Biologically selective drug-eluting stent

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Expert Team

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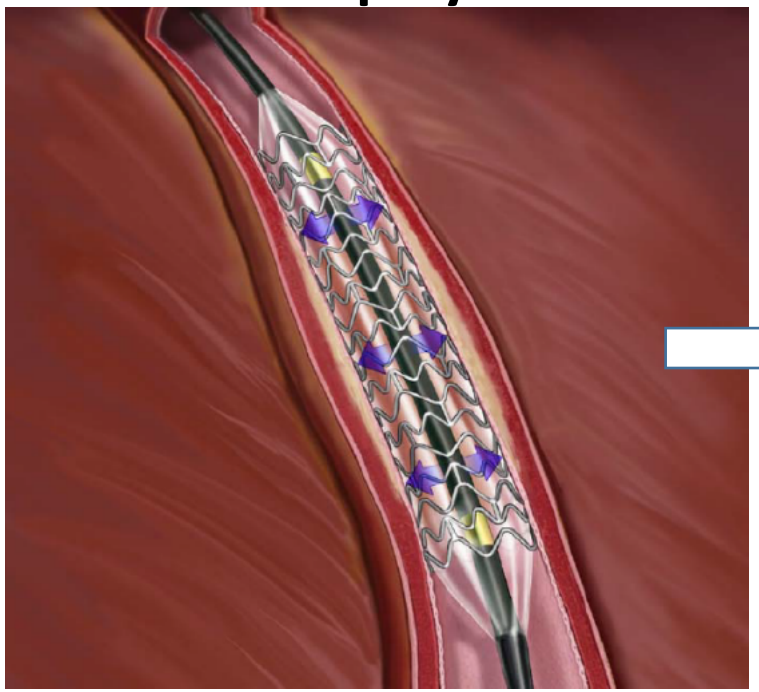
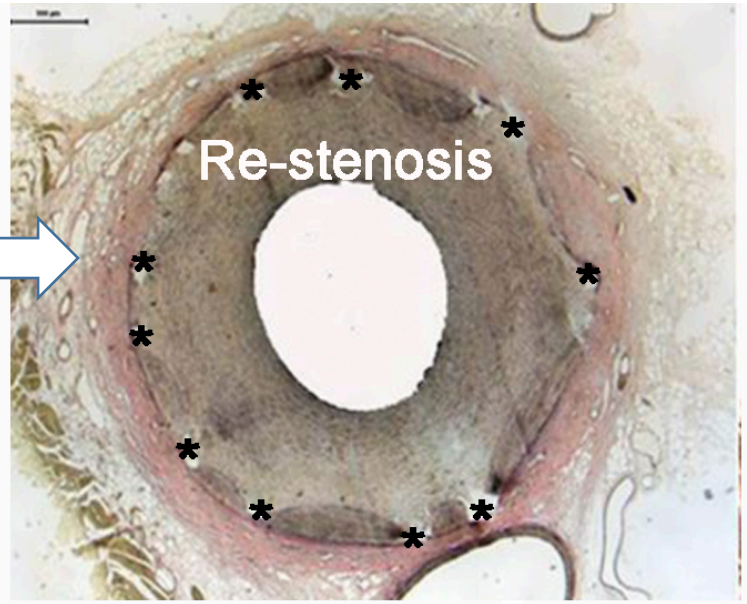
The Problems with the Current Drug-Eluting Stents (DES): In-Stent Re-Stenosis, Clotting, Requirement for Dual Anti-Platelet Therapy

