



TAXUS® Drug-Eluting Coronary Stent A Commercial Success for NIH TT

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Office of Technology Transfer

National Institutes of Health

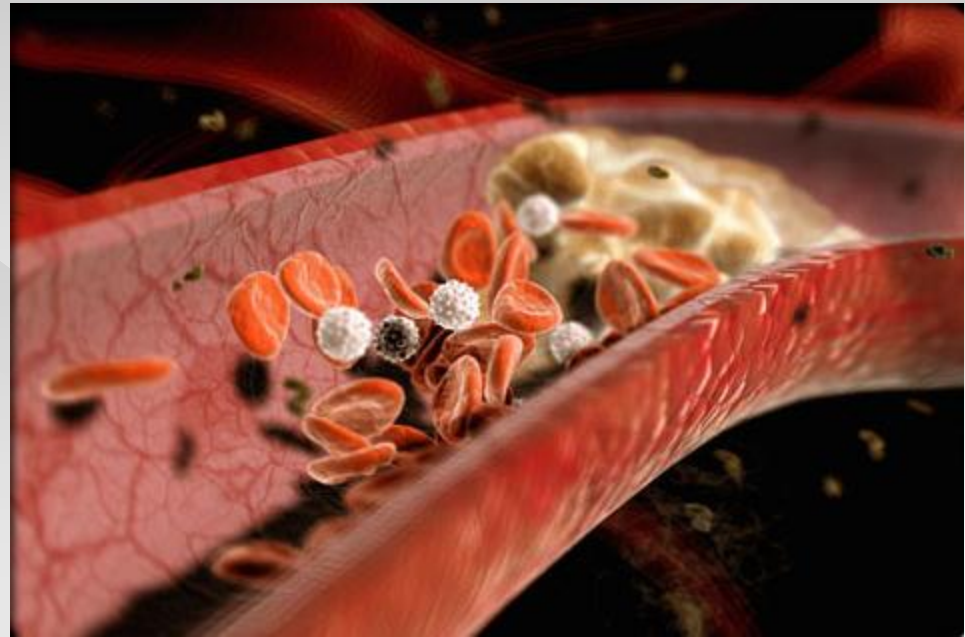
U.S. Department of Health & Human Services



National Institutes of Health – Bethesda



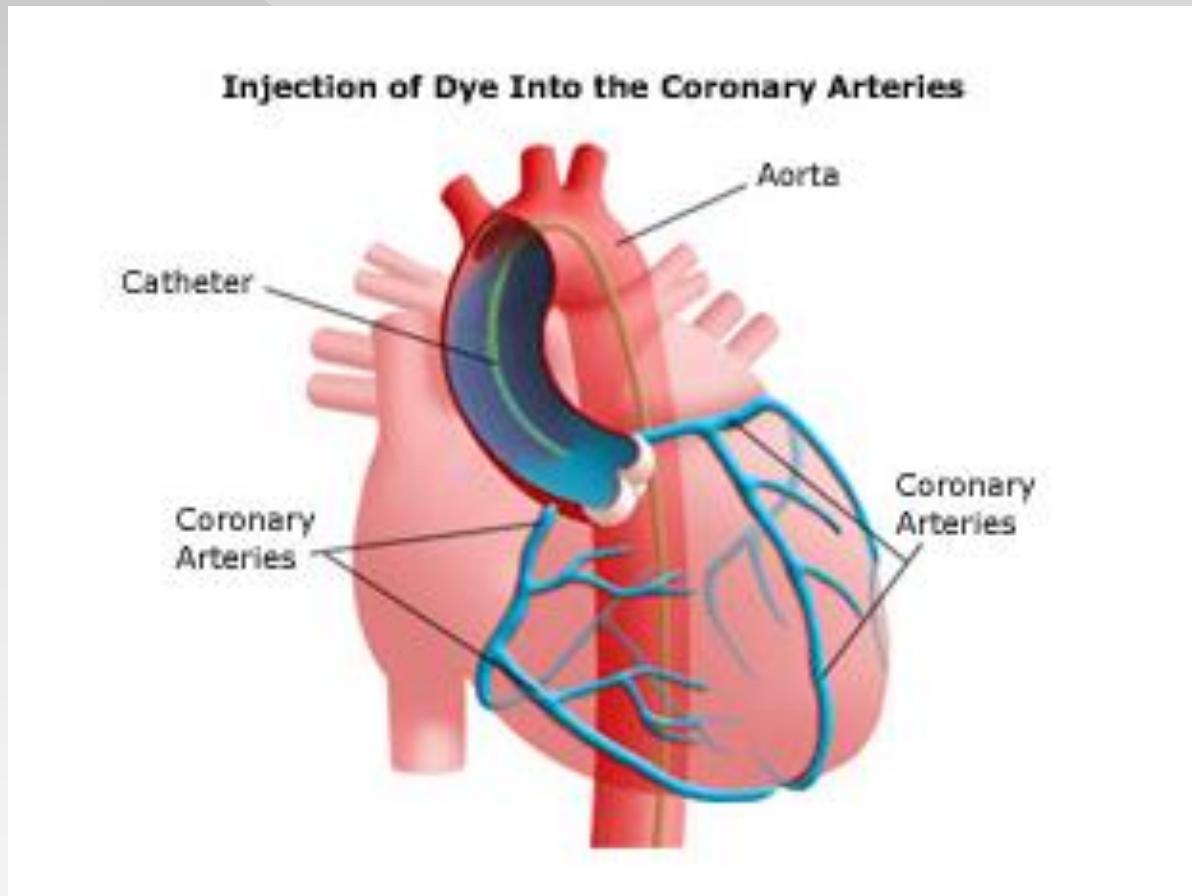
Coronary Heart (Artery) Disease (CHD)



