

# **Curing Cancer**

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# The War on Cancer is Declared

## Richard Nixon, 1971

- "I will also ask for an appropriation of an extra \$100 million to launch an intensive campaign to find a cure for cancer, and I will ask later for whatever additional funds can effectively be used. The time has come in America when the same kind of concentrated effort that split the atom and took man to the moon should be turned toward conquering this dread disease. Let us make a total national commitment to achieve this goal."

# NCI Funding 2005-07

Cancer Site	2005 Spending (actual, in millions)	2006 Spending (estimated, in millions)	2007 Spending (estimated, in millions)
Breast	\$560.1	\$557.3	\$551.1
Colorectal	\$253.1	\$251.9	\$249.1
Lung	\$266.1	\$264.8	\$261.9
Prostate	\$309.0	\$309.0	\$305.6

The US spent \$5.6 billion on cancer research in 2006

# Cancer Research – A Super Fraud?

- "Everyone should know that most cancer research is largely a fraud and that the major cancer research organizations are derelict in their duties to the people who support them." - Linus Pauling PhD (Two-time Nobel Prize winner).

# What went right?

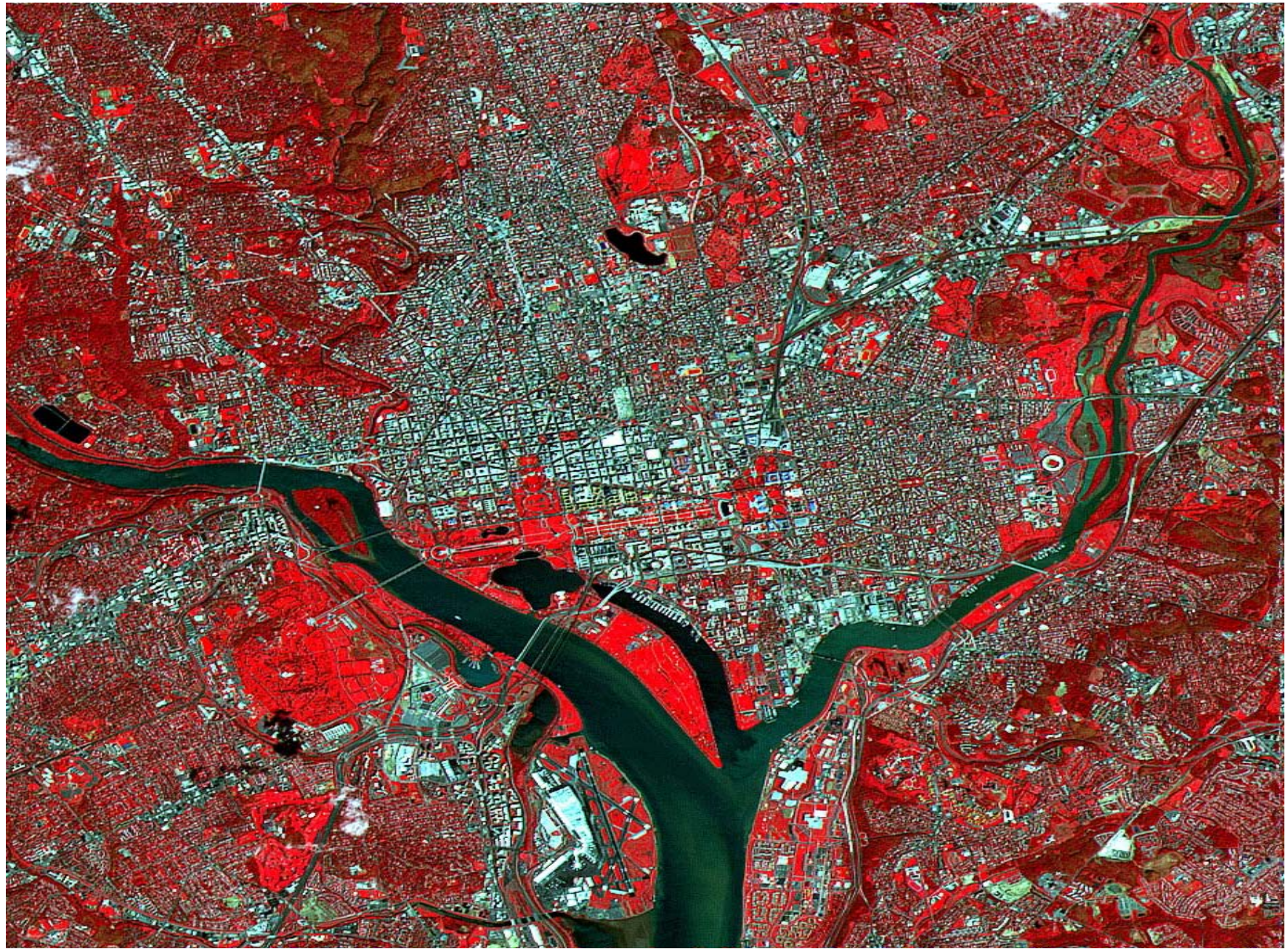
- Have cured and conquered some cancers
  - Leukemia
  - Lymphoma
  - Germ Cell cancers
  - Childhood Cancers
- Screening/Early Detection/Prevention
  - Breast, Colon, Cervix, Skin

