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A Phosphorylcholine Polymer Platform for Cancer Drug Delivery

Todd Emrick

University of Massachusetts Amherst

Et al.

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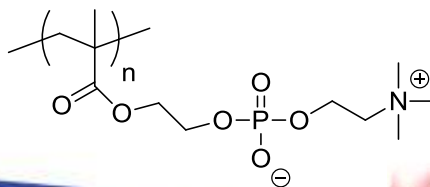
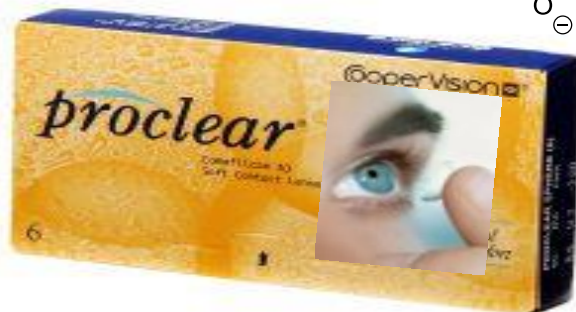
A Phosphorylcholine Polymer Platform for Cancer Drug Delivery

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)

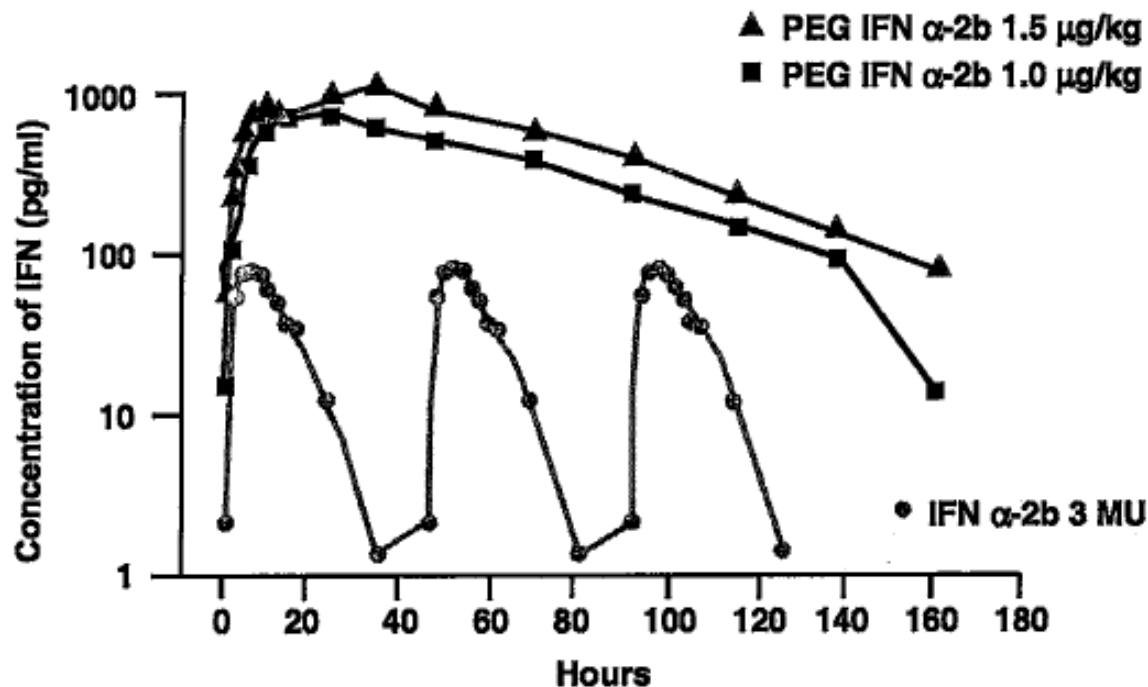


Stent devices
Endeavor (Medtronic)
Trimaxx and Dexamet (Abbott)
BioDivYsio (Biocompatibles)