Stent deployment

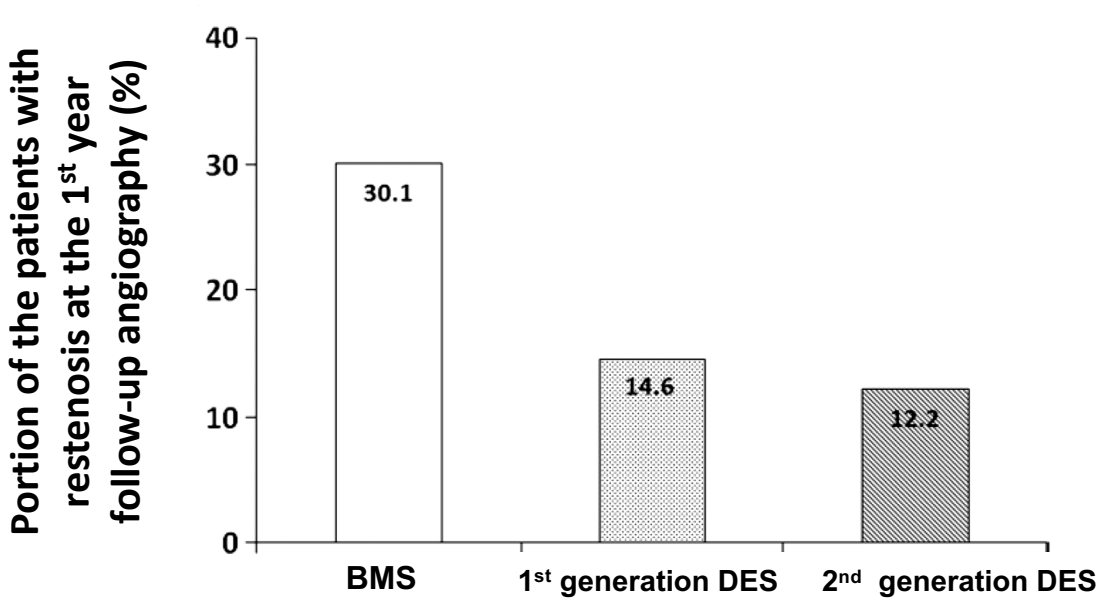


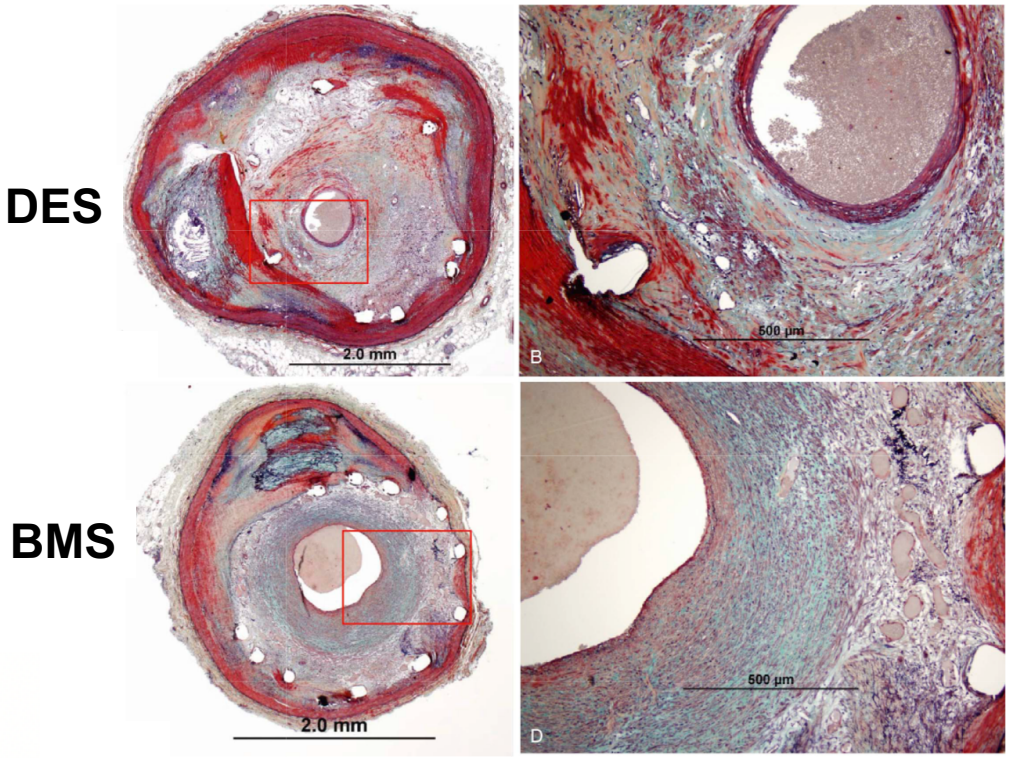
Re-narrowing of treated vessels

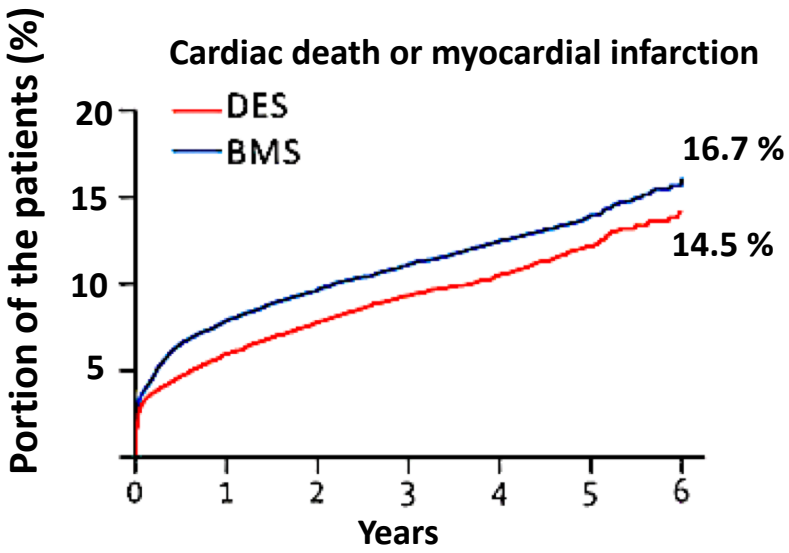


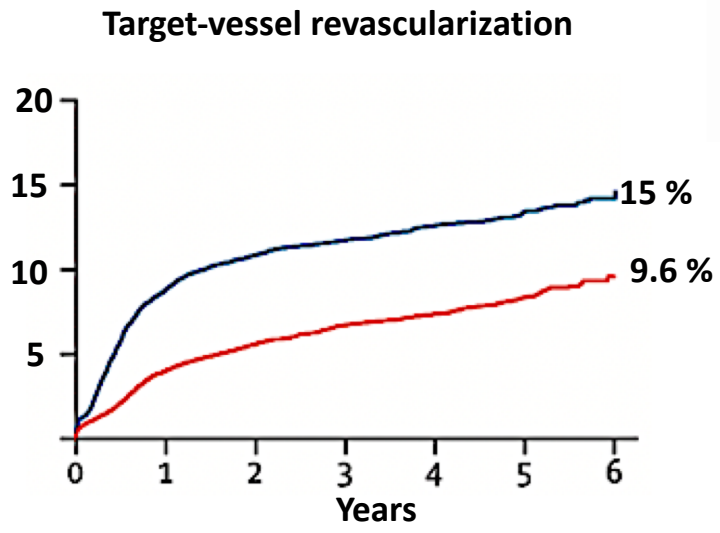
- DES have sirolimus, everolimus, paclitaxel etc→ stop growth of Endothelium: increases clotting risk.
- Therefore, patients with DES need strong, long-term anti-coagulants: increases bleeding risk.
- STILL: After DES treatment, re-stenosis remains a significant problem: need for Coronary Bypass Surgery.

