A tumor-targeting delivery method for chemotherapeutics and other cargo

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Unmet Need

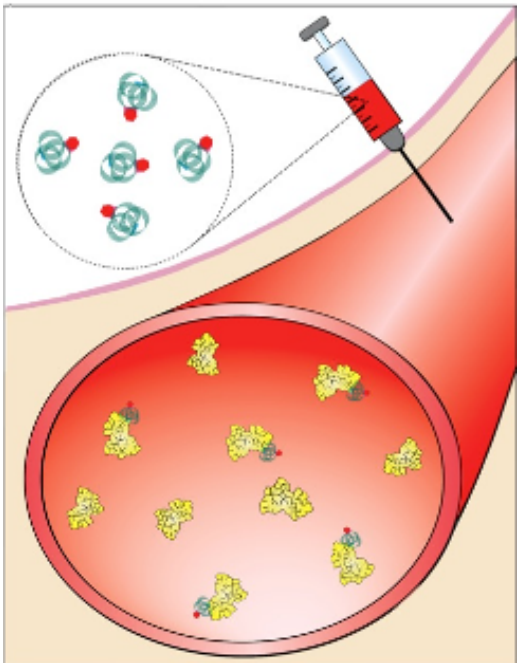
Delivery and therapeutic efficacy of small molecule imaging agents and chemotherapeutics are hampered by their short half-life, low solubility, non-selectivity to cancer cells, and toxic side effects. Small molecule chemotherapeutics, although in routine use for cancer treatment, suffer from a short circulation half-life and indiscriminate accumulation in healthy tissues that result in systemic toxicities and hence limit their maximum dose. These limitations inhibit accumulation of chemotherapeutics in tumors at therapeutic levels and limit their clinical application. Efforts in past decades have been focused on developing macromolecular and nanoparticulate drug formulations that prevent first-pass elimination in kidneys and allow for selective accumulation in tumors via the enhanced permeation and retention (EPR) effect. However, the interaction of these macromolecule and nanoparticle carriers with serum proteins and components of the immune system is not well understood and is affected by several factors such as their interfacial chemistry, size, shape and stability which makes their optimization difficult. Therefore, there remains a need for new delivery systems that can overcome these disadvantages yet provide efficacy for delivery of small molecule imaging agents and chemotherapeutics.

Technology

Duke inventors have developed a tumor-targeting composition for delivering chemotherapeutics or imaging agents. Specifically, an albumin binding domain is conjugated to cargo which harnesses favorable pharmacokinetics and pharmacodynamics through its binding specificity to endogenous albumin. When conjugated to doxorubicin, this technology demonstrated superior therapeutic efficacy in a colon carcinoma model in mice and a pancreatic adenocarcinoma xenograft model in nude mice compared to free doxorubicin and aldodoxorubicin.

Advantages

- A safer drug delivery approach than those that use exogenous albumin



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Links

- From the lab of Dr. Ashutosh Chilkoti

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- Could be used to deliver a variety of cargo to tumors
- Decreases the chance for non-specific interactions compared to aldoxorubicin, an albumin-binding prodrug
- Demonstrated improved therapeutic efficacy in colon and pancreatic cancer models

Publications

- Conjugate of Doxorubicin to Albumin-Binding Peptide Outperforms Aldoxorubicin (Small, 2019)
- US Patent App 16/964,832