Al-AhmadyLab
Advanced Therapeutic Innovations

Targeted Nanomedical Approaches Against Multiple Myeloma

Asifuddin Syed, Sergio Rutella, Ivan Campeotto, Firas Al-Kaisi, **Zahraa Al-Ahmady**

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CRS 2024 Annual Meeting AND Exposition
JULY 8-12, 2024 • BOLOGNA, ITALY

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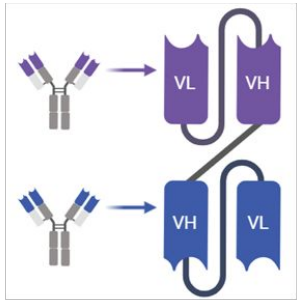
ACROSS DISCIPLINES

Multiple Myeloma: Conventional Approaches to BCMA Targeting

Multiple myeloma (MM) is an ***incurable haematological cancer*** with a relapsing course and significant morbidity secondary to the disease pathology and due to its treatment.

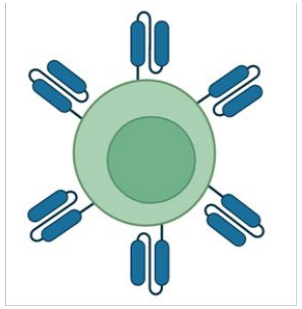
Antibody-Drug Conjugates (ADCs)

- Cytopenia
- Ocular toxicities



Bispecific T-Cell Engager Antibodies (BiTEs)

- Cytokine Release Syndrome (CRS)
- Short half-life

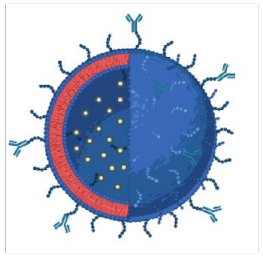


Chimeric Antigen Receptor T Cells (CAR-T Cells)

- Cytokine Release Syndrome
- Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS)
- Secondary Infections – Prolonged Lymphodepletion
- **Availability, Complex Manufacturing, Costs**

A Targeted Nanomedicine Based Approach for Myeloma

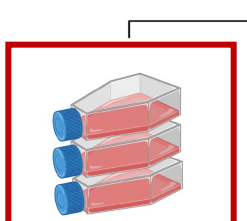
We propose the design of an *anti-BCMA targeted lipid nanoparticle* that when internalised will deliver a payload of MMAF directly into the MM cells. This novel approach has the potential to eliminate off-target side effects and to be available off-the-shelf.

