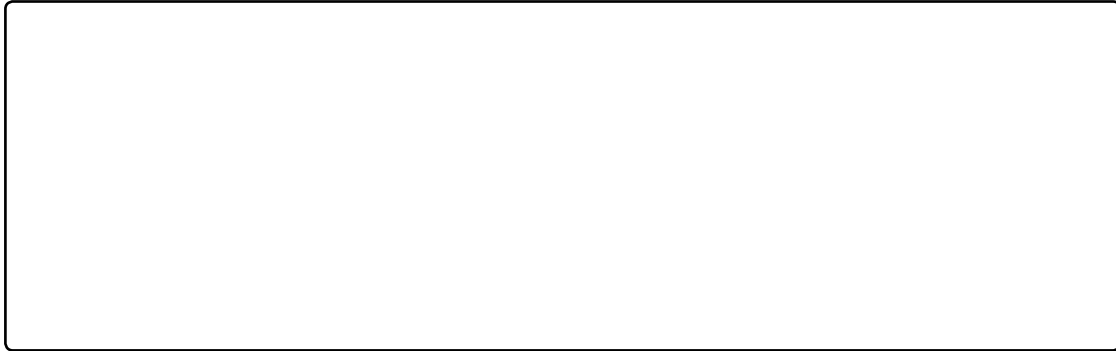


## Harnessing Mitotic Catastrophe for Targeted Cancer Treatment

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### Introduction

Abstract: Mitotic catastrophe is a form of cell death that occurs when a cell undergoes mitosis despite the presence of DNA damage or other cellular stressors. This process is characterized by the formation of micronuclei and the presence of lagging chromosomes. In cancer cells, mitotic catastrophe is often induced by DNA-damaging agents, leading to the formation of tetraploid cells that are highly susceptible to further genetic instability and cell death. Understanding the mechanisms of mitotic catastrophe and its role in cancer progression is crucial for developing targeted therapies that exploit this vulnerability. This review discusses the key mechanisms involved in mitotic catastrophe, including DNA damage response, spindle assembly checkpoint, and apoptotic pathways. It also explores strategies to induce mitotic catastrophe in cancer cells and the potential of this approach as a novel cancer treatment strategy.

### Understanding mitotic catastrophe

Mitotic catastrophe is a form of cell death that occurs when a cell undergoes mitosis despite the presence of DNA damage or other cellular stressors. This process is characterized by the formation of micronuclei and the presence of lagging chromosomes. In cancer cells, mitotic catastrophe is often induced by DNA-damaging agents, leading to the formation of tetraploid cells that are highly susceptible to further genetic instability and cell death. Understanding the mechanisms of mitotic catastrophe and its role in cancer progression is crucial for developing targeted therapies that exploit this vulnerability. This review discusses the key mechanisms involved in mitotic catastrophe, including DNA damage response, spindle assembly checkpoint, and apoptotic pathways. It also explores strategies to induce mitotic catastrophe in cancer cells and the potential of this approach as a novel cancer treatment strategy.

### The key mechanisms involved in mitotic catastrophe include:

#### DNA Damage Response (DDR):

The DNA damage response (DDR) is a complex signaling pathway that is activated in response to DNA damage. It involves the activation of various proteins, including ATM, ATR, and Chk1/2, which lead to cell cycle arrest and DNA repair. In cancer cells, DDR is often dysregulated, leading to the accumulation of DNA damage and the induction of mitotic catastrophe.

#### Spindle Assembly Checkpoint (SAC):

The spindle assembly checkpoint (SAC) is a critical mechanism that ensures the proper segregation of chromosomes during mitosis. It involves the activation of the APC/C complex, which leads to the degradation of cyclin B and the inhibition of the APC/C complex. In cancer cells, SAC is often dysregulated, leading to the formation of micronuclei and the induction of mitotic catastrophe.

#### Apoptotic Pathways:

Apoptotic pathways are a series of signaling events that lead to the programmed cell death of a cell. In cancer cells, the activation of apoptotic pathways is often inhibited, leading to the survival of cells that should undergo apoptosis. This inhibition can be overcome by targeting key components of the apoptotic pathway, leading to the induction of mitotic catastrophe and cell death.

Understanding the mechanisms of mitotic catastrophe and its role in cancer progression is crucial for developing targeted therapies that exploit this vulnerability. This review discusses the key mechanisms involved in mitotic catastrophe, including DNA damage response, spindle assembly checkpoint, and apoptotic pathways. It also explores strategies to induce mitotic catastrophe in cancer cells and the potential of this approach as a novel cancer treatment strategy.

### Strategies to Induce Mitotic Catastrophe in Cancer Cells

Targeted therapies that exploit the vulnerability of cancer cells to mitotic catastrophe are a promising approach for cancer treatment. These therapies include DNA-damaging agents, spindle assembly checkpoint inhibitors, and apoptotic pathway activators. The combination of these therapies may lead to synergistic effects, leading to the induction of mitotic catastrophe and cell death in cancer cells.

biomarkers for response need to be addressed for the successful implementation of these treatments. This approach

represents a promising frontier in cancer therapy, with the potential to revolutionize treatment protocols and enhance

patient outcomes.



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