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## Molecular mechanisms in multiple myeloma drug resistance | Journal ...

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## mutations in 19s proteasome subunits represent a novel mechanism ...

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the  $\beta 5$ -subunit of proteasome (PSMB5), has marked efficacy against multiple myeloma and ...

Keywords: Drug resistance, Mechanism, Proteasome inhibitor, Bortezomib, PSMB5 ..... Resistance Mechanisms to Novel Therapies in Myeloma.



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알림 만들기

### The proteasome inhibitor PS-341 inhibits growth, induces apoptosis, and overcomes drug resistance in human multiple myeloma cells

T Hideshima, P Richardson, D Chauhan... - Cancer research, 2001 - AACR

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### [HTML] A novel orally active proteasome inhibitor induces apoptosis in multiple myeloma cells with mechanisms distinct from Bortezomib

D Chauhan, L Catley, G Li, K Podar, T Hideshima... - Cancer cell, 2005 - Elsevier

... In that study, we utilized a novel methodology to measure proteasome activity by immunoblotting using DansylAhx ... Mechanisms mediating anti-MM activity of NPI-0052 ... on FADD-caspase-8 signaling axis than does Bortezomib, further confirming differential mechanism of action ...

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### Molecular mechanisms of novel therapeutic approaches for multiple myeloma

T Hideshima, KC Anderson - Nature Reviews Cancer, 2002 - nature.com

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### Molecular sequelae of proteasome inhibition in human multiple myeloma cells

N Mitsiades, CS Mitsiades, V Poulaki... - Proceedings of the ..., 2002 - National Acad Sciences

... Physiology; Plant Biology; Population Biology; Psychological and Cognitive Sciences; Sustainability Science; Systems Biology. Molecular sequelae of proteasome inhibition in human multiple myeloma cells. Nicholas Mitsiades ...

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### Novel therapies targeting the myeloma cell and its bone marrow microenvironment

T Hideshima, D Chauhan, K Podar, RL Schlossman... - Seminars in ..., 2001 - Elsevier

... 341 both acts directly on MM cells and inhibits paracrine MM growth mechanisms in the ... Elliott B, B... CS, M... D... P... A... I...

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Novel mechanism of drug resistance to proteasome inhibitors in multiple myeloma

Zhou J *et al.* Drug resistance in MM

Jianbiao Zhou, Wee-Joo Chng

#### Abstract

Multiple myeloma (MM) is a cancer of antibody-secreting plasma cells in bone marrow, which represents the second most common hematological malignancy. MM is a highly heterogeneous disease and can be classified into a spectrum of subgroups based on their molecular and cytogenetic abnormalities. In the past decade, novel therapies, especially, the first-in-class proteasome inhibitor bortezomib, have been revolutionary for the treatment of MM patients. Despite these remarkable achievements, myeloma remains incurable with a high frequency of patients suffering from a relapse, due to drug resistance. Mutation in the proteasome  $\beta 5$ -subunit (PSMB5) was found in a bortezomib-resistant cell line generated via long-term coculture with increasing concentration of bortezomib in 2008, but their actual implication in drug resistance in the clinic has not been reported until recently. A recent study discovered **four resistance-inducing PSMB5 mutations from a relapsed MM patient receiving prolonged bortezomib treatment**. Analysis of **the** dynamic clonal evolution revealed that two subclones existed at the onset of disease, while the other two subclones were induced. Protein structural modeling and functional assays demonstrated that all



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## The resistance mechanisms of proteasome inhibitor ...

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4177604>

Mar 01, 2013 · The summary of possible **bortezomib resistance mechanisms**. The **mechanisms of proteasome inhibitor bortezomib resistance** mainly focused on the **modifications** of the **mechanisms** of its action. Mutations at key points of  $\beta 5$  subunit of **proteasome (PSMB5)** ...

Cited by: 99

Author: Shuqing Lü, Jianmin Wang

Publish Year: 2013

## Proteasome inhibitors – molecular basis and current ...

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4508135>

Apr 08, 2014 · **Proteasome inhibitors in multiple myeloma**. Generally, UPR allows the **cell** to survive reversible environmental conditions, such as chemical insult or nutrient deprivation. However, during **prolonged stress** caused by PIs, UPR activation leads to **cell cycle arrest** [ ...

Cited by: 96

Author: Lenka Kubiczkova, Ludek Pour, Lenka Se...

Publish Year: 2014

## Resistance Mechanisms to Novel Therapies in Myeloma ...

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The number of **novel therapies** for the **treatment of multiple myeloma (MM)** is rapidly increasing with **proteasome inhibitors**, immunomodulatory agents and **monoclonal antibodies** being the most well-known therapeutic classes whilst **histone deacetylase inhibitors**, **selective inhibitors** of nuclear export and CAR-T cells amongst others also being actively investigated.

Author: Craig T. Wallington-Beddoe, Douglas ...

Publish Year: 2018

## Novel cell line models to study mechanisms and overcoming ...

<https://www.sciencedirect.com/science/article/pii/S0925443919301140>

Jun 01, 2019 · Experimental data on resistance mechanisms of multiple myeloma (MM) to **ixazomib (IXA)**, a second-generation proteasome inhibitor (PI), are currently lacking. We generated **MM cell lines** with a 10-fold higher resistance to IXA as their sensitive counterparts, and observed cross-resistance towards the **PIs carfilzomib (CFZ)** and bortezomib (BTZ).