- narrowing or occlusion of coronary arteries
- angina pectoris – acute myocardial infarction
- > 1 million/year in the U.S.

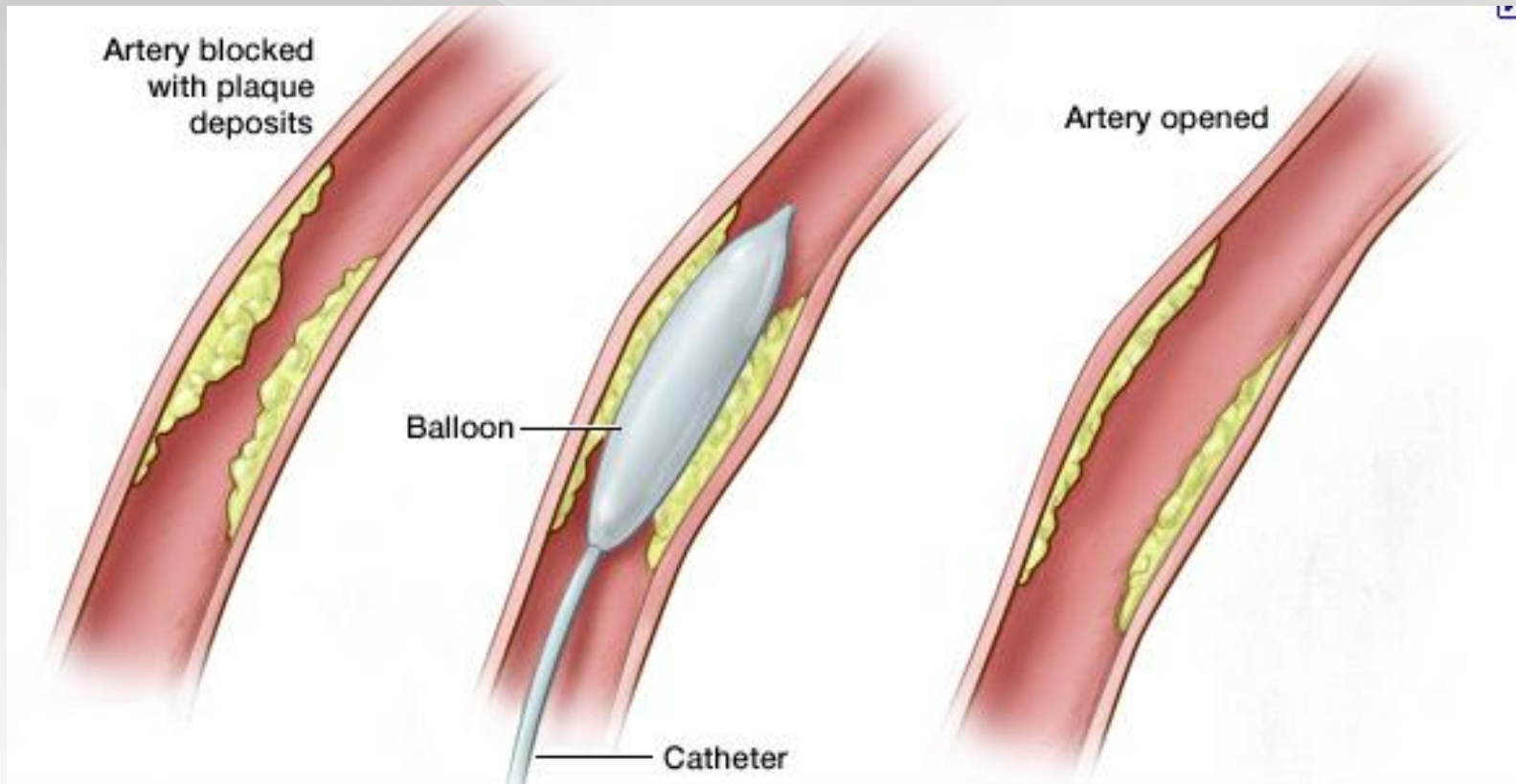
Evolution of CHD Treatment Procedures

- 1950's - coronary angiography for diagnosis



