Washington University in St. Louis
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TARGETED LIPOSOME DRUG DELIVERY SYSTEM TO IMPROVE MULTIPLE MYELOMA TREATMENT

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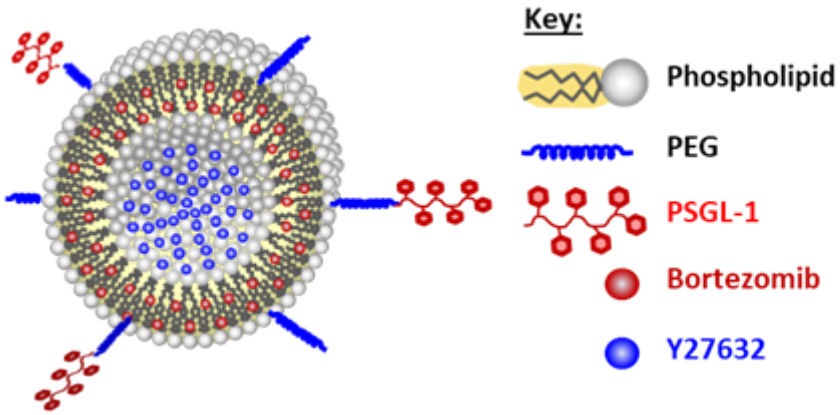
Technology Description

Researchers in Prof. Kareem Azab's laboratory have developed a liposome drug delivery vehicle to improve efficacy and reduce side effects of multiple myeloma treatment. This system is designed to target compounds to the bone marrow microenvironment (BMME) and simultaneously deliver a chemotherapeutic agent (e.g., bortezomib "BTZ") along with an agent that disrupts the BMME and enhances the effects of the chemotherapy.

Patients receiving conventional treatment (e.g., BTZ) for multiple myeloma (MM) experience toxic side effects and often develop resistance and relapse. The efficacy of this chemotherapy could be enhanced by re-sensitizing the MM cells with agents that disrupt the interaction between MM and BMME. This technology uses a novel strategy harnesses that sensitizing activity of BMME disruption and specifically targets drugs tumor associated endothelium. Specifically, the liposome nanoparticle drug delivery system has three features: a targeting antibody (anti-PSGL-1) that specifically homes to the BMME (not the tumor itself); a unique drug payload that combines both BTZ and a disrupting agent (Y27632, the ROCK inhibitor) to enhance the effects of BTZ; and synchronized delivery of the two drugs to overcome drug resistance. The rationally-designed approach drug cocktail improves the efficacy of treatment with the drug cocktail while reducing toxic side effects with specific targeting.



PSGL-1-Targeted liposomes simultaneously deliver a chemotherapeutic agent (e.g., BTZ) with an agent that disrupts the interaction between BMME and MM cells (e.g., Y27632) in order to overcome resistance to BTZ and other conventional MM drugs.

Stage of Research

The inventors have demonstrated that PSGL-1 targeted liposome delivery of bortezomib and Y27632 enhanced responsiveness to bortezomib in vitro and in vivo. In a mouse model of multiple myeloma, this treatment delayed tumor progression and prolonged survival significantly more than controls. It also reduced the severe side effects of bortezomib.

Publications: Federico, C., Muz, B., Sun, J., Alhallak, K., King, J., Kohnen, D. R., ... & Azab, A. K. (2018). Overcoming Drug Resistance in Myeloma By Synchronized Delivery of Therapeutic and Bone Marrow Disrupting Agents By Nanoparticles Targeting Tumor-Associated Endothelium. *Blood*, 132(Supplement 1), 1931-1931.

Applications

- **Multiple myeloma drug delivery –** targeted, synchronized delivery of a chemotherapeutic agent and an enhancing drug

Key Advantages

- **Improved efficacy:**
  - synchronized delivery of two drugs could prevent resistance and enhance cytoxicity
  - targeting antibodies increase the accumulation of treatment agents at the tumor location
  - delayed tumor progression and prolonged survival in mouse models
- **Targeted treatment for reduced side effects:**
  - specific targeting with PSGL-1 directs therapy to endothelial cells in tumor microenvironment and the nearby multiple myeloma cells
  - reduced off-target effects compared with untargeted drug delivery
  - reduced hair loss and weight loss in mouse model

Patent Application: WO2021096951

Related Web Links: Azab Profile; Azab Lab