Novel Approaches to Drug Delivery to Vessel Walls to Prevent Restenosis After Open Vascular Surgery

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Financial Disclosure

• Nothing to disclose

The enemy - Intimal hyperplasia

Failed saphenous vein graft

Problem Solved for intraluminal drug delivery

• Drugs have been developed that prevent intimal hyperplasia

Drug coated stent
Drug coated balloons
No clinically available method of drug delivery following open cardiac or vascular surgery

Over 500,000 open vascular reconstructions in the US each year

Failure rates following open surgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Failure Rate</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysis access</td>
<td>50%</td>
<td>1</td>
</tr>
<tr>
<td>CABG with vein</td>
<td>40%</td>
<td>10</td>
</tr>
<tr>
<td>Fem-pop/tib bypass</td>
<td>30-60%</td>
<td>5</td>
</tr>
<tr>
<td>Carotid endarterectomy</td>
<td>5%</td>
<td>5</td>
</tr>
</tbody>
</table>

Approach - Nanoparticle mediated drug delivery to the periadventital arterial wall in conjunction with open surgery

Why nanoparticles (NP)?
Local drug delivery to the arterial wall

- High loading capacity
- Sustained drug release
- Targeted drug delivery

Sustained and targeted perivascular drug delivery using NPs

Rapamycin (or any drug)

PLOS ONE: February 21, 2014

Study protocol
- PLGA nanoparticles
- Rapamycin
- Pleuronic Gel (3 day dissolution)
- Rat carotid injury model
- Control: free rapamycin in a pleuronic gel
NPs prolong rapamycin release \textit{in vitro}\hspace{1cm}

Rat carotid injury model of restenosis

Nanoparticle uptake by the vessel wall

Green labeled nanoparticles

Rapamycin plus nanoparticles produces sustained delivery and \textit{durable inhibition of IH}\hspace{1cm}

UW Bioengineering: Innovative nanoparticle: \textit{unimolecular micelle}\hspace{1cm}

Unimolecular micelle-triblock gel prolonged release of rapamycin over 3 months\hspace{1cm}

Triblock gel: PLGA-PEG-PLGA copolymer (30 d durability)
3 month outcomes of rapamycin-loaded unimol-NPs in triblock gel

5-Year Goal
Perivascular nanoplatform in humans

Coming attractions

Thank you!