# The view from 35,000 feet



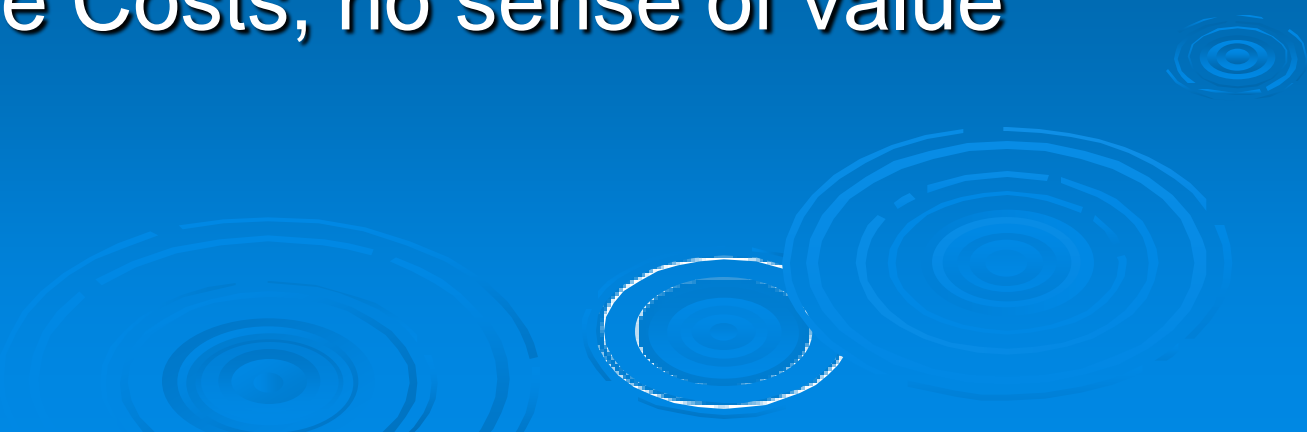
Everything looks the same from up here





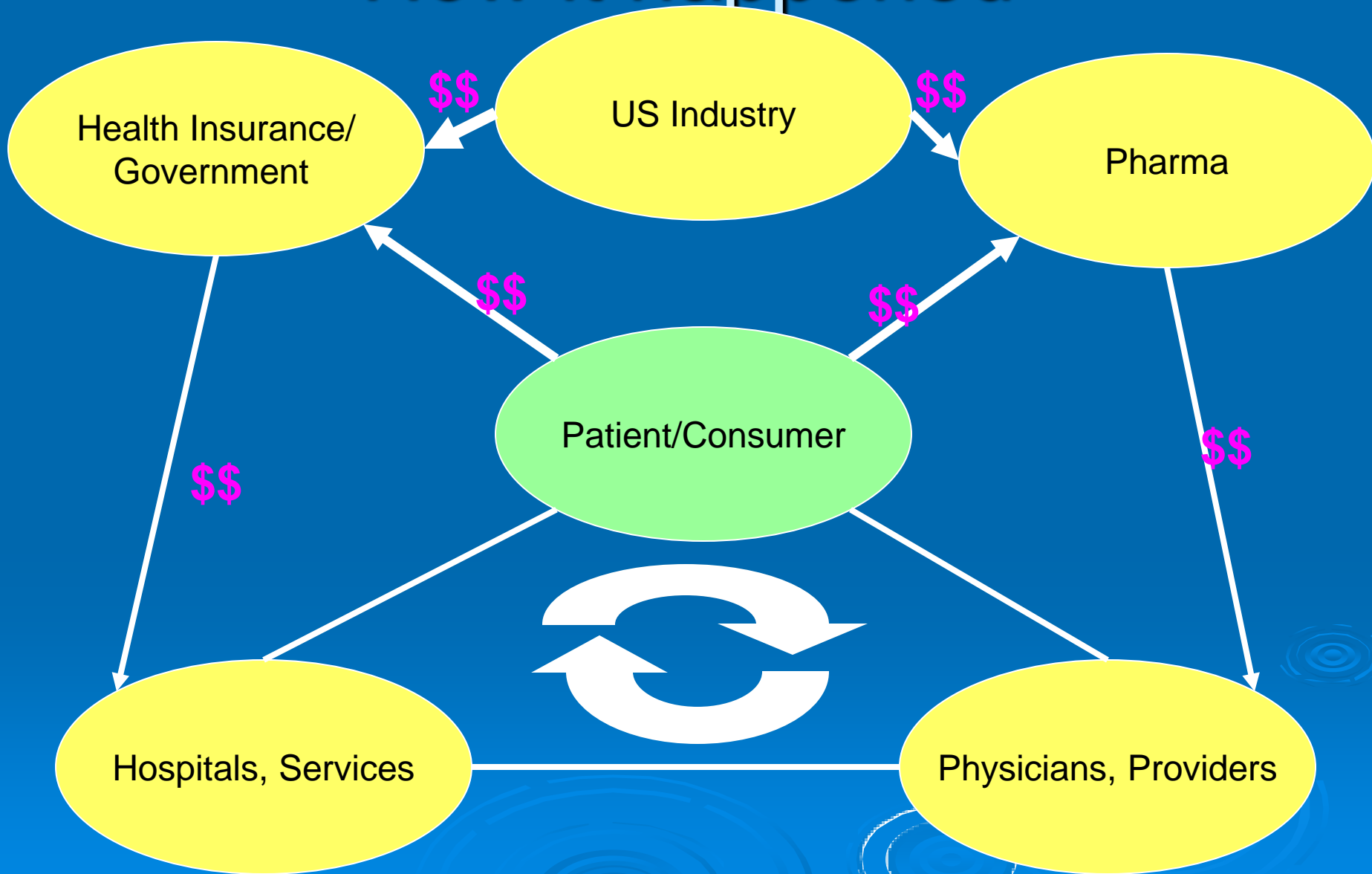


# What went wrong?

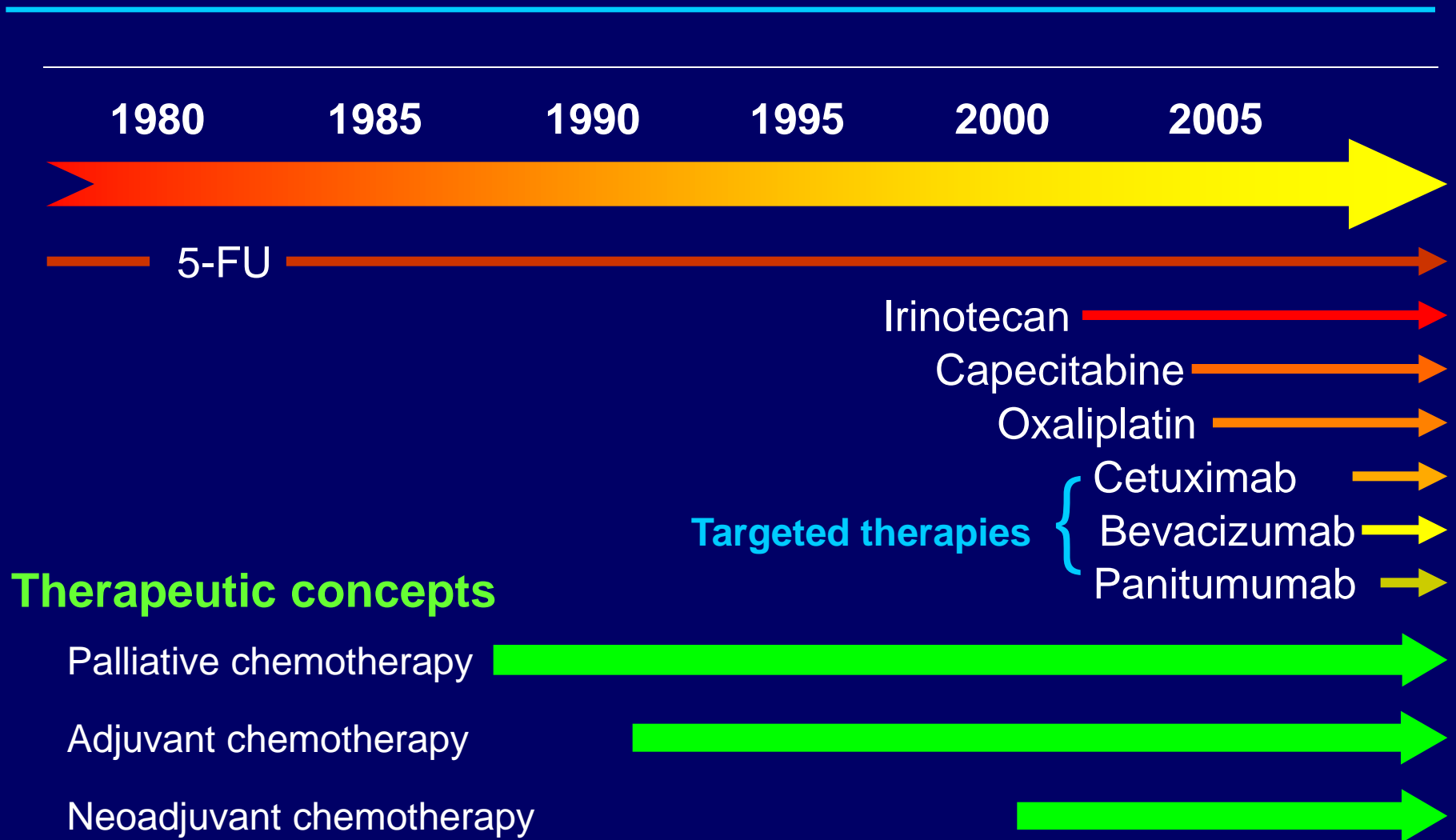
- Adenocarcinomas
  - Progression free survival
  - Declaring response rates do not correlate with survival
  - Accepting low response rates
  - Health Care Costs, no sense of value
- 



