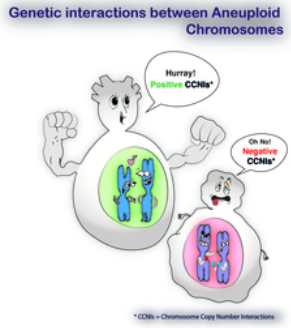
Making sense of chromosomal chaos

05/12/2018



(/fileadmin/_processed_/csm_Final_Cover_art_SF_5b9a991bd4.jpg)

When cells divide, chromosomes must be accurately segregated. Sometimes errors occur, leading to aneuploidy, a state where cells have an incorrect number of chromosomes. This chromosomal instability is in most cases harmful for cells, yet aneuploidy and high rates of errors in chromosome segregation are frequently observed in cancers, especially those that are resistant to treatment. How can cells adapt to and thrive in such a disadvantageous state?

Scientists from Christopher Campbell's lab at the Max F. Perutz Laboratories, a joint venture of the University of Vienna and the Medical University of Vienna, now report findings that could help answer this question. The scientists artificially induced high levels of segregation errors in yeast and examined how the cells react over time. They discovered that among the cells that manage to adapt to this stress, specific numbers and combinations of chromosomes, or karyotypes, are often found. This hints that cells find a way to adapt by obtaining a karyotype consisting of chromosomal abnormalities that help them stabilize the defects caused by missegregation – they turn a disadvantage into something positive. First author Madhwesh Ravichandran explains in detail: "Only a few cells survived the stress induced by high rates of chromosome missegregation and almost all of them had a complex karyotype with multiple chromosomal gains and losses. Thus for the first time we were able to develop a model to observe the formation of complex karyotypes and explore the patterns that govern their formation by making use of the powerful genetic techniques available in budding yeast."

Most interestingly, the scientists identified which chromosomes support this adaption and also found that there are genetic interactions between aneuploid chromosomes that play a key role in determining the optimal adapted karyotype. Group leader Christopher Campbell explains: "We were actually quite surprised to see such strongly divergent patterns in the karyotypes of the adapted yeast. The common thinking in the field is that the negative effects of aneuploidy are quite general and would be similar for all chromosomes, but the specificity of the patterns strongly suggests that this is often not the case, especially when multiple aneuploid chromosomes are present."

When comparing the patterns in the yeast data to cancer karyotypes the group found strong similarities, hinting that aneuploid cancer cells may also form distinct aneuploidy patterns that are affected by genetic interactions between chromosomes. The most pressing questions therefore are the exact character of these interactions and the specifics of the adaptation process both in human and non-human cells.

Publication in Genes & Development: (http://genesdev.cshlp.org/content/32/23-24/1485)

Madhwesh C. Ravichandran, Sarah Fink, Matthew N. Clarke,Franziska Christina Hofer and Christopher S. Campbell

Genetic interactions between specific chromosome copy number alterations dictate complex aneuploidy patterns.

DOI: 10.1101/gad.319400.118