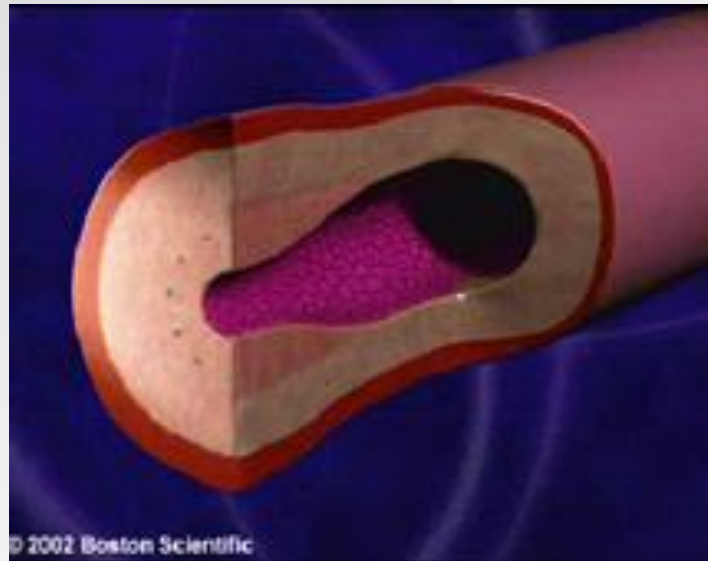
Evolution of CHD Treatment Procedures

- 1970's – balloon angioplasty for opening



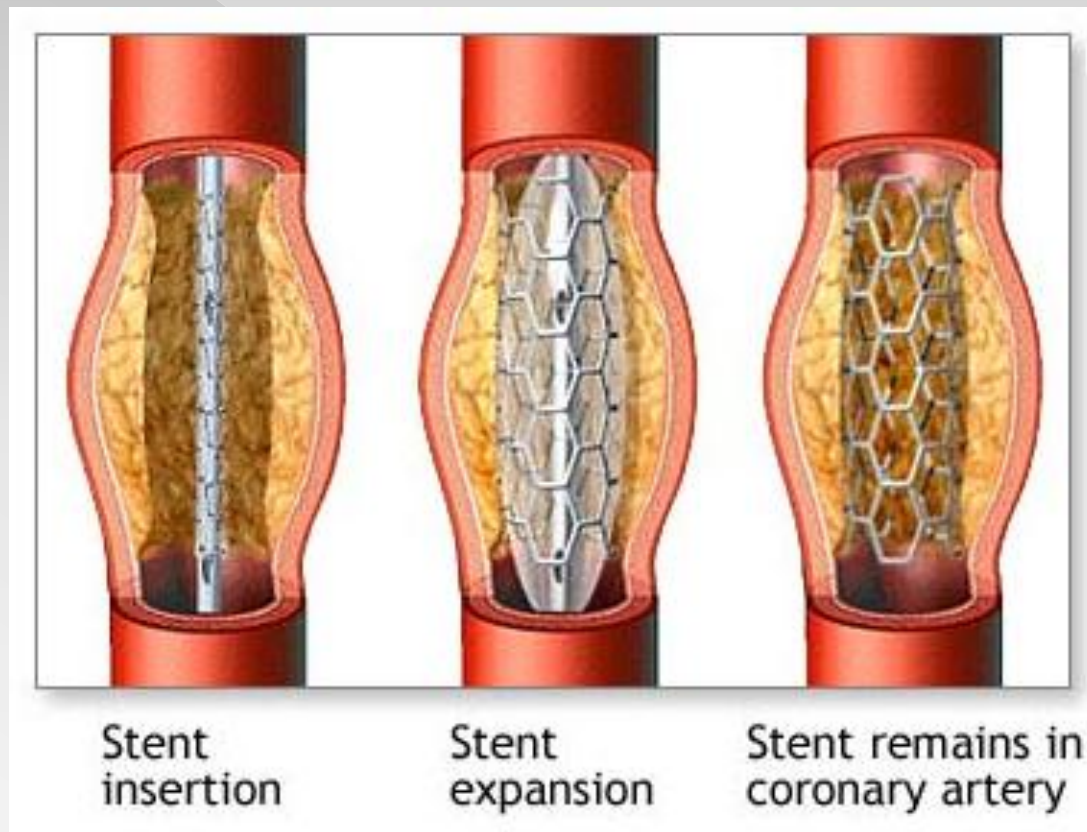
Problems with Coronary Balloon Angioplasty