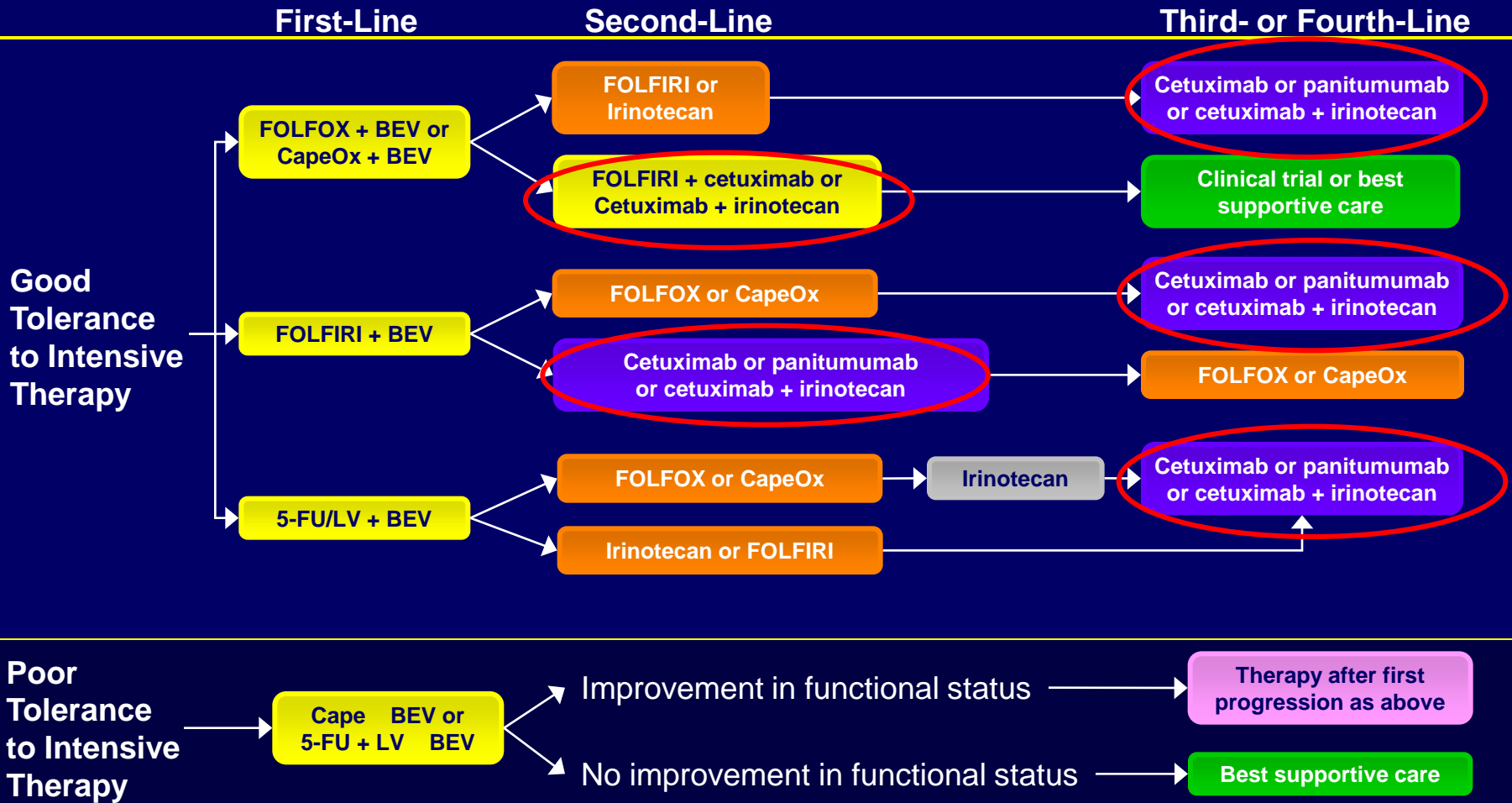
# How it happened



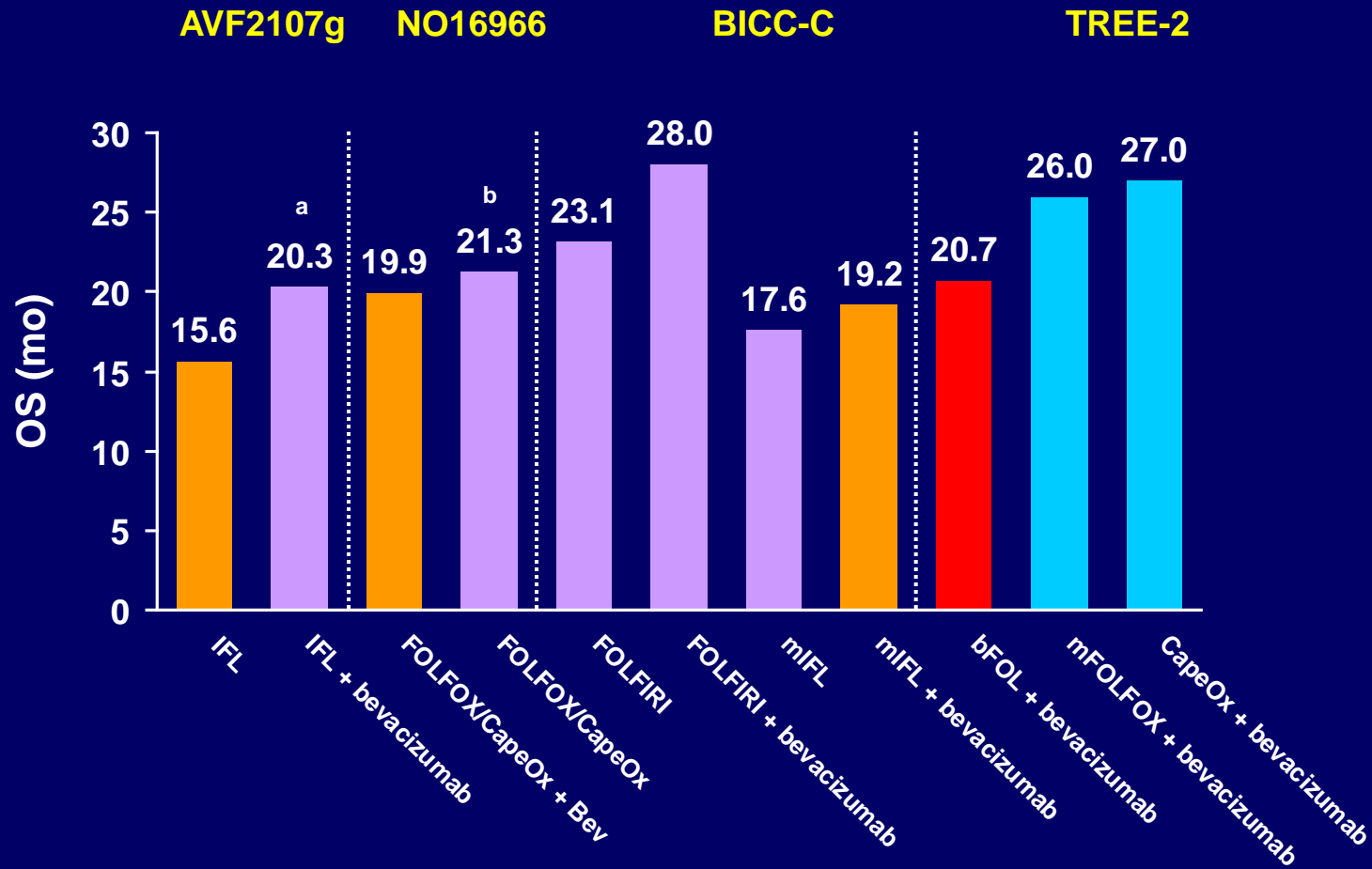
# “Success” in the Treatment of Colorectal Cancer



