a growth advantage.

Human embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) hold great promise for regenerative medicine and serve as cellular models to study disease as well as development. The unique capacity of these cells to self-renew in culture enables the maintenance and the expansion of the population, but this comes at the expense of accruing genetic and epigenetic changes over time.

It is thought that cells maintained for many passages in the pluripotent state are subject to strong selection favoring those cells containing genetic variants that enhance their capacity to self-renew. However it is often difficult to disentangle changes that simply reflect variants existing in the human population from those acquired during culture.

The International Stem Cell Initiative set out to compare—at an unprecedented scale—the genomes of human ESC lines at early and late passages. Prior initiatives by this consortium have examined marker expression by human ESC lines and compared the media used for their culture. In the present work, they aimed to identify common genetic changes that occur in human ESCs as a result of prolonged culture and to identify genetic or epigenetic alterations that might confer growth advantages to the cells.

The researchers performed karyology, high-resolution single-nucleotide polymorphism and DNA methylation analysis in 125 ethnically diverse human ESC lines and 11 iPSC lines, from 38 laboratories worldwide.

Most of the ESC (and iPSC) lines studied remained karyotypically normal after many passages, but the results revealed a progressive tendency to acquire changes on chromosomes 1, 12, 17 and 20 over time in culture. The karyotypic and structural-variant data pointed to a region in chromosome 20 that was amplified in more than 20% of the late-passage cell line populations. This region contained the anti-apoptotic gene *BCL2L1*, a strong candidate in driving adaptation to culture. The authors detected many other structural variations and DNA methylation changes, but these occurred with no link to time in culture.

It will be interesting to directly test the role that the amplification of the *BCL2L1* gene has in the growth and culture adaptation of ESC lines and to determine whether it affects their differentiation potential.

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RESEARCH PAPERS

The International Stem Cell Initiative. Screening ethnically diverse human embryonic stem cells identifies a chromosome 20 minimal amplicon conferring growth advantage. *Nat. Biotechnol.* **29**, 1132–1144 (2011).