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

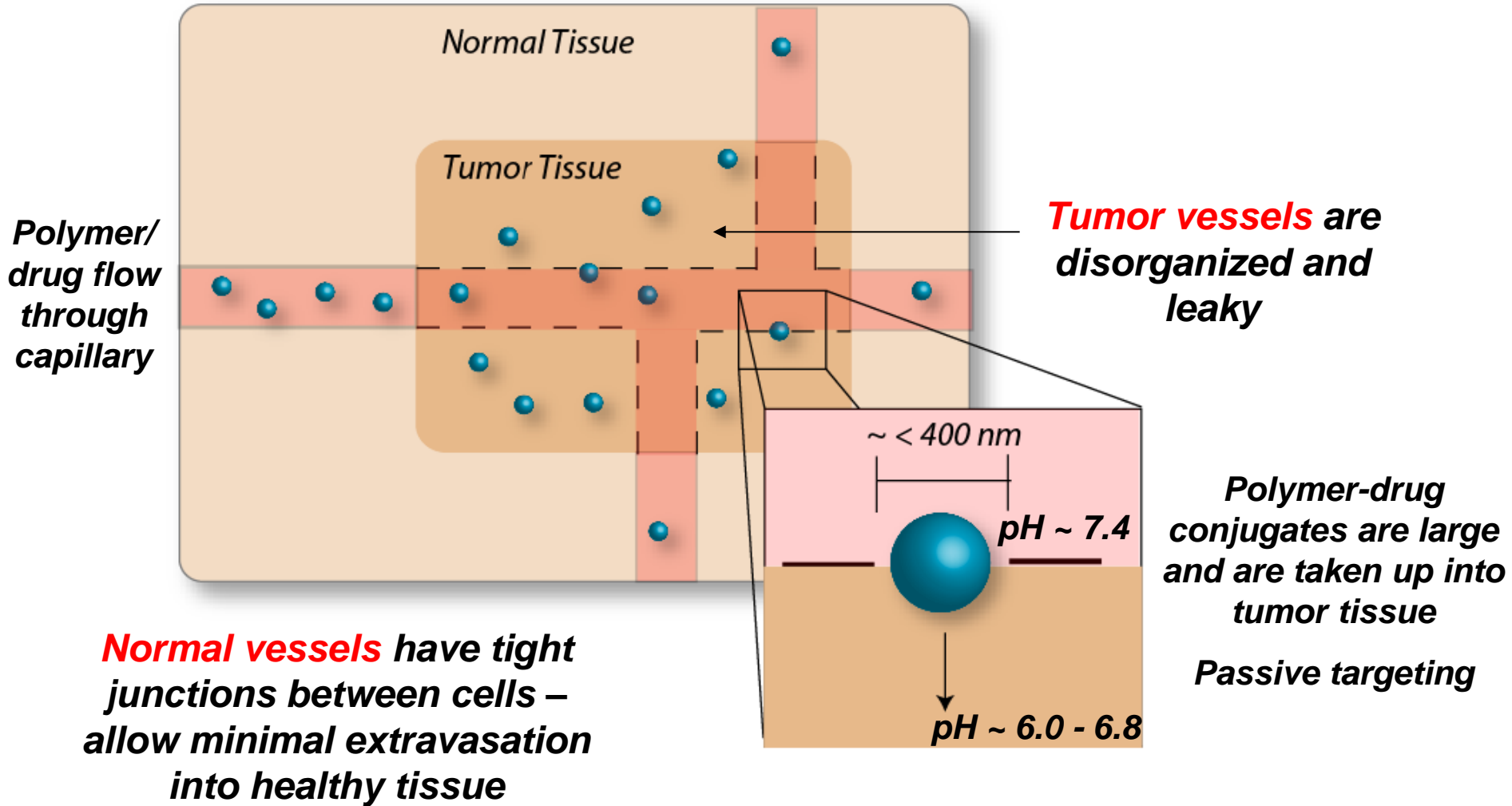
Future

*Longer lasting
protein therapeutics*

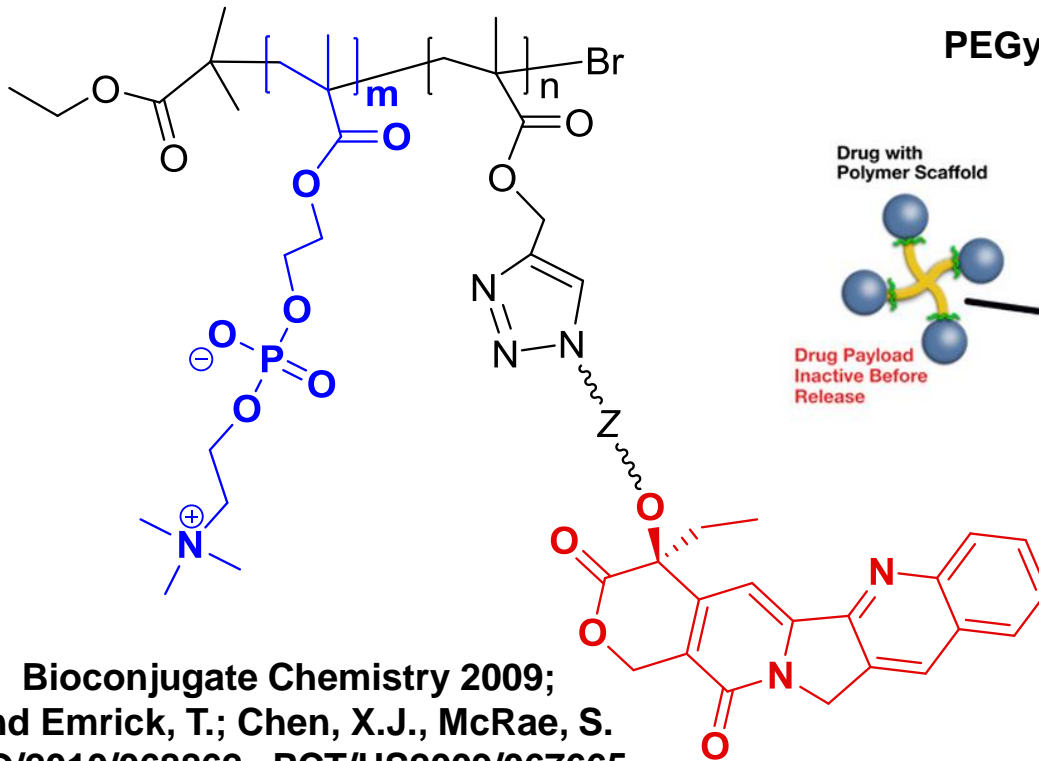


Why Polymers? Polymers Enhance Drug Delivery