# NCCN Guidelines: Advanced/MCRC



# First-Line Bevacizumab in MCRC: Overall Survival

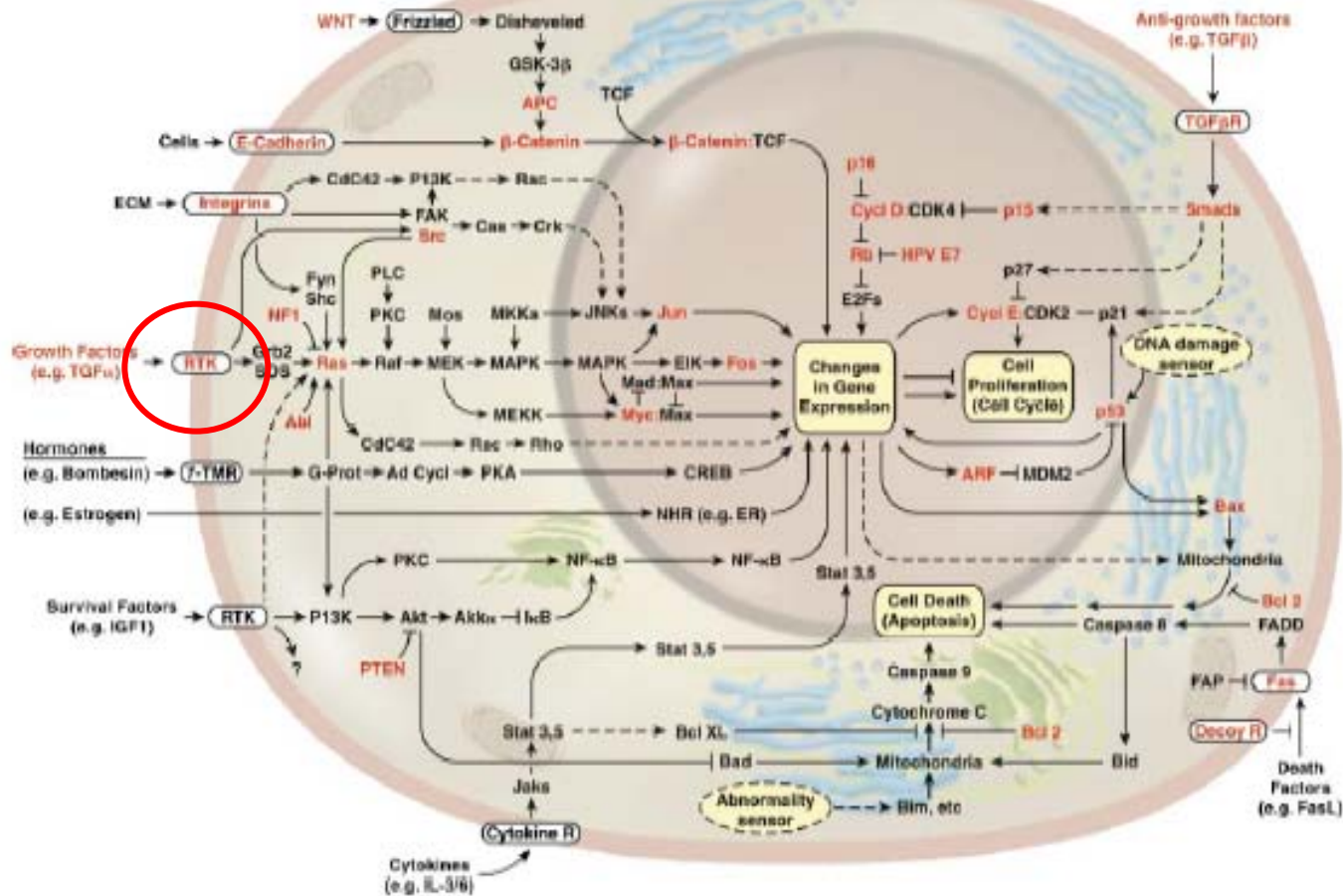


<sup>a</sup> $P < 0.001$ ; <sup>b</sup> $P = 0.0769$ .

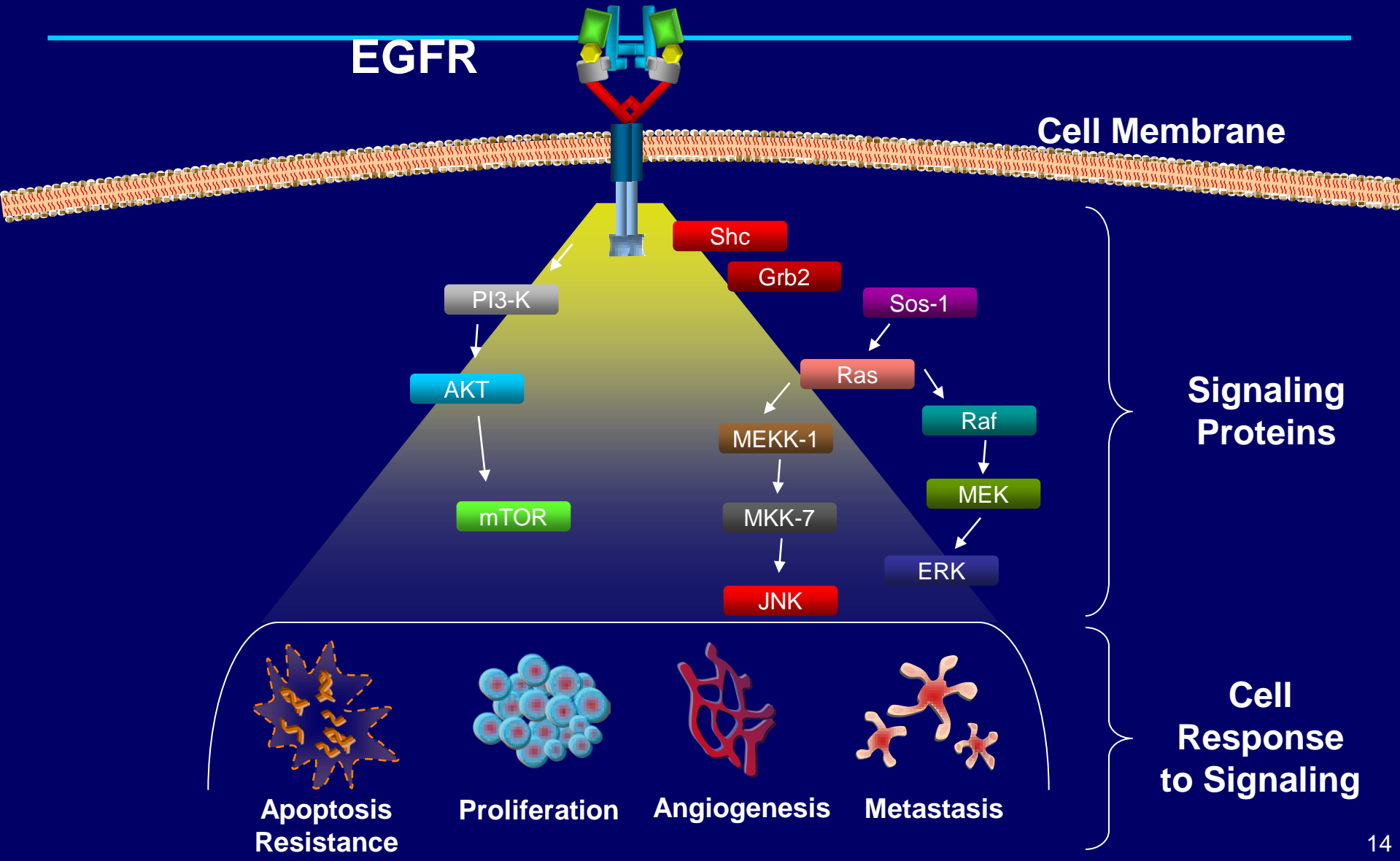
Fuchs et al. ASCO, 2007. Abstract 4027; Hochster et al. ASCO, 2006. Abstract 3510;  
Hurwitz et al. *N Engl J Med.* 2004;350:2335; Saltz et al. *J Clin Oncol.* 2008;26:2013.