- Risk of uncontrollable plaque disruption
- Vascular recoil - coronary occlusion & AMI
- Up to 40% - renarrowing of artery (restenosis)



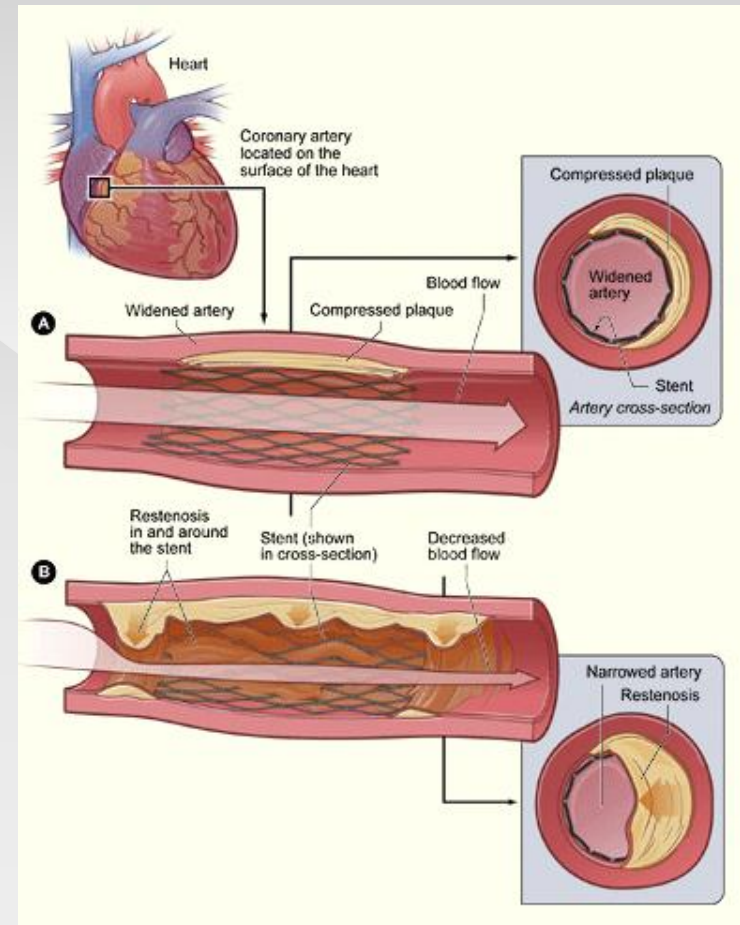
How Improve Balloon Angioplasty for CHD?

- 1990's - add bare metal mesh scaffold (stent)