The Problems with the Current Drug-Eluting Stents: Clotting, Requirement for Anti-Coagulants, and In-Stent Re-Stenosis









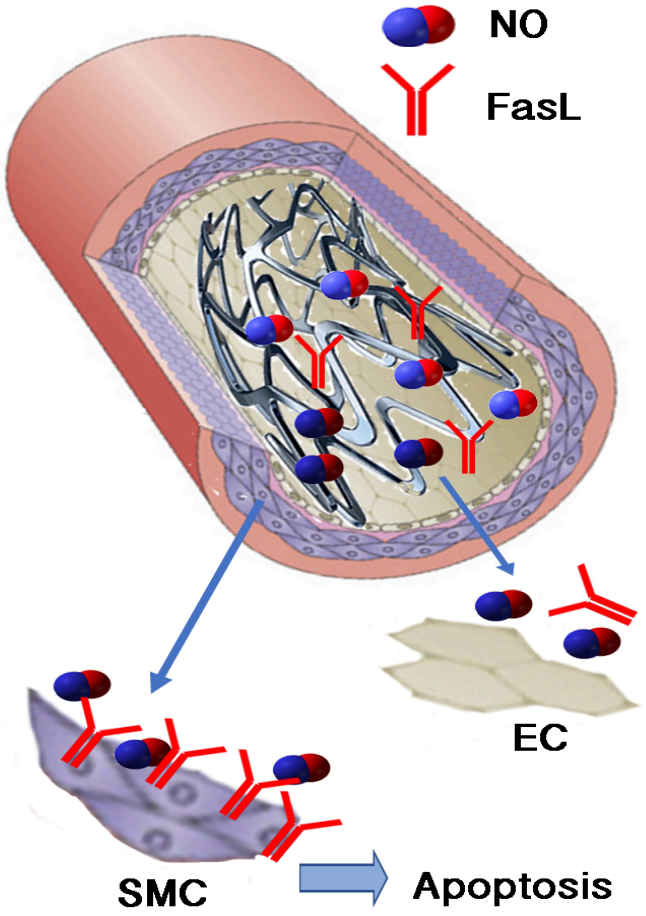
Cassese S, Heart 2013;0:1-7
Bhatt. DL Cardiovascular Intervention. 2015
Piccolo, Lancet 2019; 393: 2503–10

Market Opportunity

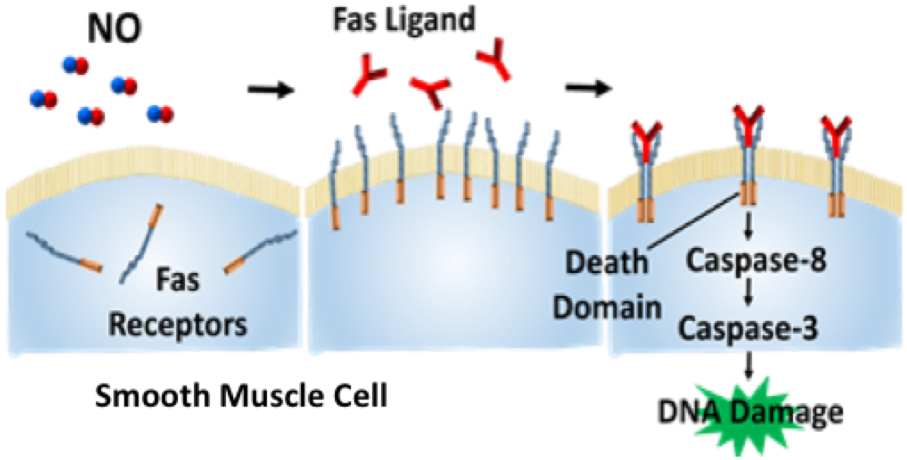
- Over 1 million coronary stents placed each year in the US alone.
- 10% of current DES fail due to in-stent restenosis over 5 years
- Cumulatively, 100,000 interventions for stent failures/year in the US alone.
- Re-imbursement for DES typically > $1,500 per stent placed.
- If capture just 5% of the coronary DES market: $75 MM in revenues/year.
- Total Addressable Market: > $1.5 B per year.

The Solution: A "smart" Drug Combination: Drug-Eluting Stent that Releases Fas Ligand (FasL) with Nitric Oxide (NO)

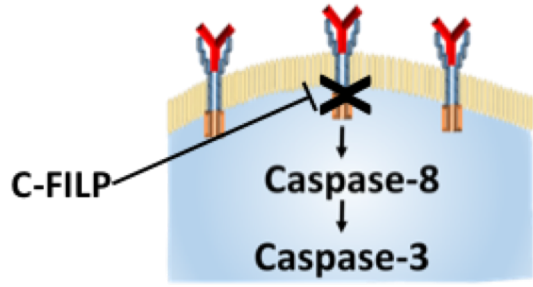
Next-generation drug-eluting stent: Differentiates between endothelial and smooth muscle cells: Inhibits and kills Smooth Muscle, while sparing the critical Endothelium that lines the artery.