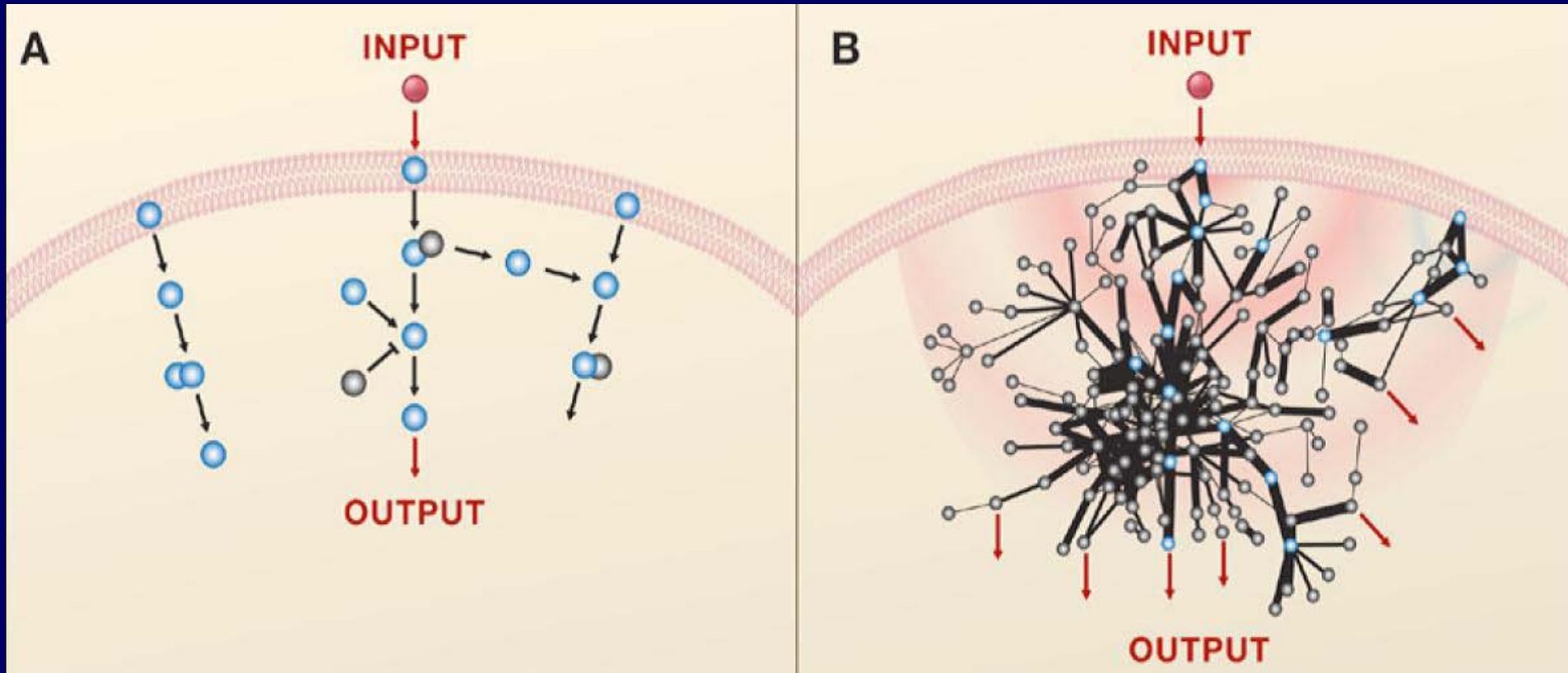
# EGFR: One of Many Signaling Modules in Cancer Cells



