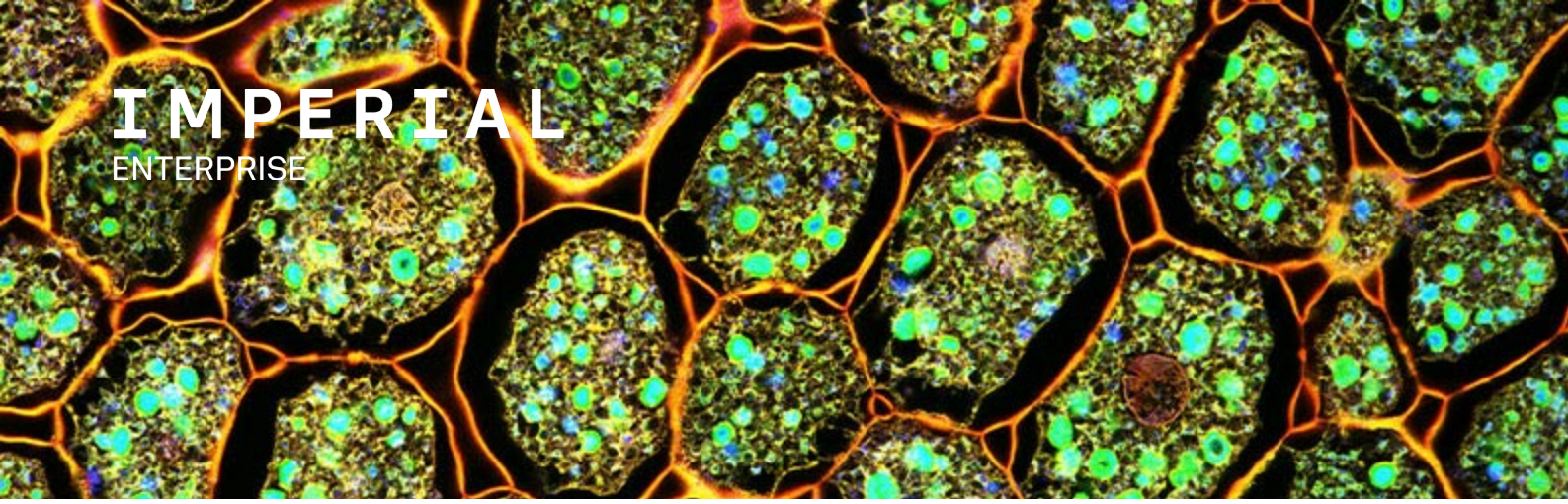

Novel Polypeptide “Warhead” Targeting MYC for Cancer Therapy

A polypeptide-based ('bioPROTAC') technology designed to degrade the MYC oncoprotein inside cells, applicable in cancer treatment and prevention

Proposed Use

This technology has application in cancer therapy, specifically targeting MYC-driven cancers. MYC is overexpressed in most human cancers, making it a critical target for therapeutic intervention. An intrinsically disordered warhead derived from MYC's Compaction Region 1 (CR1) can be used to target MYC for irreversible intracellular degradation, leading to tumour regression. This approach is particularly promising for treating cancers such as liver cancer, leukaemia, lymphoma, and various solid tumours.

The technology's ability to selectively degrade MYC offers a novel and effective strategy for cancer treatment, potentially improving patient outcomes and reducing mortality rates .

Problem Addressed

MYC is a transcription factor overexpressed in most human cancers, driving tumour growth and progression. Despite its critical role in cancer, MYC has been considered "undruggable" due to its intrinsically disordered structure, which lacks binding pockets for conventional drugs. This presents a significant challenge in developing effective therapies targeting MYC. The novel polypeptides derived from MYC's Compaction Region 1 (CR1) address this problem by leveraging previously unknown self-interaction properties of CR1. These polypeptides can be employed as "warheads" in bioPROTACs (Proteolysis-Targeting Chimeras) to selectively degrade MYC in cancer cells. This approach not only neutralizes MYC's oncogenic activity but also offers a new pathway for developing anti-MYC therapies, potentially transforming cancer treatment and improving patient survival rates.

Technology Overview

The technology involves polypeptides derived from the Compaction Region 1 (CR1) of the MYC oncoprotein. CR1 exhibits strong selectivity for MYC, making it a viable target for therapeutic intervention. A fusion of CR1 with ubiquitin ligases to create bioPROTACs, which target MYC for proteasomal degradation. Experimental data demonstrate the effectiveness of CR1-based bioPROTACs in degrading MYC and inhibiting its transcriptional activity. This technology offers a novel approach to cancer therapy by targeting a previously "undruggable" protein, providing a new avenue for developing treatments for MYC-driven cancers. The flexibility and specificity of CR1-based polypeptides make them a promising tool for both diagnostic and therapeutic applications in oncology.

We are seeking research collaborations and prospective third-party licensees for this technology.

Benefits

- **Targeted Therapy**: Efficiently degrades MYC in cancer cells by channelling overexpressed MYC into the intracellular protein destruction machinery
- **Novel Approach**: Addresses the "undruggable" nature of MYC.
- **Effective Degradation**: Based on a bioPROTAC design for efficient intracellular MYC degradation.
- **Broad Applicability**: Suitable for various types of cancer.
- **Improved Outcomes**: Potentially enhances patient survival rates.
- **Therapeutic Versatility**: Applicable in both monotherapy and combination therapy.

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Novel Polypeptide “Warhead” Targeting MYC for Cancer Therapy

Intellectual property information

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Inventor information

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Dr. Weinzierl's research focuses on the structure and function of gene-specific transcription factors (GSTFs) acting as human oncoproteins.

Oncoproteins are proteins that fulfil important regulatory functions in the cell and are either mutated or dysregulated in cancer cells. Many of these also play key roles in normal ageing (senescence) processes.

One of the most important oncoproteins - responsible for around 2/3 of all human cancers - is the oncoprotein c-MYC (or ‘MYC’ for short). Most of the functionally active parts of MYC are intrinsically disordered and cannot form the defined and stable three-dimensional structure that many other folded proteins display. The laboratory thus focuses extensively on computational simulations of the structural ensembles of such intrinsically disordered proteins (IDPs) to gain new, experimentally verifiable insights into structure/function relationships of MYC. The laboratory is also pioneering high-throughput robotic approaches to identify the locations of transcriptional activation domains and regions involved in protein-protein interactions in IDPs.

Such studies will provide new insights into the central role of oncoprotein GSTFs in normal and pathological cellular conditions.