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A Phosphorylcholine Polymer Platform for Cancer Drug Delivery

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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)

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

Future

Longer lasting protein therapeutics

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

pH ~ 7.4

pH ~ 6.0 - 6.8

~ < 400 nm
**PolyMPC-CPT:** the first polyMPC pro-drug

**NKTR-102**
PEGylated Irinotecan (CPT11, Camptosar)

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

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

Bioconjugate Chemistry 2009;  
and Emrick, T.; Chen, X.J., McRae, S.  

4-arm star PEGylation
PolyMPC-Doxorubicin pro-drugs

polyMPC-DOX
Increasing wt percent Dox loading →

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**

- **Pro-drug**
  - DOX signal
  - Nuclear stain
  - Overlay
  - Phase contrast overlay

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**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