# What is the Role of the Epidermal Growth Factor Receptor (EGFR) in Cancer?



# Pathway vs. Network signaling

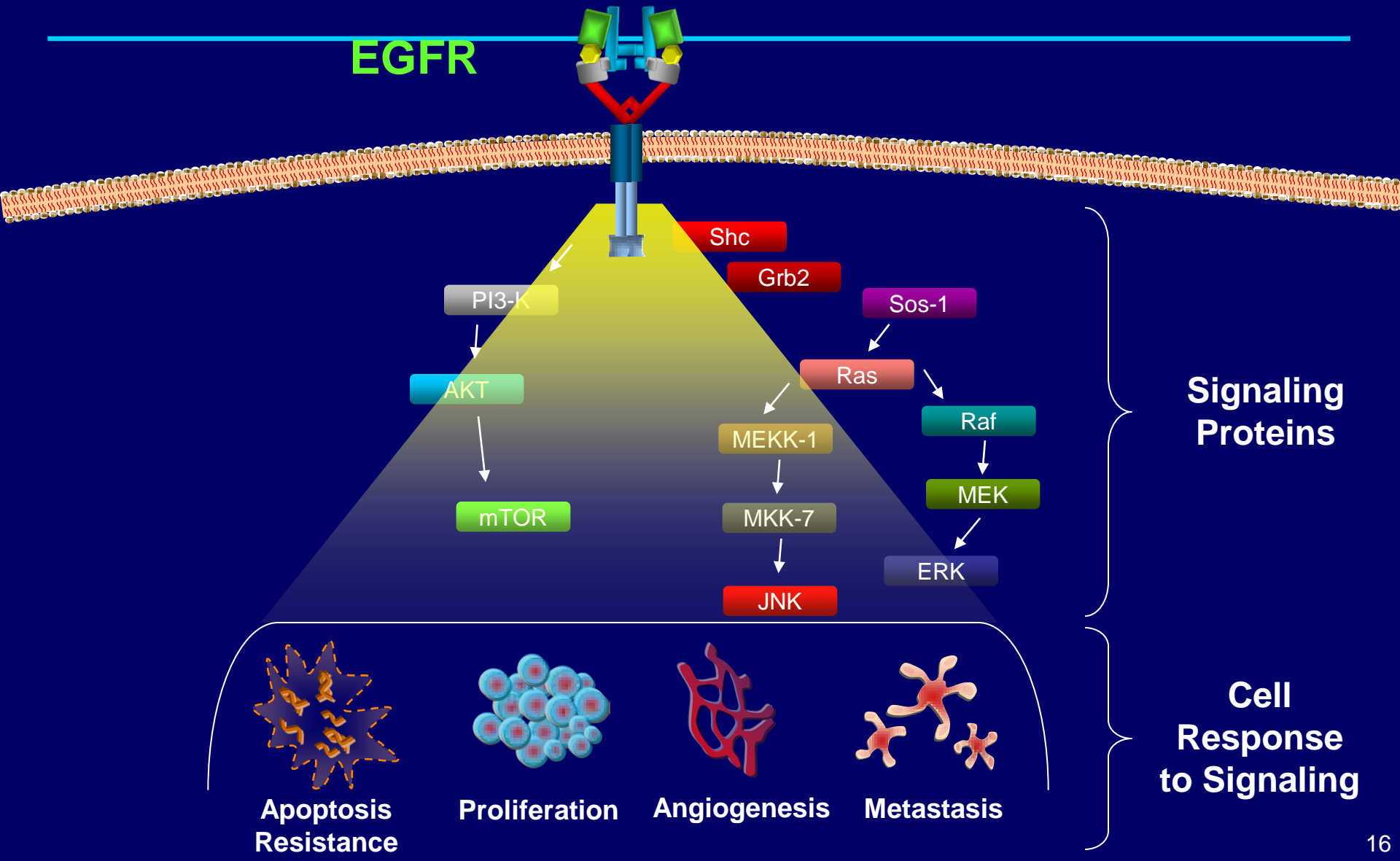


**Pathway**

**“Newtonian”**

**Network**

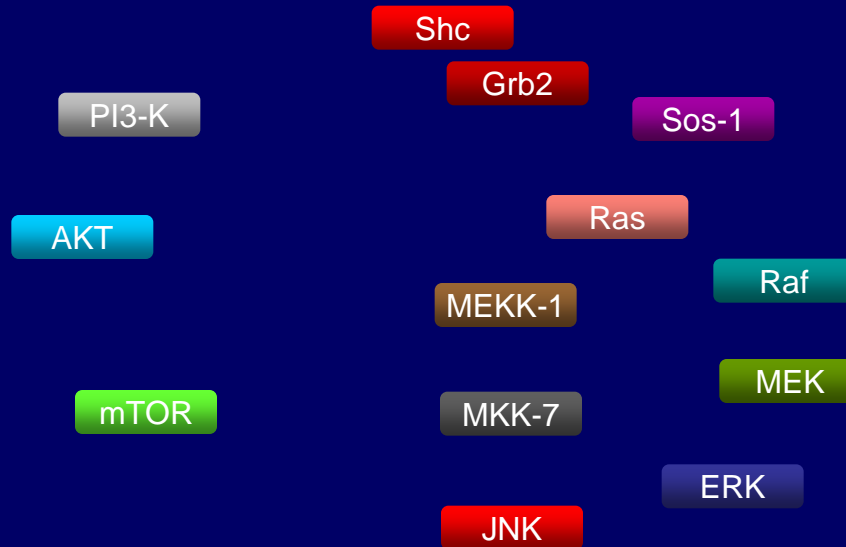
**“Chaotic”**

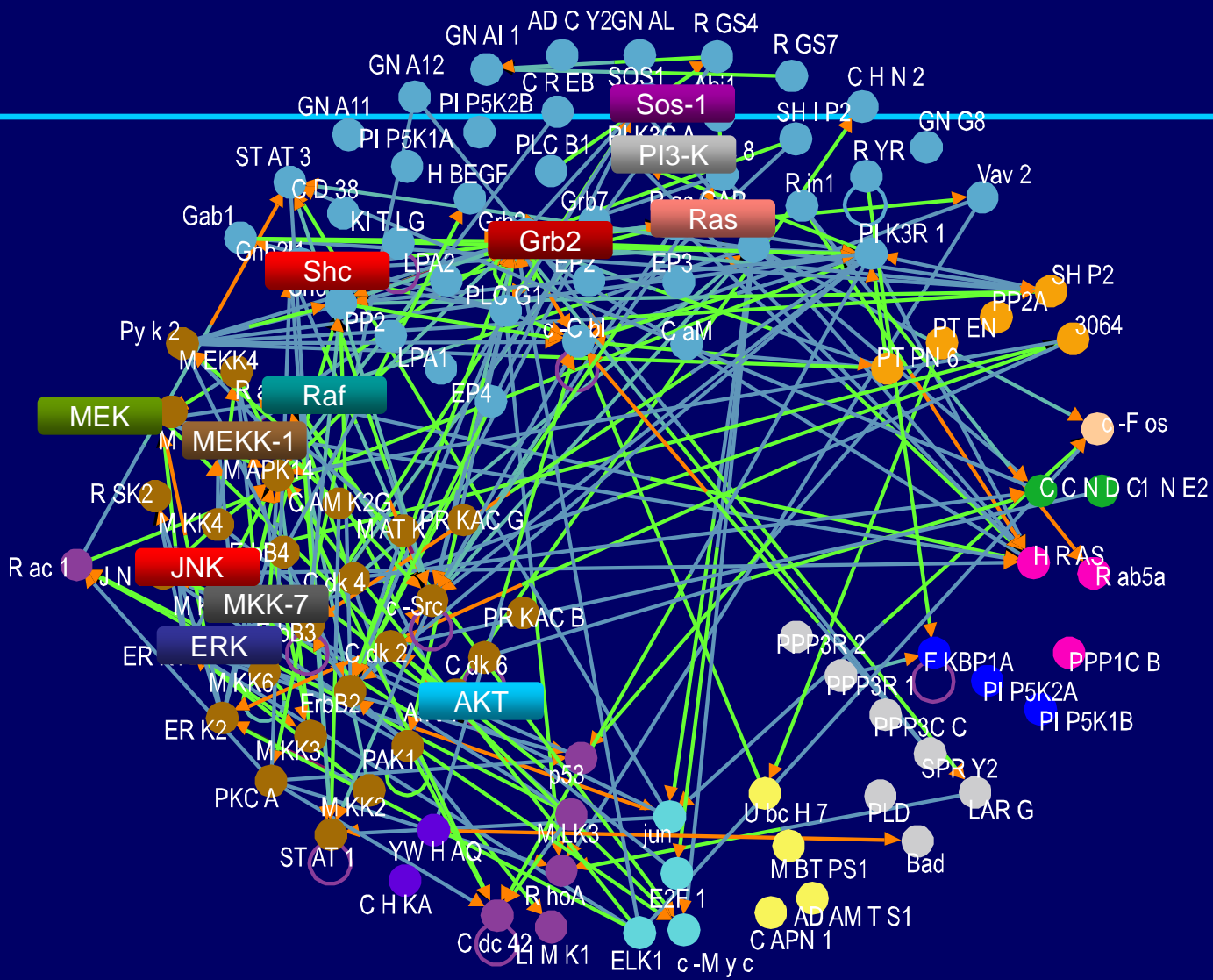




# Which Target?

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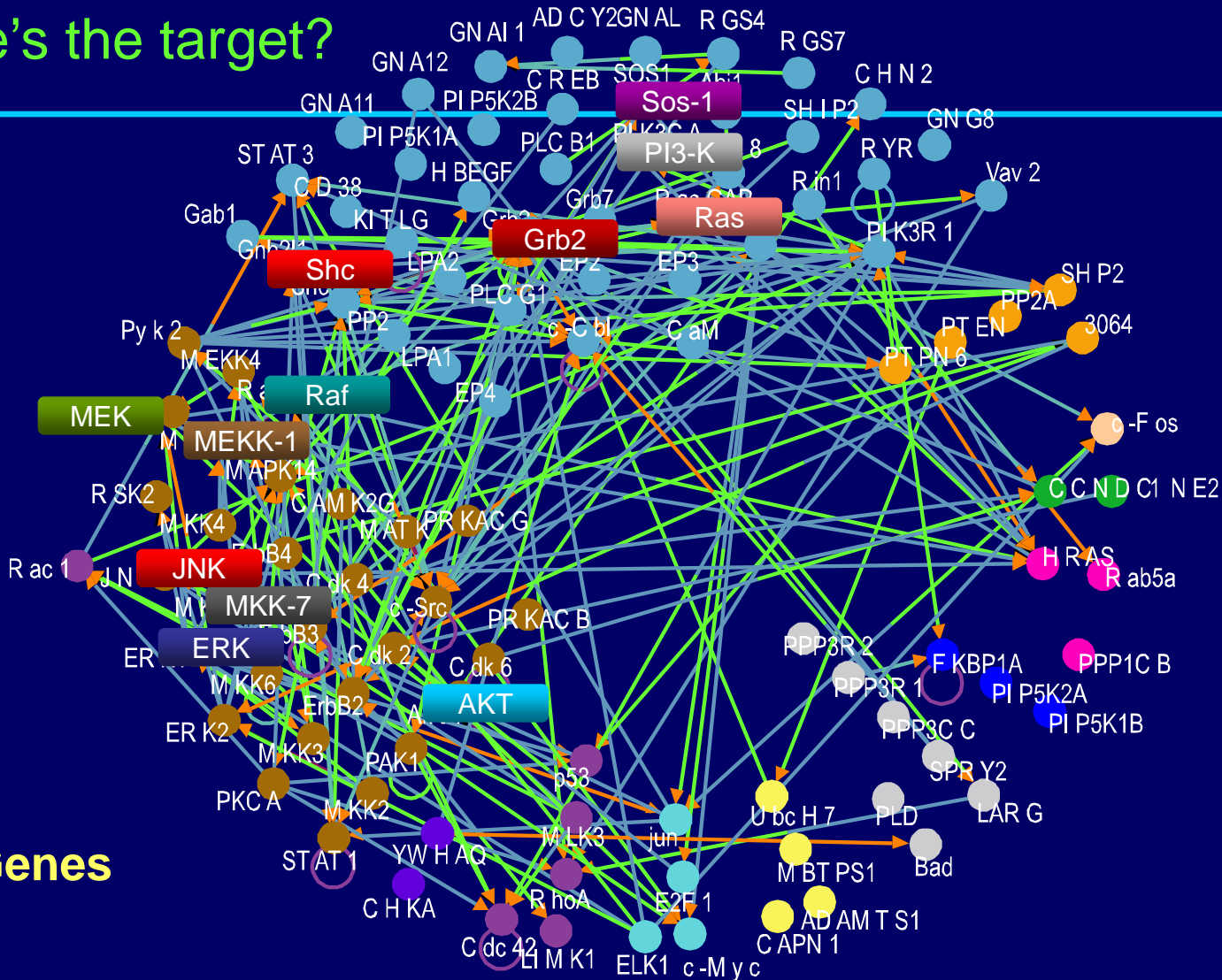