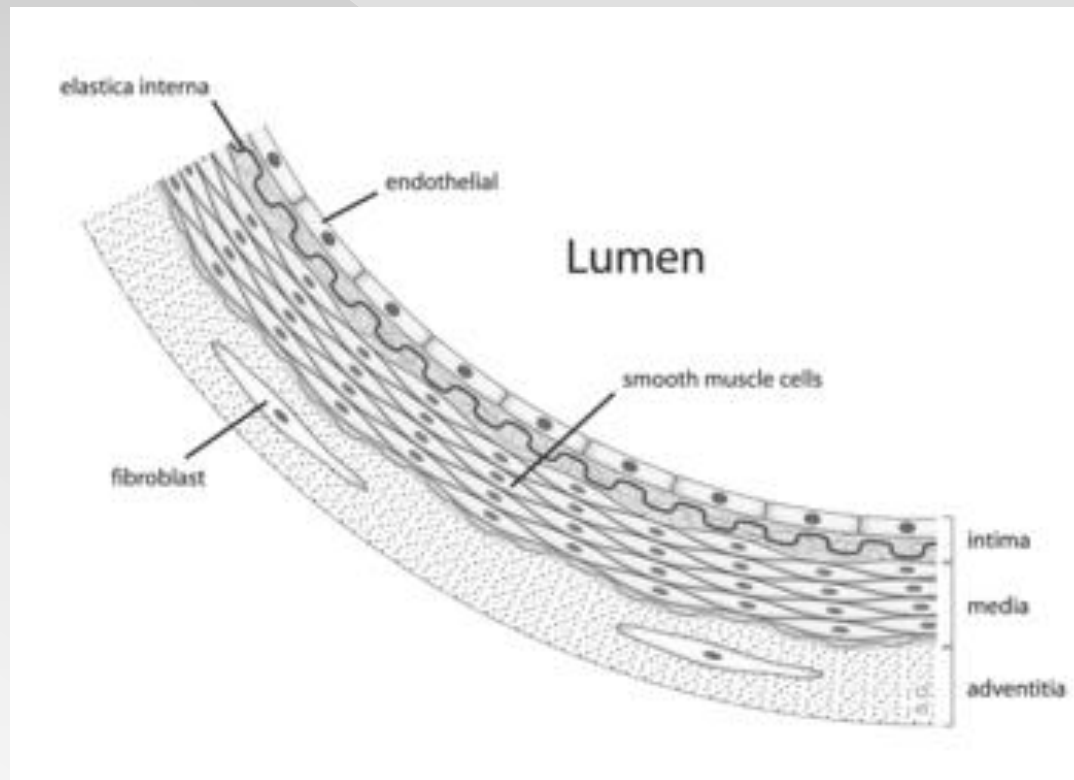
Still Problems with Bare-Metal Stents

- Subacute stent thrombosis
- Late in-stent restenosis



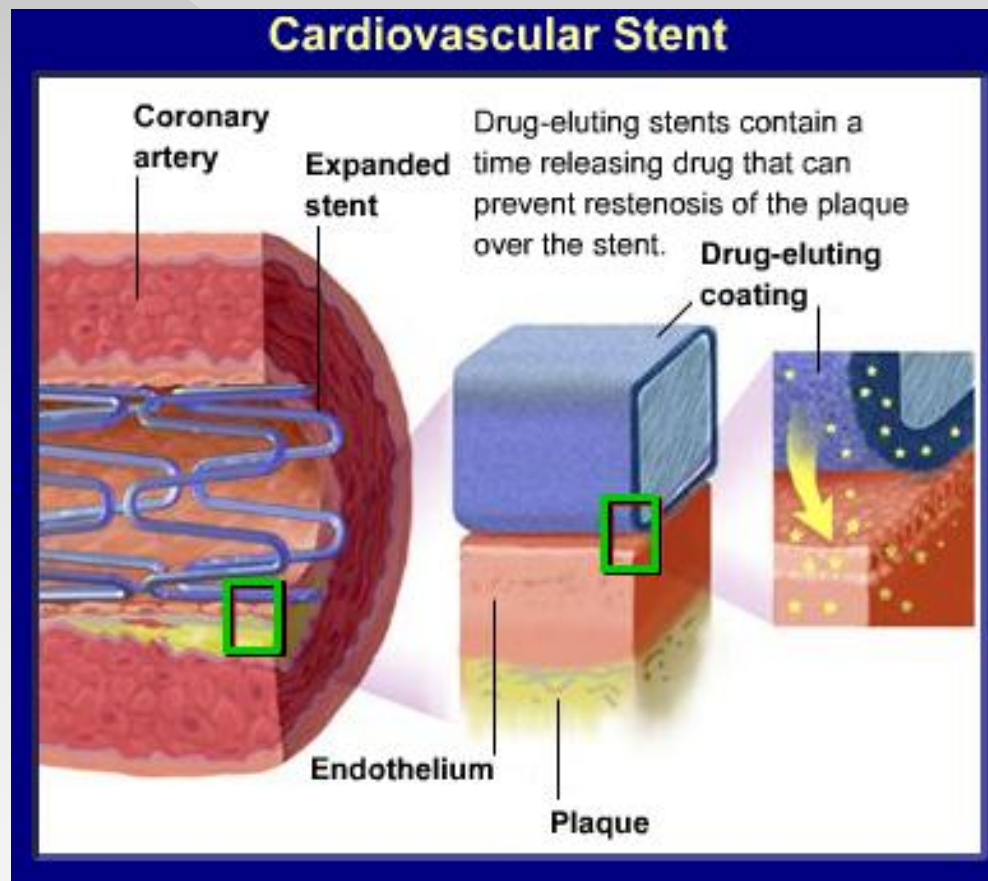
Analysis of the Problem

- Late in-stent restenosis – mainly due to proliferation & migration of smooth muscle cells from intima into lumen



Need for Further Innovation – 1990s

- New concept – Coat metal stents with drugs that will prevent or inhibit restenosis