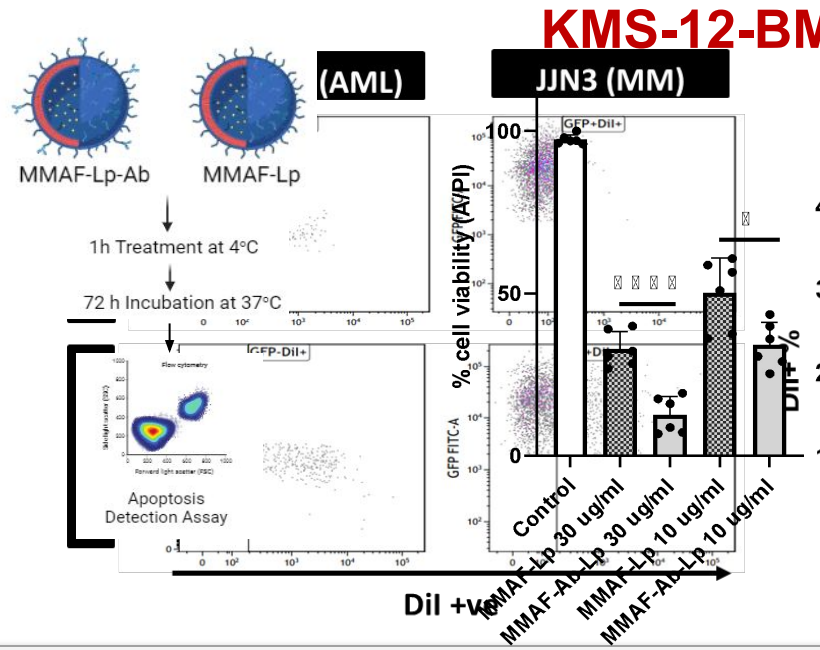


Size
MMAF-Lp: 105.133 ± 15.82 nm
MMAF-Ab-Lp: 107.07 ± 7.76 nm

Zeta Potential
MMAF-Lp: -19.32 mV
MMAF-Ab-Lp: -20.77 mV

MMAF-Ab-Lp





A significant reduction in KMS-12-BM and JJN3 cell viability was observed from MMAF-Lp-Ab compared to non-targeted MMAF-Lp

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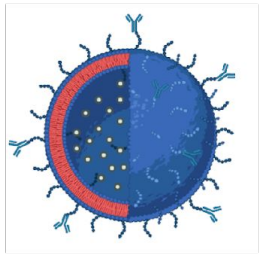

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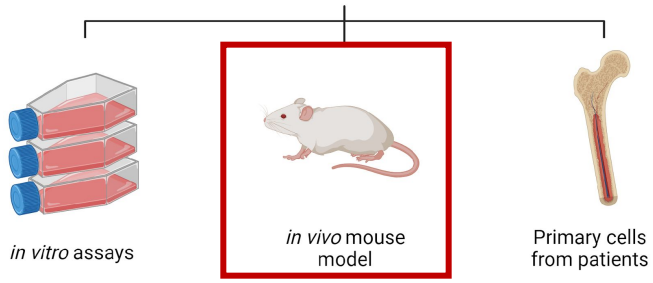

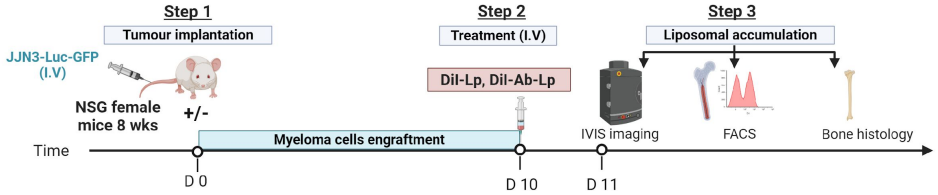

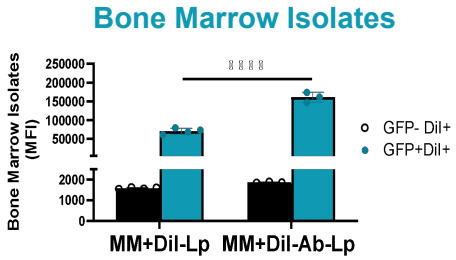

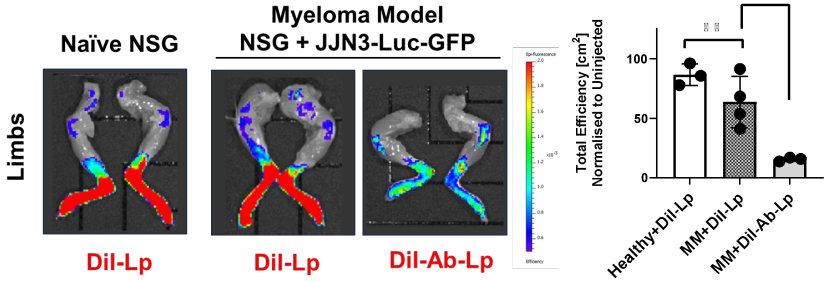

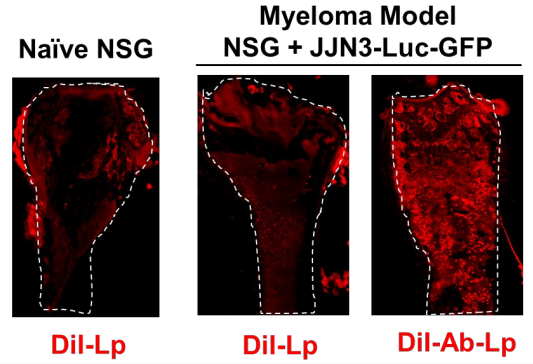

Selective uptake of Dil-Ab-Lp by myeloma cells with a reduced non-specific interactions.