Smooth Muscle Cells are Sensitized to FasL by the Release of NO: Results in Smooth Muscle Cell death.



In contrast, Endothelial Cells Resist the FasL-NO combination.

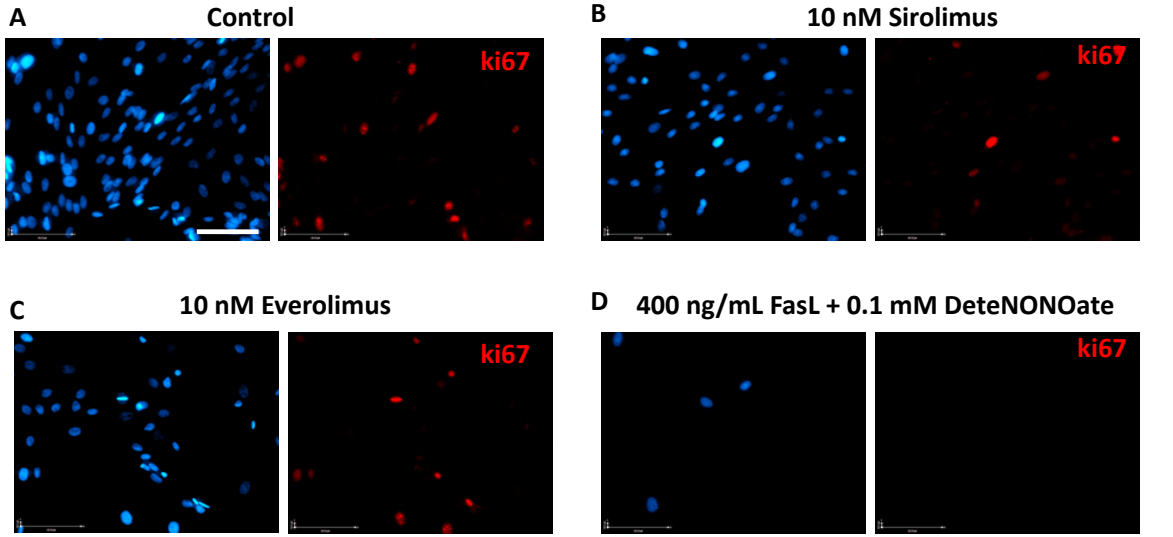


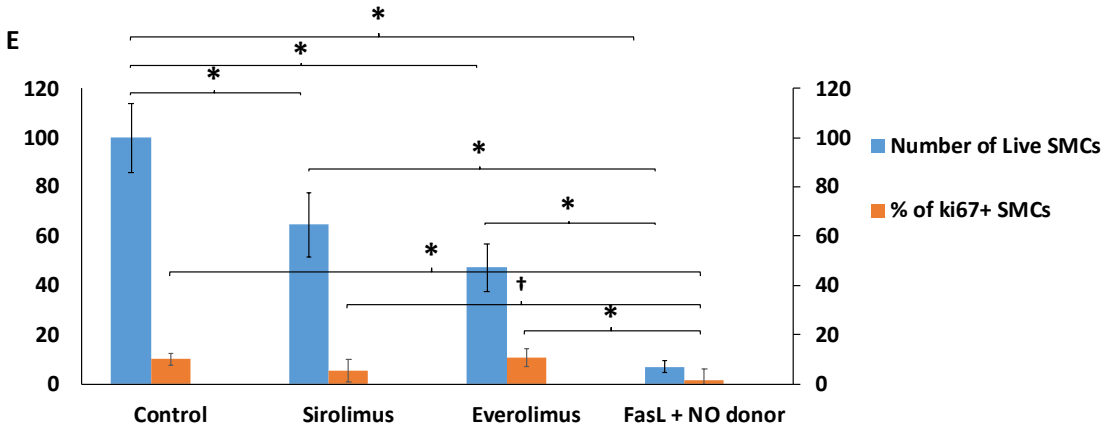
This FasL-NO combination leads to

- **More-potent inhibition of in-stent restenosis; AND**
- **Resistance to in-stent clotting**