Courtesy of I. Serebriiskii and E. Golemis, Fox Chase Cancer Center

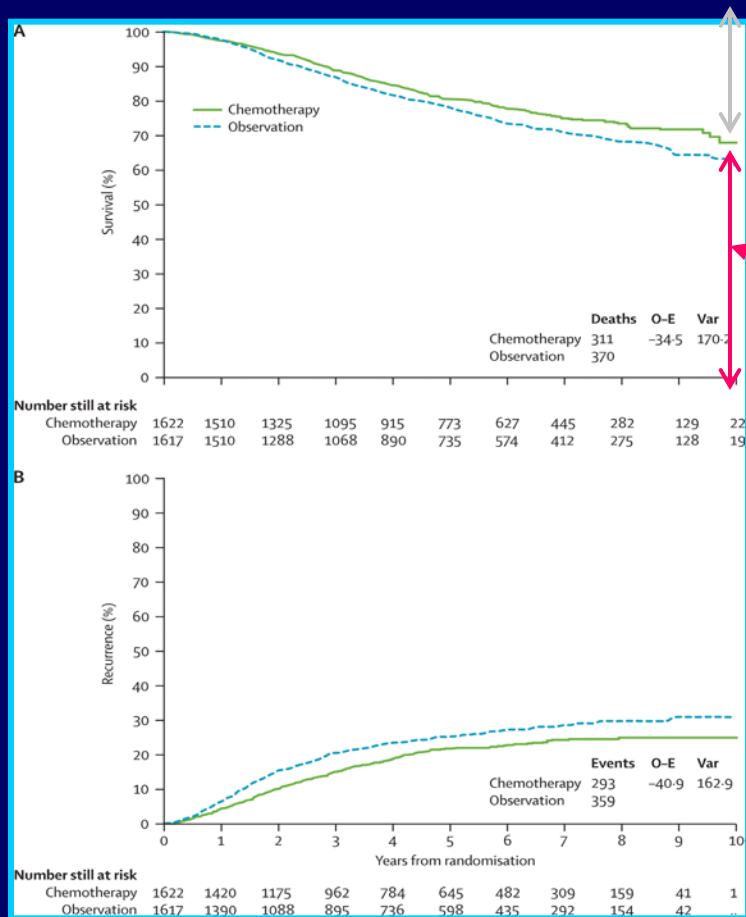
# The EGF Receptor Interactome

Where's the target?



