123-ANEUPLOIDY IN CANCER AND RESISTANCE TO CHEMOTHERAPY

Two articles in Developmental Cell[1,2] deal with cancer resistance to chemotherapy. Both underline the importance, in this regard, of the instability of the genome due to aneuploidies and variations in copy number, the latter being a consequence of the former. It is noteworthy that somatic aneuploidies are not subject to the highly selective filter of the complex process of embryonic development. Therefore, these events, when not detrimental, could fuel cancer evolution.

In this context it is interesting to keep in mind that the phenomenon of aneuploidy is exploited as fuel for species evolution by some organisms. Two examples:

A 2014 paper in PloS biology[3] states: "Candida albicans, the most prevalent human fungal pathogen, is generally diploid. However, 50% of isolates that are resistant to fluconazole (FLC), the most widely used antifungal, are aneuploid and some aneuploidies can confer FLC resistance". Another paper, in press in PNAS[4], suggests that Leishmania (a protozoan) exploits the frequent variations in chromosome and gene copy number to regulate gene expression levels for adaptation.

1- Chromosomal instability accelerates the evolution of resistance to anti-cancer therapies
Lukow DA, Sausville EL, Suri P, Chunduri NK, Wieland A, Leu J, Smith JC, Girish V, Kumar AA, Kendall J, Wang Z, Storchova Z, Sheltzer JM. Dev Cell. 2021 56:2427-2439.
https://www.sciencedirect.com/science/article/abs/pii/S153458072100592X?via%3Dihub

2- Gene copy-number changes and chromosomal instability induced by aneuploidy confer resistance to chemotherapy.
Ippolito MR, Martis V, Martin S, Tijhuis AE, Hong C, Wardenaar R, Dumont M, Zerbib J, Spierings DCJ, Fachinetti D, Ben-David U, Foijer F, Santaguida S. Dev Cell. 2021 56:2440-2454.
https://www.sciencedirect.com/science/article/abs/pii/S1534580721005621?via%3Dihub

3- Harrison BD, Hashemi J, Bibi M, Pulver R, Bavli D, Nahmias Y, Wellington M, Sapiro G, Berman J: A tetraploid intermediate precedes aneuploid formation in yeasts exposed to fluconazole. PLoS Biol 12:e1001815 (2014)
https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1001815

4- Bussotti G, Piel L, Pescher P, Domagalska MA, Rajan KS, Cohen-Chalamish S, Doniger T, Hiregange DG, Myler PJ, Unger R, Michaeli S, Spath GF: Genome instability drives epistatic adaptation in the human pathogen Leishmania. **Proc Natl Acad Sci U S A** 118 in press (2022)
https://www.pnas.org/content/118/51/e2113744118.long