What is DNA Damage Response?

DNA Damage Response (DDR) is a term describing the systems in our cells that protect against DNA damage.

Many cancers are known to have defects in their DNA Damage Response systems which makes them dependent on, and therefore highly sensitive to, inhibition of the remaining DNA Damage Response systems.

Targeting DNA Damage Response defects can preferentially kill cancer cells, while minimising the impact on normal cells and the potential for more selective, better tolerated therapies to improve survival in multiple cancers.

What happens to DNA Damage Response in Cancer?

Every day, DNA in our cells is damaged tens of thousands of times by natural causes and external factors. Fortunately, before they grow and divide, our cells pause to check for damage and repair any damage through DNA Damage Response or DDR which comprises many different systems.

Repairing the damage allows the cell to continue on its cycle of replication and division.

In a cancer cell with DNA Damage Response defects, if we develop compounds that inhibit the remaining DNA Damage Response systems on which it relies, the DNA damage the cancer cell accumulates will be unsustainable, causing it to die. Normal cells have intact DNA Damage Response systems and continue to repair any damage and survive.

How can DNA Damage Response Inhibition be used to fight cancer?

An early event in the formation of many cancers is a defect in a DNA Damage Response system. Cancer cells can lose the ability to pause and check DNA for damage, as well as the ability to repair any damaged DNA.

This loss of repair and inability to check for damage means that the cancer cell carries damage through as it grows and divides.

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Why target DNA Damage Response in oncology?

Many cancers are known to have defects in DNA Damage Response systems. These cancer cells are heavily reliant on the remaining DNA Damage Response systems, which can be exploited by using highly targeted treatments.

Selectivity for cancer over normal cells

Potential new treatment options

Which targets are we exploring?

Maximising DNA damage by inhibiting repair systems

Preventing repair by inhibiting checkpoints

The greatest potential of DNA Damage Response inhibition is likely to lie in combination with each other and with other classes of anticancer agents.

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