Prolonged Circulation; Enhanced Permeation and Retention



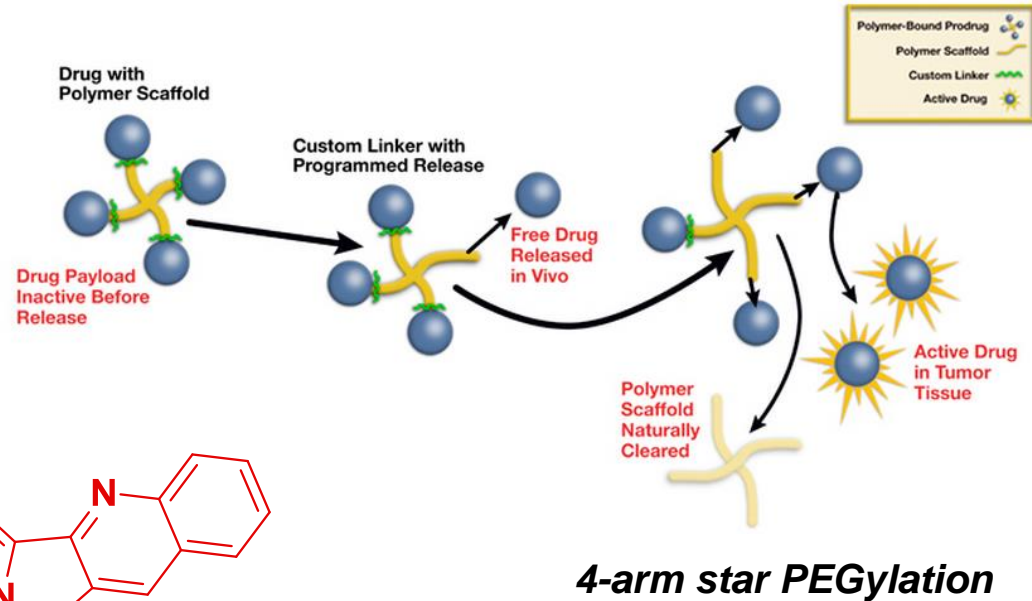
PolyMPC-CPT: the first polyMPC pro-drug



Bioconjugate Chemistry 2009;
and Emrick, T.; Chen, X.J., McRae, S.
WO/2010/068862 PCT/US2009/067665

