A Phosphorylcholine Polymer Platform for Cancer Drug Delivery

Todd Emrick
University of Massachusetts Amherst, tsemrick@mail.pse.umass.edu

Sallie Schneider
Pioneer Valley Life Sciences Institute, sallie.schneider@bhs.org

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A Phosphorylcholine Polymer Platform for Cancer Drug Delivery

Todd Emrick & Sallie Schneider
UMass Amherst Polymer Science and Engineering
and the Pioneer Valley Life Sciences Institute
PolyMPC: current applications and future potential

Current

Contact lenses
Proclear (Copper Vision)

Stent devices
Endeavor (Medtronic)
Trimaxx and Dexamet (Abbott)
BiodivYsio (Biocompatibles)

PolyMPC is extremely hydrophilic and biocompatible: Ishihara, Nakabayashi, Iwasaki, Armes, Lewis,..

Future

Longer lasting protein therapeutics
Why Polymers? Polymers Enhance Drug Delivery  
Prolonged Circulation; Enhanced Permeation and Retention

Normal vessels have tight junctions between cells – allow minimal extravasation into healthy tissue

Tumor vessels are disorganized and leaky

Polymer-drug conjugates are large and are taken up into tumor tissue  
Passive targeting

Polymer/drug flow through capillary
PolyMPC-CPT: the first polyMPC pro-drug


Drug loading: 18 wt %, CPT equivalent solubility: 36.7 mg/mL

Drug loading: 3.7 wt %, CPT equivalent solubility: 6.7 mg/mL

NKTR-102
PEGylated Irinotecan (CPT11, Camptosar)

4-arm star PEGylation

Drug with Polymer Scaffold
Custom Linker with Programmed Release
Free Drug Released in Vivo
Drug Payload Inactive Before Release
Polymer Scaffold Naturally Cleared
Active Drug in Tumor Tissue
PolyMPC-Doxorubicin pro-drugs

DOX release from polyMPC-DOX conjugates at pH 5.0 and 7.4

Half-life of polyMPC-Dox samples range from 8-28 hours, depending on molecular weight and drug loading

PolyMPC-Dox soluble in water and injectable saline at very high DOX loading
In vitro and in vivo evaluation

Cell uptake  MCF7 24 h

Maximum tolerated dose (MTD) of polyMPC-Dox

Nuclear uptake seen for polyMPC-Dox

MTD values of 50 mg/kg or greater
About 10 times that of Dox alone
About twice that of Doxil

Bioconjugate Chemistry 2012
In vivo experiments in mice: 4T1 breast cancer model

Highly invasive and spontaneously metastatic tumor line
Large tumor starting volume; 1 injection

Survival
Doxil: 40% at 7 days, 0% at 14 days
polyMPC-Dox: 100% at 7 days
50% at 14 days

Survival
Day 15 with Dox: 10% survival
Day 15 with polyMPC-Dox: 90% survival