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Investigating the mechanisms of action of anticancer drugs using novel proteomic techniques

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Track: Research
Theme: Treatment

ABSTRACT

Introduction: Understanding the mechanisms of action of anticancer drugs is critical for improving therapeutic outcomes and developing next-generation treatments. Proteomics, the large-scale study of proteins and their functions, has emerged as a powerful tool in oncology research, providing insights into drug mechanisms, biomarker discovery, and resistance mechanisms **Purpose:** This study employs two advanced proteomic techniques to investigate the mechanisms of action of two anticancer agents: Compound B, a novel immunomodulatory drug, and Bortezomib, a first-generation proteasome inhibitor. **Materials and Methods:** The mechanism of action of Compound B was studied using pull-down assays and LC-MS analysis in T-cells to identify its immunological targets. Cytokine and chemokine levels were measured using ELISA and MSD V-plex kits to assess its immunostimulatory effects. For Bortezomib, metabolic labeling with unnatural amino acids, such as azidohomoalanine (AHA), was used for the first time to explore its effects on protein synthesis and degradation in multiple myeloma cells. **Results:** Compound B significantly increased the production of several immunostimulatory cytokines, including IL-13, IL-6, and IL-2. Proteomic analysis identified 21 significant proteins, with cyclin-dependent kinase 6 (CDK6) emerging as a potential target, consistent with its role in immunomodulatory pathways. For Bortezomib, proteomic analysis revealed significant upregulation of key neddylation enzymes, highlighting changes in protein dynamics, including synthesis and degradation. **Conclusion:** These findings provide new insights into the mechanisms of Compound B and Bortezomib, highlighting potential therapeutic targets and strategies to enhance cancer treatments.

Keywords: Immunotherapy, cancer treatment, proteomics, target identification, multiple myeloma