Online Proceedings

POSTER SESSION 3

Balcony, Easel 106

2:30 PM to 4:00 PM

Development of a Doxorubicin-Loaded Cyclic Polymer Drug Delivery System

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Mentor: Suzie Pun, Bioengineering
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The most common form of cancer treatment is the use of small-molecule chemotherapeutic agents. However, due to non-specific distribution and uptake, these drugs have a host of complications that limit their efficacy and usage. Polymer nanocarriers have been demonstrated to improve drug pharmacokinetics, enhancing therapeutic benefit of the drugs. The feasibility of cyclic micelle-like polymer nanoparticles for use as a delivery vehicle for doxorubicin (abbreviated as DOX), a potent chemotherapeutic drug, is discussed here. It is hypothesized that cyclic polymers will afford a more efficacious pharmacokinetic release profile than their linear counterparts. A linear polymer is functionalized with "click"able moieties at each end, which are then joined to create a single cyclized polymer. The polymer is decorated with poly(ethylene glycol) (PEG) chains to reduce immunogenicity, and carboxylic acid groups to electrostatically complex with the positively-charged DOX molecule. Upon addition of DOX, the polymer self-assembles into unimolecular micelle-like structures. When the construct accumulates in a tumor microenvironment due to the enhanced permeability and retention (EPR) effect, the low pH of the tumoral interstitium protonates the carboxylic acid groups, releasing DOX locally. Using a unimolecular micelle-like approach, less polymer can be used to deliver the same therapeutic payload, relative to other similar approaches that utilize pluralities of potentially toxic polymers to form micelle structures. The polymer's average molecular weight is around 11530 Da and the polydispersity of the reaction is 1.067. Gel Permeation Chromatography, Nuclear Magnetic Resonance, Fourier-Transform Infrared Spectroscopy, Ultraviolet-Visible Spectroscopy and Dynamic Light Scattering are used to confirm chemical identity, drug loading efficiency, particle size, and polydispersity. Cytotoxicity studies conducted with MDA-MB-231 invasive ductal carcinoma cells *in vitro* demonstrate the feasibility of this construct.

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Identifying Targeting Ligands to Nephrin and NEPH-1 by SELEX

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Mentor: Suzie Pun, Bioengineering
Mentor: Gary Liu, Bioengineering

Many cases of chronic kidney disease are caused by loss of podocytes, kidney cells that are part of the filtration barrier between the blood and urine, resulting in declining kidney function. Current therapies do not prevent podocyte loss and rely on systemic small-molecule drug delivery, which is less effective and can lead to significant complicating side effects. Therefore, targeted drug delivery to podocytes could more effectively protect against injury, prevent further loss, and halt disease progression to kidney failure. To effectively deliver drugs to these cells, ligands that bind with high affinity to proteins specific to podocytes must be developed. Aptamers, DNA- or RNA-based ligands, are advantageous because they can be generated using standard techniques and are easily reproduced. Here, systemic evolution of ligands by exponential enrichment (SELEX) was used to identify aptamers that bind to His-tagged nephrin and NEPH-1, two membrane proteins highly specific to podocytes. First, a large library (on the order of 6×1014 sequences) of randomized single-stranded DNA (ssDNA) was incubated with nephrin or NEPH-1, and protein-aptamer complexes were isolated using His-tag capture beads. Beads were washed to remove any unbound ssDNA, and bound ssDNA were then isolated. This pool will be narrowed further by applying additional selection stringencies over the course of several rounds, ultimately resulting in a small final pool of aptamers with high specificity and affinity to these desired targets. Libraries from selected rounds will be tested for binding to target proteins to monitor selection. Through SELEX, we anticipate finding a small pool of aptamers capable of binding to recombinant nephrin and NEPH-1, and will next validate individual aptamer sequences for their ability to bind to these proteins in vivo. These identified aptamers can be further used to develop a targeted drug delivery platform to podocytes.