

the importance of genes that are critical in the pathogenesis, progression, and are potentially essential in the treatment of hematologic malignancies. This study highlights the importance of genetic understanding in the study of large populations, and we believe that the integration of these genetic and molecular discoveries presupposes the transformation of the management of these diseases.

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#### PLASMINOGEN ACTIVATING RECEPTOR UROKINASE (U-PAR): INTERACTION AND IMPLICATIONS IN TUMOR MICROENVIRONMENT IN LEUKEMIAS

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**Objectives:** The urokinase-like plasminogen activator receptor (uPAR) interacts with its ligand (uPA) to convert plasminogen into plasmin, which degrades components of the extracellular matrix. Plasminogen activation can influence many normal and pathological processes through interactions that culminate in cell activation, adhesion, migration and extravasation. This study aimed to describe the implications of uPAR-mediated plasminogen activation in leukemias, exploring its interaction with the tumor microenvironment. **Materials and methods:** This is an integrative review following the Preferred Reporting Items for Systematic Reviews guidelines for reports, searching for published data available on the descriptors “uPAR”, “leukemia” and “genetic expression”. The research was carried out on the MEDLINE (PubMed), Science Direct, Google Scholar and Scielo platforms, covering the last 10 years (2015-2024) with only 23 articles meeting the criteria for approaching the proposed theme. **Results:** Studies have shown high levels of suPAR and positive surface expression of uPAR associated with decreased chemosensitivity in patients with M0-M5 AML, where blasts expressing the surface receptor have been observed. The increase in uPAR levels was related to hyperfibrinolysis in patients with acute promyelocytic leukemia (APL) and associated with increased invasive proteolytic activity, interaction of tumor cells with the immunosuppressive microenvironment, causing immune

evasion and dysfunction of effector cells. Similar results were demonstrated in patients with AML, ALL and biphenotypic leukemia, where high uPAR expression was associated with the invasive capacity of leukemia cells, and involved in the interaction of tumor cells with a suppressive microenvironment, which may influence the lymphocyte-mediated immune response. In addition to observations on altered expression, transcription variants were identified that can act as ceRNAs (uPAR  $\Delta 5/ \Delta 6/$  uPAR  $\Delta 6/7$ ) in myeloid lineage cells, demonstrating higher levels in monoblasts. **Discussion:** The high expression of the receptor in leukemic blasts of AML M0-M5 evidences its role in the invasion and metastasis of malignant cells. The ability of the receptor to influence the immune response has been shown to be an indicator of poor prognosis and a potential marker of risk stratification. The direct interaction of stromal and leukemic cells denotes the formation of a competitive niche that can favor malignant cells. In addition, the identified variants suggest a negative modulation in the cell-matrix interaction, favoring the proliferation and progression of leukemia. In short, if there is no conversion of plasminogen into plasmin, which is also involved in angiogenesis, it leads to a decrease in nutrients and O<sub>2</sub> in leukemia cells. **Conclusion:** The studies pointed to the contribution of the receptor in tumor progression, immune evasion and resistance to treatment, suggesting that the receptor is a target in the therapeutic potential, that is, the key molecule to limit the interactions of the plasminogen activation system, in order to suppress tumorigenesis. The recent development of anti-urokinase receptor antibodies has shown promise in blocking the interactions of the receptor and its ligand, thereby inhibiting the proteolytic cascade. In addition, the recipient can also improve the effectiveness of hematopoietic stem cell transplants.

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#### RECONSTITUIÇÃO DO SISTEMA IMUNOLÓGICO HUMANO EM MODELO MURINO IMUNOSSUPRIMIDO

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**Objetivos:** Padronizar o processo de humanização do sistema imune de camundongos imunodeficientes da linhagem NSG, utilizando células-tronco hematopoéticas CD34<sup>+</sup>. **Materiais e métodos:** Amostras de sangue de cordão umbilical (UCB) humano foram obtidas do biobanco do Hospital da Mulher Prof. Dr. José Aristodemo Pinotti (CAISM/UNICAMP) e criopreservadas em nitrogênio líquido. Para a obtenção de