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Cancer Drug Resistance

Review

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Dodging the bullet: therapeutic resistance mechanisms in pediatric cancers

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Abstract

While advances in the treatment of pediatric cancers have improved survival to > 80% across all tumor types, drug resistance continues to limit survival for a considerable number of patients. We review the known mechanisms of resistance in pediatric cancers, including processes that impair conventional chemotherapies, newer classes of targeted small molecule antineoplastic drugs, and monoclonal antibodies. We highlight similarities and differences in treatment approach and resistance between pediatric and adult cancers. We also discuss newer areas of research into drug resistance, including extracellular and immune factors.

Keywords: Tumor microenvironment, drug efflux, chemoresistance, inhibition of apoptosis, BCL2, pediatric cancer

INTRODUCTION

Pediatric cancer therapies have made significant advances over the last 70 years, with 5-year overall survival rates rising from < 20% in the 1960's to > 80% today[1]. Those improvements have not been uniform, however, across pediatric cancer histologies, including significant mortality among patients with acute myeloid leukemia, high-risk neuroblastoma, metastatic sarcomas, and specific brain tumors[1,2]. Resistance to cancer therapies, including chemotherapies and radiation therapy, have been an area of study for many decades, identifying some key mechanisms that allow cancer cells to remain viable. The development of new therapeutic approaches, including tyrosine kinase inhibitors, monoclonal antibodies, and