additional 30Mb fragment of chromosome 15 inserted into chromosome 19.
Being a cancer cell line, HAP1 is prone to genetic instability, which is further compounded by its tendency for 'diploidisation'. CRISPR/Cas9 gene editing coupled with prolonged in vitro cell culturing can cause unintended 'off-target' cytogenetically visible mutations.
To gain an insight into chromosomal instability (CIN) and karyotype heterogeneity we characterised 19 HAP1 cell lines, including two double haploids, using M-FISH, a single cell-based assay. We focussed on novel numerical (N) and structural (S) CIN and explored the potential causal factors that triggered this. For each cell line we examined its ploidy, gene editing status and its length of in vitro cell culturing.
Sixteen of the 19 cell lines had been edited with passage numbers ranging from 10 to 35. Diploidisation in the 17 near-haploid cell lines ranged from 4% to 33% and percentage of CIN in [1n & 2n] metaphases ranged from 7% to 50%, with two cell lines showing no CIN. The most common S-CIN observed were translocations, both non-reciprocal and Robertsonian along with gain of deleted chromosomes, in [1n] metaphases. Interestingly, 11 cell lines showed a prevalence of S-CIN associated with chromosome 13, with Robertsonian translocation being the most common. Furthermore, we showed for the first time that the additional chromosome 15 fragment is inserted into 19p rather than 19q.
In summary, our study has revealed karyotype instability in most HAP1 cell lines and emphasizes the importance of maintaining the cell lines at low passage and the need for regular monitoring to prevent karyotype heterogeneity which may have implications for downstream applications.

7.P14 Duplication of the long arm of chromosome 1 in primary myelofibrosis is a malignity factor

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Primary myelofibrosis (PMF) is one of the Myeloproliferative neoplasms (MPN), which presents a preferential proliferation of megakaryocytes and granulocytes in the bone marrow (BM). One of the causes of morbidity and mortality in PMF is the progression to Acute Myeloid Leukemia (AML).
We present a clinical case, of a female individual, 68 years old at the time of the initial diagnosis, who presented moderate anemia and thrombocytosis, and diagnosed as myeloid metaplasia with myelofibrosis. The karyotype performed in the BM, resulted in a duplication of the long arm of chromosome 1, del(1)(q21q32). The patient remained stable and without therapy for 5 years having performed a myelogram at this time, and a bone biopsy that showed an advanced myelofibrosis. In parallel, cytogenetic studies and search for V617F mutation in the Jak2 gene, indicated the absence of the mutation V617F, and confirmed the presence of the dup(1)(q21q32). the patient started therapy with an erythropoietin substitute. Currently, with 8 years of evolution of the disease, she has no clinical complaints, without transfusions and maintaining therapy.
The dup(1)(q21q32) associated with MPN is a rare anomaly and is associated with AML evolution. Since the patient understudy did not evolve to AML, FISH, and high-resolution microarray studies were performed. The studies confirmed the observed breacpoints and did not show other changes Based on the patient's clinical history and results, we suggest that the dup(1)(q21q32) alone does not induce an evolution to AML and that the duplication of genes correlated with this pathology (ex: ARNT, among others) is not a sufficient factor for the development of a more aggressive progression. However, more studies should be carried out in order to clarify the role of this alteration in NM.

7.P15 Cryptic translocation t(5;11)(q35;p15) resulting in NUP98 / NSD1 gene fusion in adults with de novo acute myeloid leukemia (AML)

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The NUP98/NSD1 fusion, a product of the cryptic translocation t(5;11)(q35;p15.5), is a recurrent genetic change in cytogenetically normal patients with AML. It occurs most frequently in children (16%) and young (2%) AML patients, very rarely in adult patients.