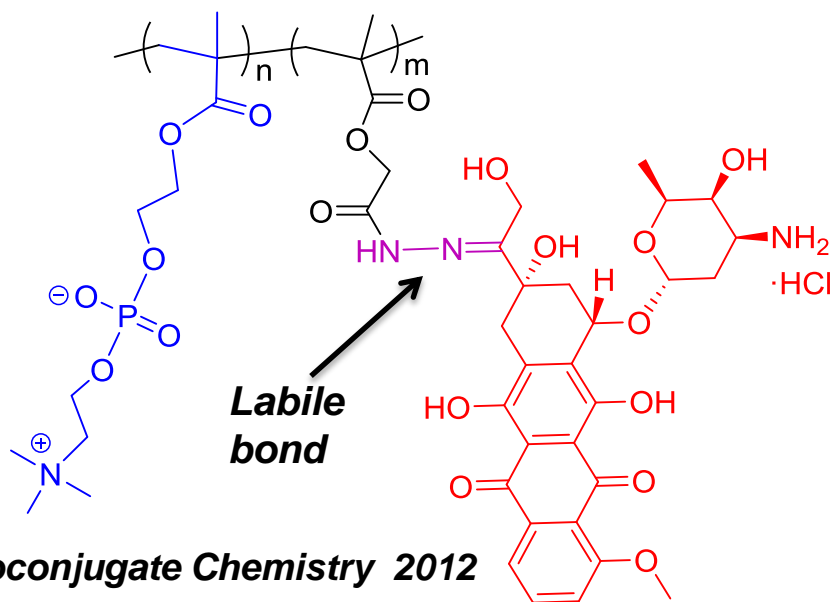
Drug loading: 18 wt %,
CPT equivalent solubility: 36.7 mg/mL

NKTR-102 PEGylated Irinotecan (CPT11, Camptosar)