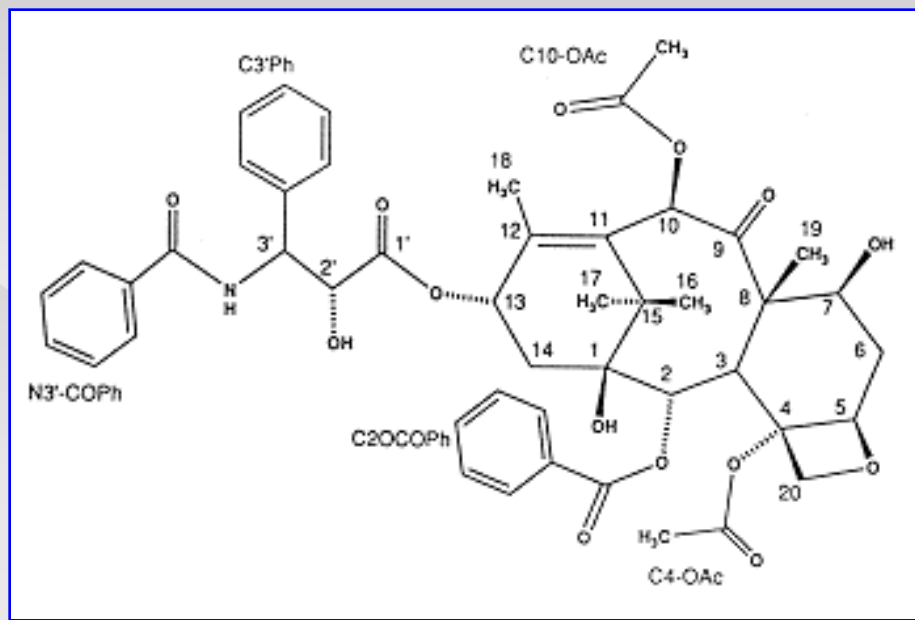
New Challenge for Improving Stents for BA

- How do you disrupt or inhibit triggering of the inflammatory process that leads to restenosis?
- What drug(s) will work, and how do you formulate them to be effective over a long period of time to prevent late in stent restenosis?

One of Several Drugs Evaluated:

- Paclitaxel (a.k.a. Taxol)

- inhibits proliferation
- inhibits migration
- inhibits inflammation
- inhibits secretion
- used to treat breast & ovarian cancer



TAXUS® Drug-Eluting Stent – IP History

NeoRx filed USPA 08/011,669 by Kunz, *et al.* on January 28, 1993

- claims a therapeutic method comprising inhibiting stenosis or restenosis of a blood vessel by administering to a mammal an effective amount of taxol or a structural analog thereof

TAXUS® Drug-Eluting Stent – IP History

Angiogenesis Technologies filed USPA 08/094,536 by Hunter, *et al.* on July 19, 1993

- claims a stent for expanding the lumen of a body passageway comprising a generally tubular structure coated with a composition comprising paclitaxel, an analogue or derivative thereof, and a polymeric composition

TAXUS® Drug-Eluting Stent – IP History

NIH filed USPA 08/099,067 by Kinsella & Sollott (NIA) on July 29, 1993

- claims a method for treating or reducing a fibroproliferative vascular disease in a patient comprising: treating said patient with a pharmaceutical preparation comprising a therapeutically effective amount of a microtubule stabilizing agent selected from the group consisting of taxol, a water soluble taxol derivative, and deuterium oxide

TAXUS® Drug-Eluting Stent – Licensing

Feb 1, 1996 – Angiotech submits license application to OTT for NIH patent rights

Apr 4, 1996 – Angiotech executes CRADA with NIA & JHU

Apr 1, 1997 - NIH Kinsella & Sollott patent issues

Jul 9, 1997 – Angiotech signs co-exclusive licenses with Cook Medical & Boston Scientific to develop & market DES & wraps

Nov 19, 1997 – Angiotech signs exclusive patent license with NIH

Feb 10, 1998 – Angiotech Hunter, *et al.* patent issues

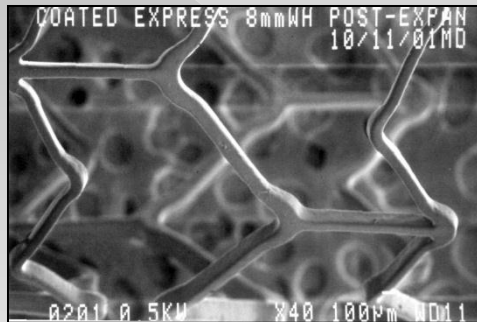
Mar 31, 1998 – NeoRx Kunz, *et al.* patent issues

Dec 17, 1998 – Angiotech signs exclusive license to NeoRx IP

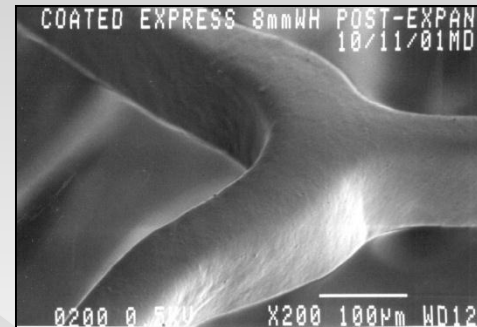
TAXUS® Stent – Commercialization

1998 on – Boston Scientific has stent and stent delivery technology & develops proprietary polymeric coating (Translute™) for TAXUS® stent

