

uma diferença estatisticamente significativa entre Ásia e América do Norte. Por fim, hiperdiploidia e hipodiploidia tiveram suas maiores frequências na América do Norte e Eurásia, respectivamente.

<https://doi.org/10.1016/j.htct.2024.09.650>

INVESTIGATION OF THE IMPACT OF THE R248Q MUTATION IN THE TP53 GENE ON THE INTERACTION OF THE P53 PROTEIN WITH THE DRUG APR-246 IN ACUTE MYELOID LEUKEMIA

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Objectives: The TP53 gene encodes the tumor suppressor protein p53, which is crucial in cancer biology. Mutations in TP53 occur in 10 to 20% of AML cases and are associated with an unfavorable prognosis and high refractoriness to chemotherapy. The compound APR-246, which reactivates the mutated form of p53, shows potential in restoring its tumor-suppressive functions. However, different mutations in the TP53 gene can influence the response to treatment, highlighting the need for specific studies. This work aims to investigate the impact of TP53 mutations in AML patients, including clinical-laboratory characteristics, therapeutic response, and clinical outcome, as well as analyze changes in protein structure and interaction with APR-246 modulated by the mutation. **Materials and methods:** Initially, two cohorts were evaluated for mutations associated with the AML phenotype: the first cohort from the Beat AML study (942 samples from 805 AML patients; only samples collected at diagnosis will be included; Nature 562:526–531, 2018 and Cancer Cell 40:850–864, 2022). The second cohort comes from The Cancer Genome Atlas (TCGA) consortium (200 samples from 200 AML patients at diagnosis; N Engl J Med 368:2059–2074, 2013). We are analyzing the mutations identified in the 64 samples with TP53 gene alterations. **Results:** In total, we identified 59 distinct mutations, including: 35 missense, 10 frameshift, 6 stop codon, and 8 splice. Among these mutations, R248Q stands out as it was identified in six samples, being the most frequent missense mutation in our cohort. **Discussion:** This mutation is considered a hotspot and is functionally classified as dominant negative; according to predictors, it is classified as pathogenic and probably damaging. Although a structural damage predictor does not indicate that the mutation leads to structural alteration, the literature suggests that this alteration leads to conformational modifications of the protein that impair its functionality. **Conclusion:** Therefore, understanding this mutation and its relevance not only in the specific phenotype but also in other neoplasms is important for evaluating how the protein containing this mutation interacts with the drug APR-246. For this, both *in silico* and *in vitro* experiments will be conducted. In the *in vitro* field, we will assess

the effects of APR-246 on specific TP53 mutations regarding proliferation, apoptosis, autophagy, and cell cycle progression in the presence of clinically used chemotherapeutic agents in AML experimental models. In the *in silico* realm, molecular docking assays followed by molecular dynamics simulations are underway. Both experiments will help understand the effect of the mutation on the interaction with the compound as well as the effect of the mutation on the dynamic system. It is expected that, due to the compound's mechanism of action, it will prevent conformational changes to avoid the detrimental phenotype.

<https://doi.org/10.1016/j.htct.2024.09.651>

AVALIAÇÃO PROGNÓSTICA DE HIPODIPLOIDIA E HIPERDIPLOIDIA EM LEUCEMIA LINFOBLÁSTICA AGUDA DE CÉLULAS B PEDIÁTRICA: REVISÃO DE LITERATURA

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Objetivo: O objetivo da revisão é sintetizar a literatura existente sobre a avaliação prognóstica de hipodiploidia e hiperdiploidia na Leucemia Linfoblástica de células B (LLA-B) pediátrica. **Metodologia:** A construção da pesquisa se deu pela busca de artigos publicados nos bancos de dados JANE, Scielo, BVS e PubMed. A coleta foi norteadada pela busca combinada nos idiomas português e inglês dos seguintes termos de busca: Cruzamento (CR): CR1: Leucemia Linfoblástica Aguda (LLA); Hipodiplóide; Hiperdiplóide. CR2: Prognóstico; alterações cromossômicas. CR3: Acute Lymphoblastic Leukemia (ALL); Hypodiploid; Hyperdiploid. CR4: Prognosis; Chromosomal changes. **Resultado:** Foram identificados 268 artigos. Destes, foram excluídos os artigos duplicados, estudos com apenas adultos, revisões e artigos fora do escopo, identificados através da leitura dos títulos e resumos. Após aplicados os critérios, 196 estudos foram descartados, 6 artigos foram selecionados e considerados para o desenvolvimento da discussão. Os artigos incluídos nesta revisão foram publicados no período de 2014 a 2024. **Discussão:** O estudo de Kerketta et al. (2017) sobre LLA-B revelou que 54% dos pacientes estudados apresentavam anormalidades citogenéticas, sendo a hiperdiploidia a mais comum. Isso corrobora com a pesquisa de Paulsson (2015), a qual aponta tal anormalidade citogenética como a mais frequente na LLA-B, ocorrendo de 25% a 30% dos casos. Essa condição envolve a presença de 51 a 67