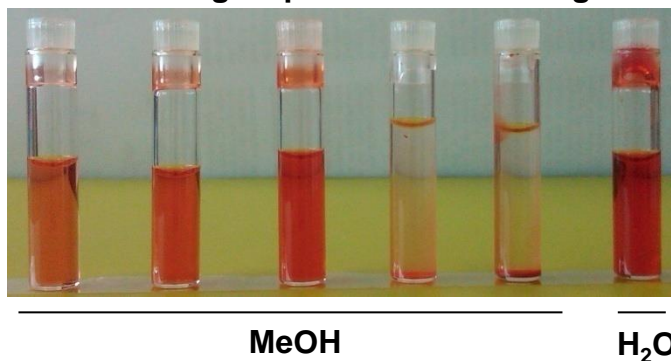


Drug loading: 3.7 wt %
CPT equivalent solubility: 6.7 mg/mL

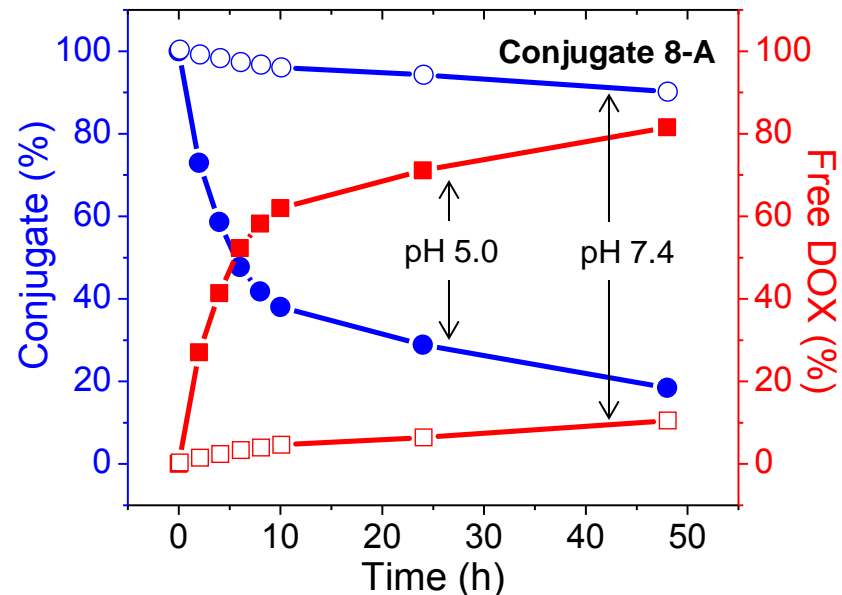
PolyMPC-Doxorubicin pro-drugs



polyMPC-DOX
Increasing wt percent Dox loading →



PolyMPC-Dox soluble in water and injectable saline at very high DOX loading

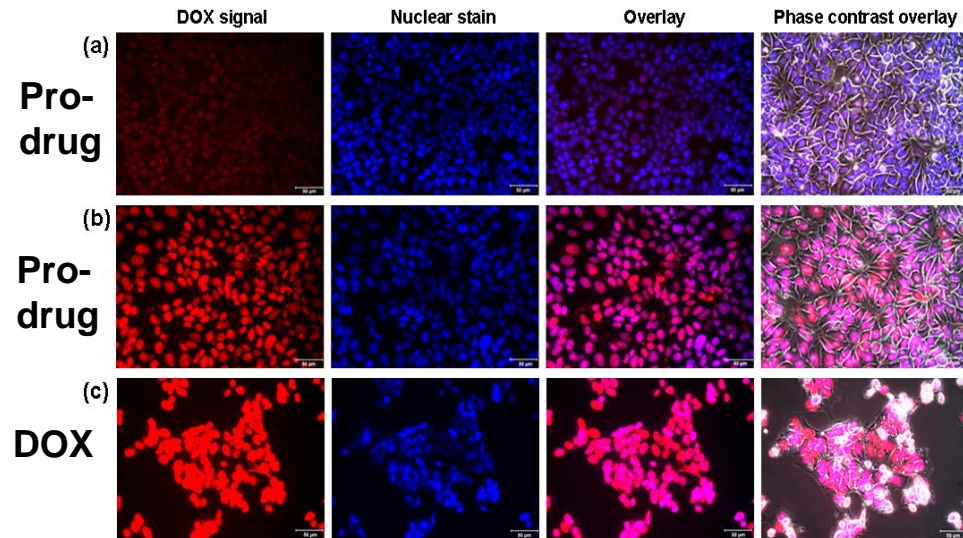


DOX release from polyMPC-DOX conjugates at pH 5.0 and 7.4

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

In vitro and in vivo evaluation

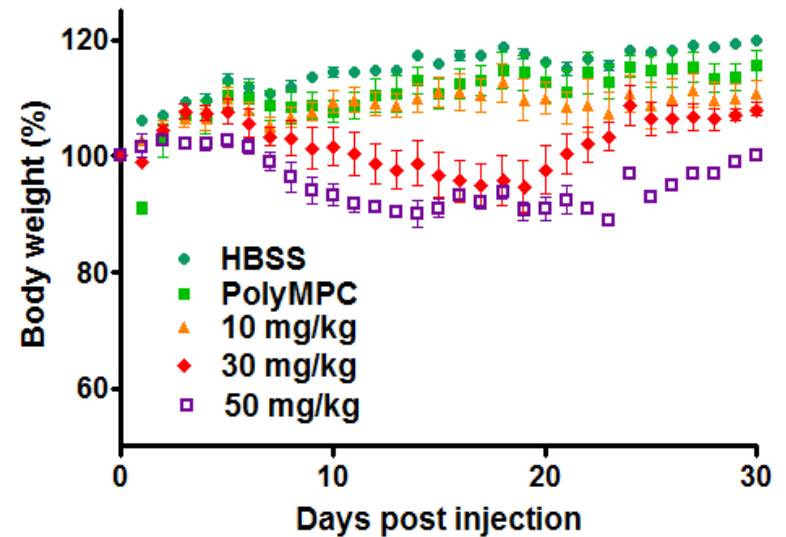
Cell uptake MCF7 24 h



Nuclear uptake seen for polyMPC-Dox