40x



200x



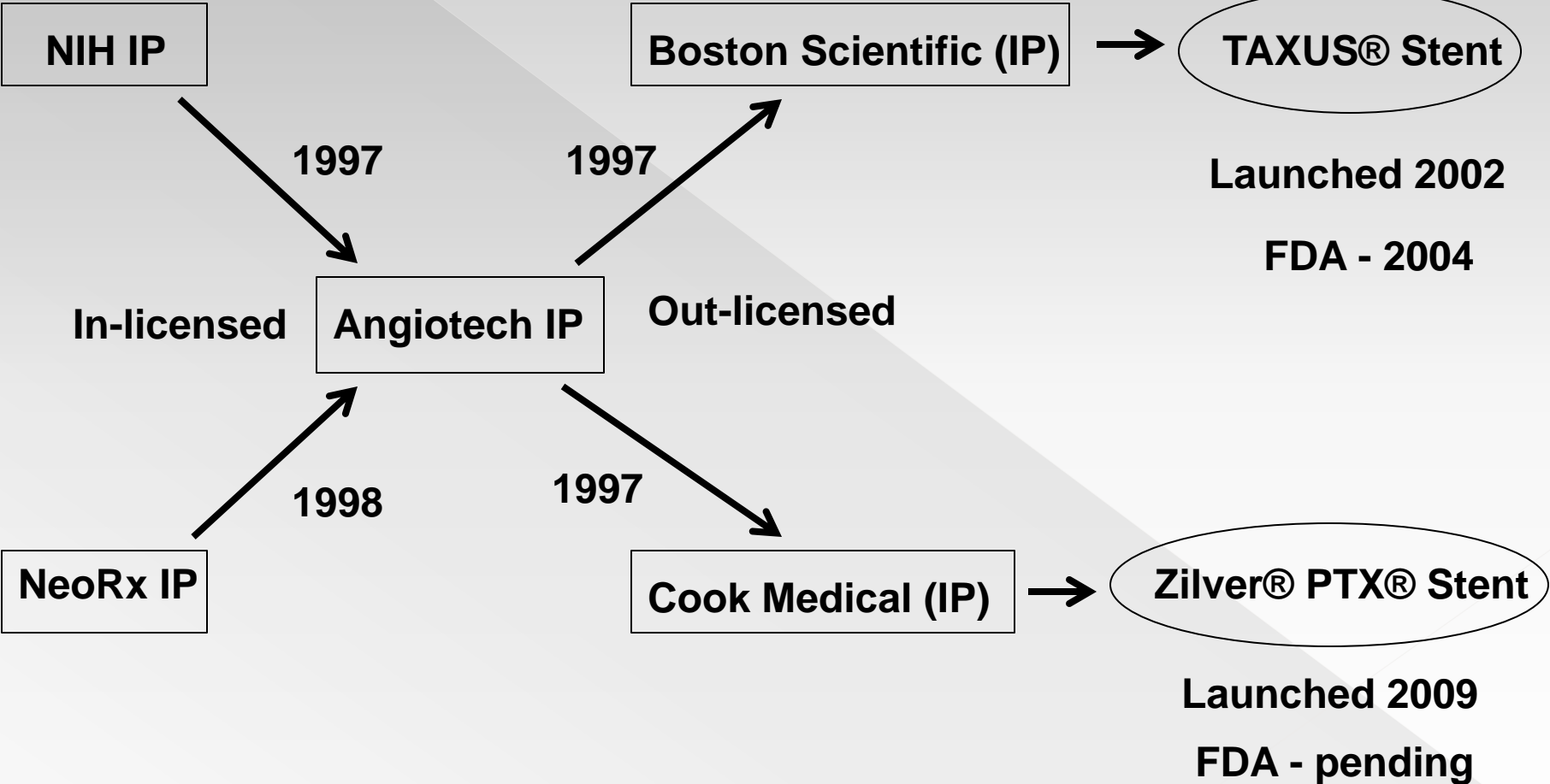
Apr 2, 2002 - First Commercial Sale by Boston Scientific

Mar 4, 2004 - TAXUS® Stent Approved by FDA for US market

Sep 25, 2004 – Cook sublicense amended to terminate co-exclusive rights to cardiovascular (CV), but retains rights to peripheral vascular (PV)