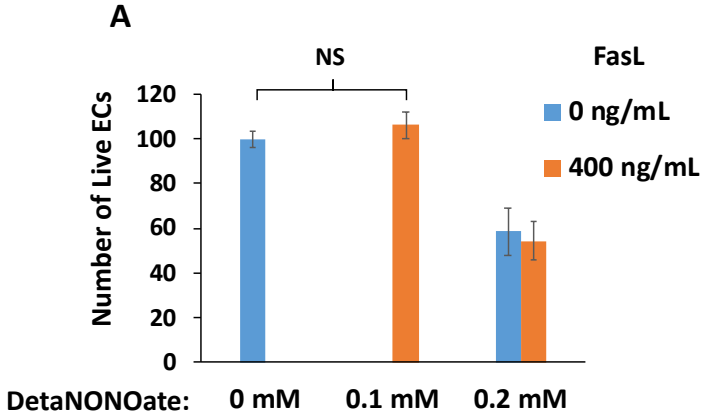
FasL-NO Drug Combination is both Highly Potent, and Highly Selective, In Vitro:

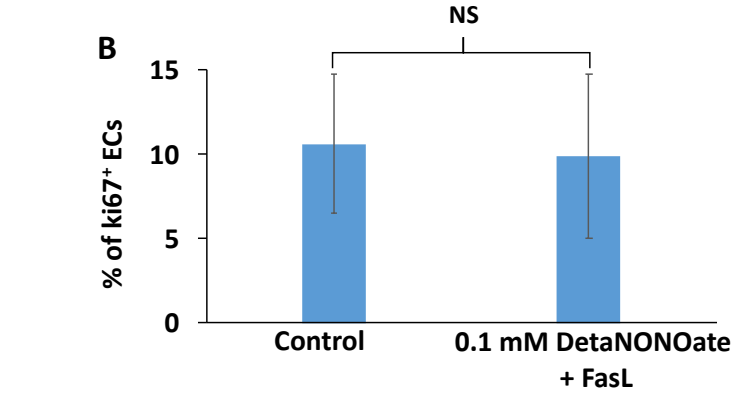
FasL-NO inhibits smooth muscle cell growth *more potently* than DES drugs everolimus and sirolimus