Bioconjugate Chemistry 2012

Maximum tolerated dose (MTD) of polyMPC-Dox



MTD values of 50 mg/kg or greater

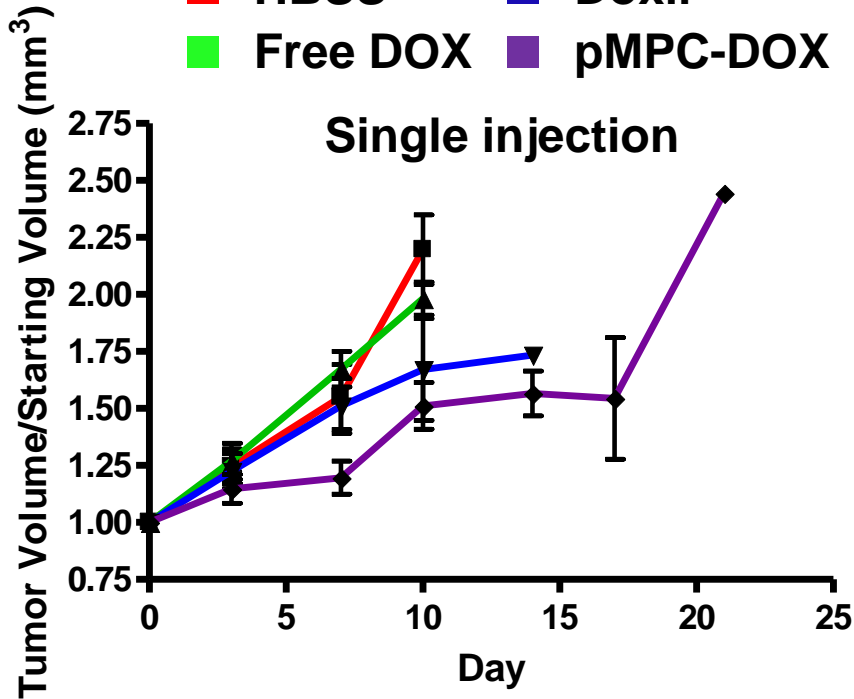
About 10 times that of Dox alone

About twice that of Doxil

In vivo experiments in mice: 4T1 breast cancer model

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

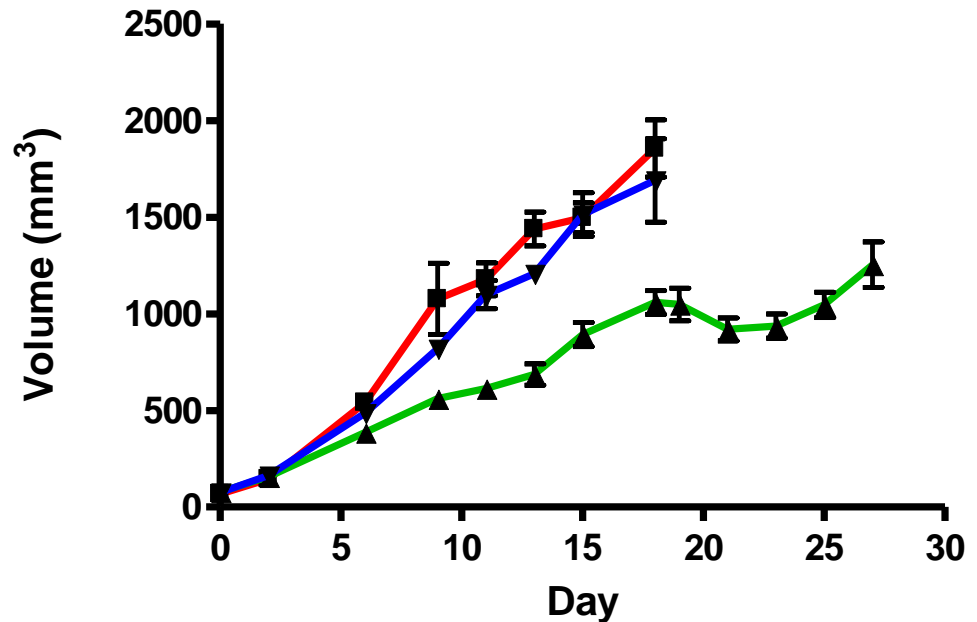
■ HBSS ■ Doxil
■ Free DOX ■ pMPC-DOX



Survival

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

Balb/c-4T1 efficacy: Tumor Volume



Survival

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