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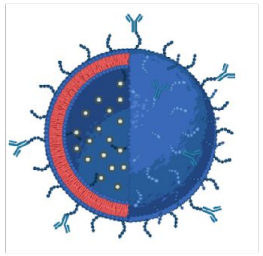

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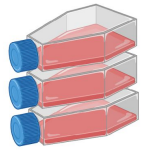
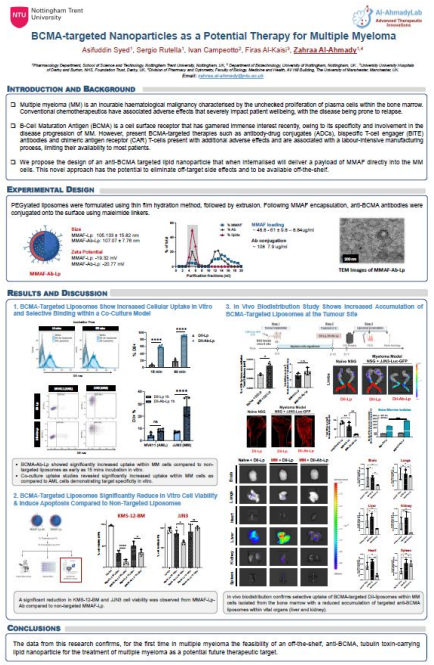


in vitro assays

in vivo mouse model

Primary cells from patients



BCMA-targeted Nanoparticles as a Potential Therapy for Multiple Myeloma

Asiluddin Syed[1], Sergio Rutella[2], Ivan Campeotto[3], Firas Al-Kaisi[4], Zahraa Al-Ahmady[1,5]

Introduction and Background

- Multiple myeloma (MM) is an incurable haematological malignancy characterised by the unchecked proliferation of plasma cells within the bone marrow. Conventional chemotherapeutics have associated adverse effects that severely impact patient wellbeing, with the disease being prone to relapse.
- B-Cell Maturation Antigen (BCMA) is a cell surface receptor that has garnered immense interest recently, owing to its specificity and involvement in the disease progression of MM. However, present BCMA-targeted therapies such as antibody-drug conjugates (ADCs), bispecific T-cell engager (BiTE) antibodies and chimeric antigen receptor (CAR) T-cells present with additional adverse effects and are associated with a labour-intensive manufacturing process, limiting their availability to most patients.
- We propose the design of an anti-BCMA targeted lipid nanoparticle that when internalised will deliver a payload of MMAF directly into the MM cells. This novel approach has the potential to eliminate off-target side effects and to be available off-the-shelf.

Experimental Design

PEGylated liposomes were formulated using thin film hydration method, followed by extrusion. Following MMAF encapsulation, anti-BCMA antibodies were conjugated onto the surface using maleimide linkers.

Results and Discussion

1. BCMA-Targeted Liposomes Show Increased Cellular Uptake In Vitro and Selective Binding within a Co-Culture Model

3. In Vivo Biodistribution Study Shows Increased Accumulation of BCMA-Targeted Liposomes at the Tumour Site

2. BCMA-Targeted Liposomes Significantly Reduce In Vitro Cell Viability & Induce Apoptosis Compared to Non-Targeted Liposomes

Conclusions

The data from this research confirms, for the first time in multiple myeloma the feasibility of an off-the-shelf, anti-BCMA, tubulin toxin-carrying lipid nanoparticle for the treatment of multiple myeloma as a potential future therapeutic target.

Bioengineering - Session #2

POSTER NUMBER: 814

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