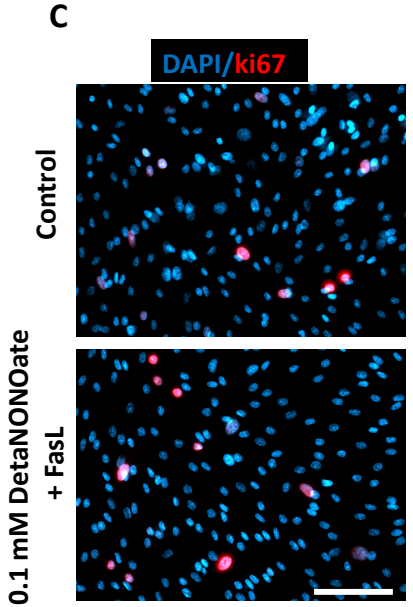




FasL-NO *does not affect* endothelial cells' viability and proliferation



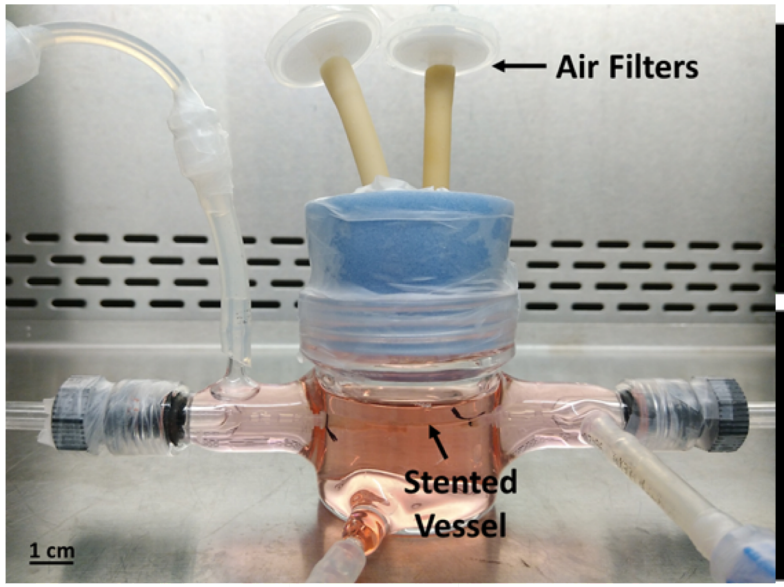


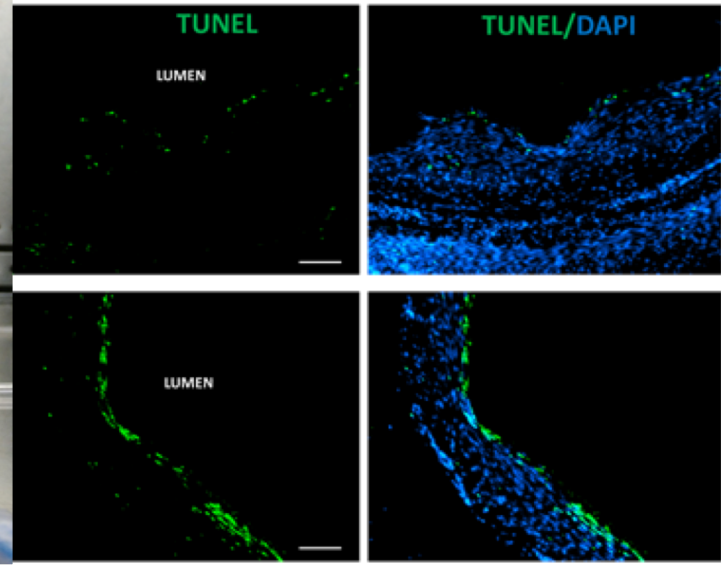


Kural et al. Biomaterials, 2019, 212:28-38.

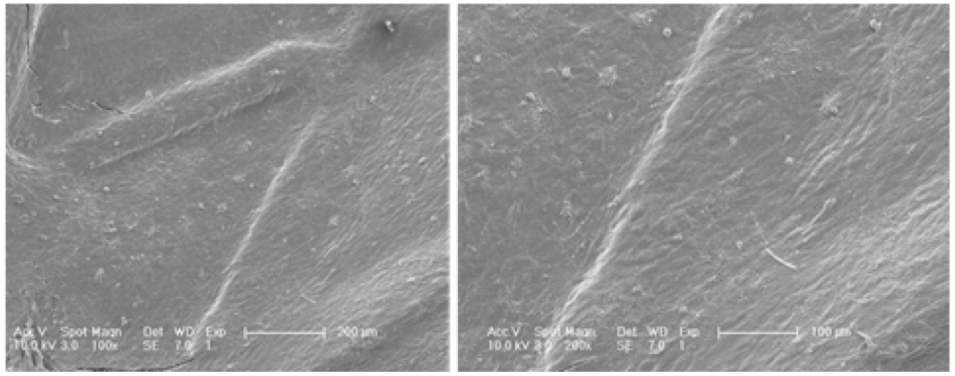
FasL-NO Eluting Stents are *Highly Potent and Selective* in Arteries: Bioreactor Studies, and In Vivo:

Bioreactor culture of stented arteries

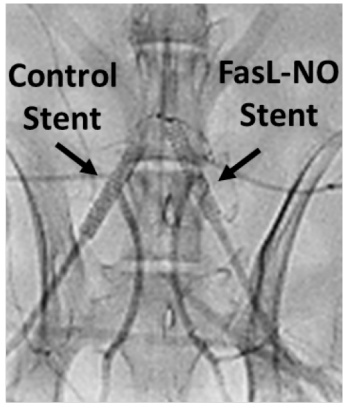




Endothelial cell recovery Day-14

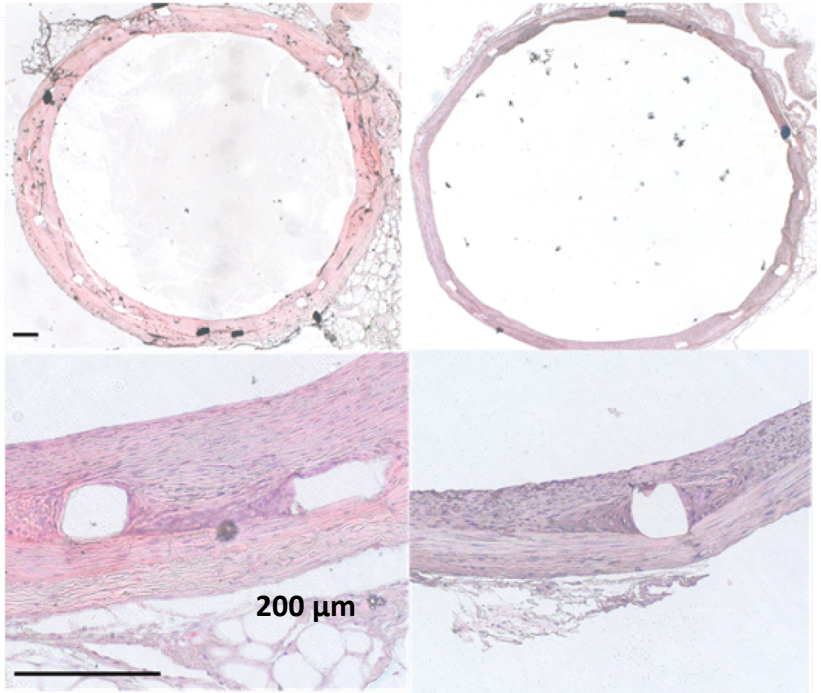


Rabbit Arterial Stent Implants



Control stent 1 month

FasL - NO stent 1 month



Intended Use of Blavatnik Funds

Design FasL-NO-eluting stent prototype:

- Stent material – Nitinol, Cobalt-Chromium, or Stainless Steel
- Prototype fabrication: outsource to Confluent Medical Inc.

Confluent offers technologies to bring Nitinol, Cobalt Chromium, and Stainless Steel stents to market:

> Design services
> Finite element analysis
> Mechanical properties testing
> Balloon/stent pillowing

<u>Approximate Budget</u>:

1. Develop prototypes with EVAc coating and characterize elution profiles – at Yale, ~ $70K.
2. Confluent prototypes Nitinol and CoCr stents with EVAc polymer coating, characterize stability/flaking/etc.
3. Confluent characterizes stent mechanics and stability – total of ~ $180k for Confluent.
4. Basic rodent toxicology studies - outsourced to WuXi Apptek, ~ $50k.
5. TOTAL: ~ $300k.

Potential Pathway to Liquidity

- Proof-of-concept design - stent/coating/drug combination – ***Blavatnik application***
- Proof-of-concept efficacy - pig coronary model (currently NIH-funded)
- Pharm/toxicology characterization, stability, potency data for IND filing
- Exit pre-Phase I, or post-Phase I-II.

Start-up company during pre-clinical characterization, before Phase-I.

Founders:
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W. Mark Saltzman, PhD

A Quantum Advancement in Drug-Eluting Stents

Value Proposition:

1,000,000 patients could benefit annually:

- Higher quality-adjusted-life years without need for additional interventions, such as repeat stenting or coronary artery bypass surgery.
- Much shorter antiplatelet treatment (free of >$200 per month and high bleeding risk).