Nov 23, 2004 – Boston Scientific sublicense amended to exclusive for CV

Summary of IP Licensing by Angiotech



Taxus® Stent - Immediate Commercial Success

BSC Worldwide Sales -



2003 - \$ 0.123 Billion

2004 - \$ 2.143 Billion

2005 - \$ 2.556 Billion

2006 - \$ 2.358 Billion

2005 >1 million sold at \$2500 ASP

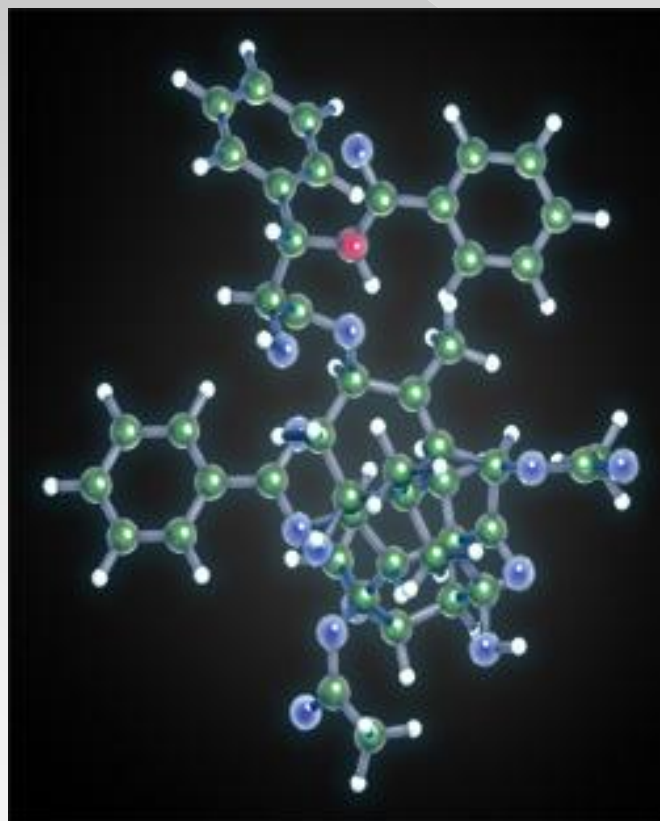
Some Unanticipated Effects of Rapid Success

Extra cash (\$\$) to grow Angiotech's business

- between 1997 and 2000 – 3 public offerings raised cash
- from 1992 to 2000 - Angiotech had < 50 employees
- 2003 to 2006 – Angiotech acquired seven companies
- 2006 - Angiotech reported >1500 employees
- but after 2007, royalty revenue declined sharply

Then - Rapid Loss of DES Market Share

BSC Worldwide Sales -



2007 - \$ 1.760 Billion

2008 - \$ 1.316 Billion

2009 - \$ 1.027 Billion

2010 - \$ 0.500 Billion

Reasons for Rapid Loss of BSC Market Share

- “uncertainty regarding late stent thrombosis” (FDA Review Panel – 4Q06)
- periodic recalls (voluntary & FDA) product lots
- U.S. launch of competing (non-paclitaxel) drug-eluting stents CHD

Summary of Successes

- The Taxus® Stent addressed an important medical problem (late in stent restenosis) in cardiac care
- Validity of a new concept (time-release coating of drugs on in-dwelling medical device to achieve therapeutic effect) was demonstrated
- Small start-up can develop IP, in-license additional IP and successfully partner, through out-licensing, with established larger companies who have complementary technology needed to commercialize an innovative new product
- Licensors do, sometimes, benefit surprisingly well from their licensees success!

www.ott.nih.gov

The screenshot shows the NIH Office of Technology Transfer (OTT) website in a Windows Internet Explorer browser window. The browser title is "NIH Office of Technology Transfer (OTT) - Windows Internet Explorer". The address bar shows "http://www.ott.nih.gov/". The search bar contains "Google". The website header includes the OTT logo, the text "US Department of Health and Human Services NATIONAL INSTITUTES OF HEALTH OFFICE OF TECHNOLOGY TRANSFER SCIENCE. IDEAS. BREAKTHROUGHS.", and a search bar with a "GO" button. Below the header, there are navigation links for "FOR NIH STAFF", "Printer Friendly", and "Text Size". The main content area features a "FEATURED TECHNOLOGIES" section with a red ribbon graphic and the text "Inhibitors of CD25 to Treat Autoimmune Diseases and Tumors". Below this, there is a "LEARN MORE" button and a "Get Adobe Flash Player" icon. To the right of the featured technologies, there are sections for "Licensing OPPORTUNITIES" with a "Brochures" button and "Learn More" link, "SUBSCRIBE TO NIH & FDA TECHNOLOGIES BY RSS FEED" with an RSS icon, and "NIH LIGHTS UP THE WORLD" with a minus sign. At the bottom, there is a "CURRENT ISSUES" section with the text "NIH to Host 'Technology Transfer Summit North America' on October 3-4, 2011 Special Conference Registration Rates of \$329 for Academics/Non-profits and \$539".



That's all Folks!