Courtesy of I. Serebriiskii and E. Golemis, Fox Chase Cancer Center

# Adjuvant therapy for colon cancer fails 95% of the time in stage II colon cancer



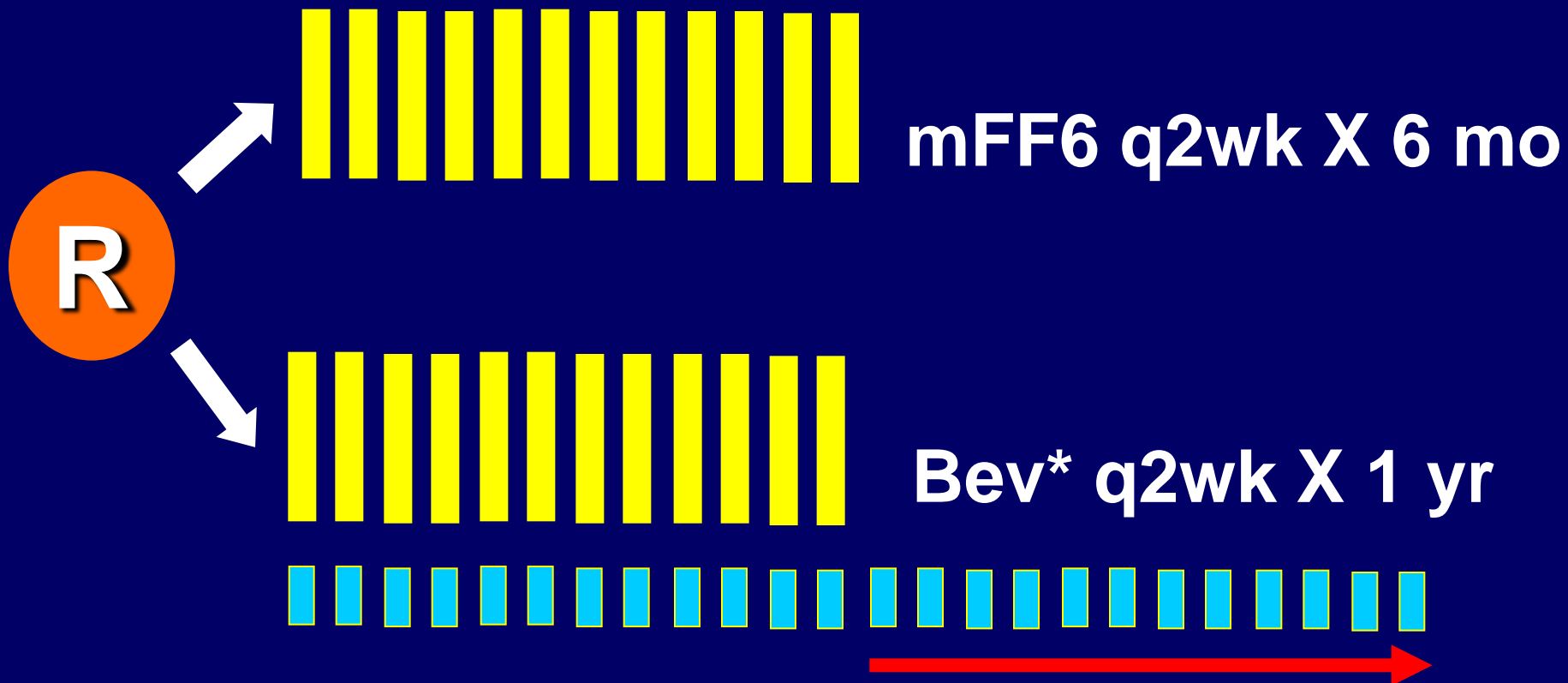
We are under-treating

We are over-treating

Quasar Lancet. 2000 May 6;355(9215):1588-96



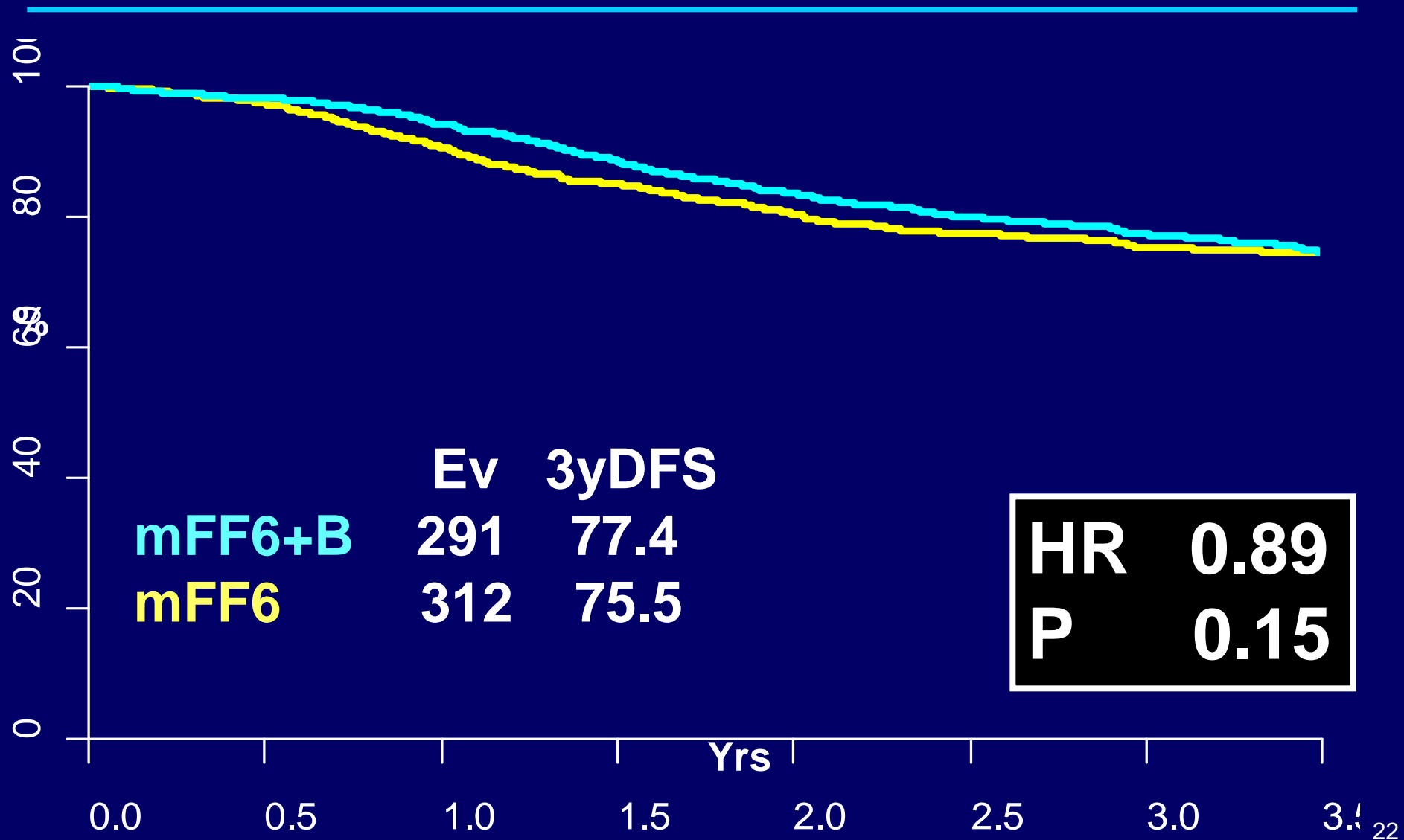
# NSABP C-08



**\*5mg/K**

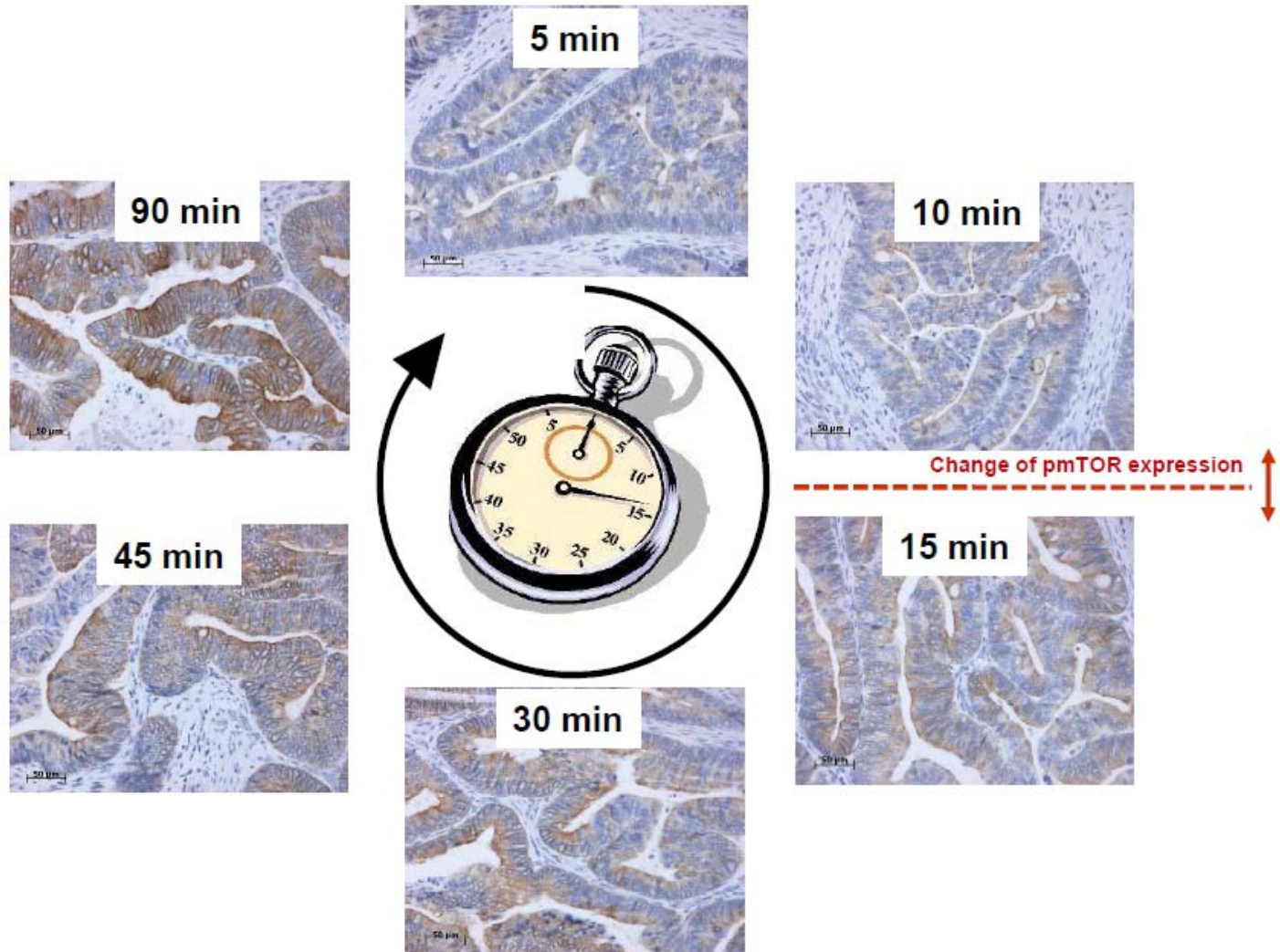
# NSABP C-08

## Disease Free Survival



# Critical: Postsurgical ischemia

## pmTOR-immunostaining (Ventana)



# Inconvenient Truths...

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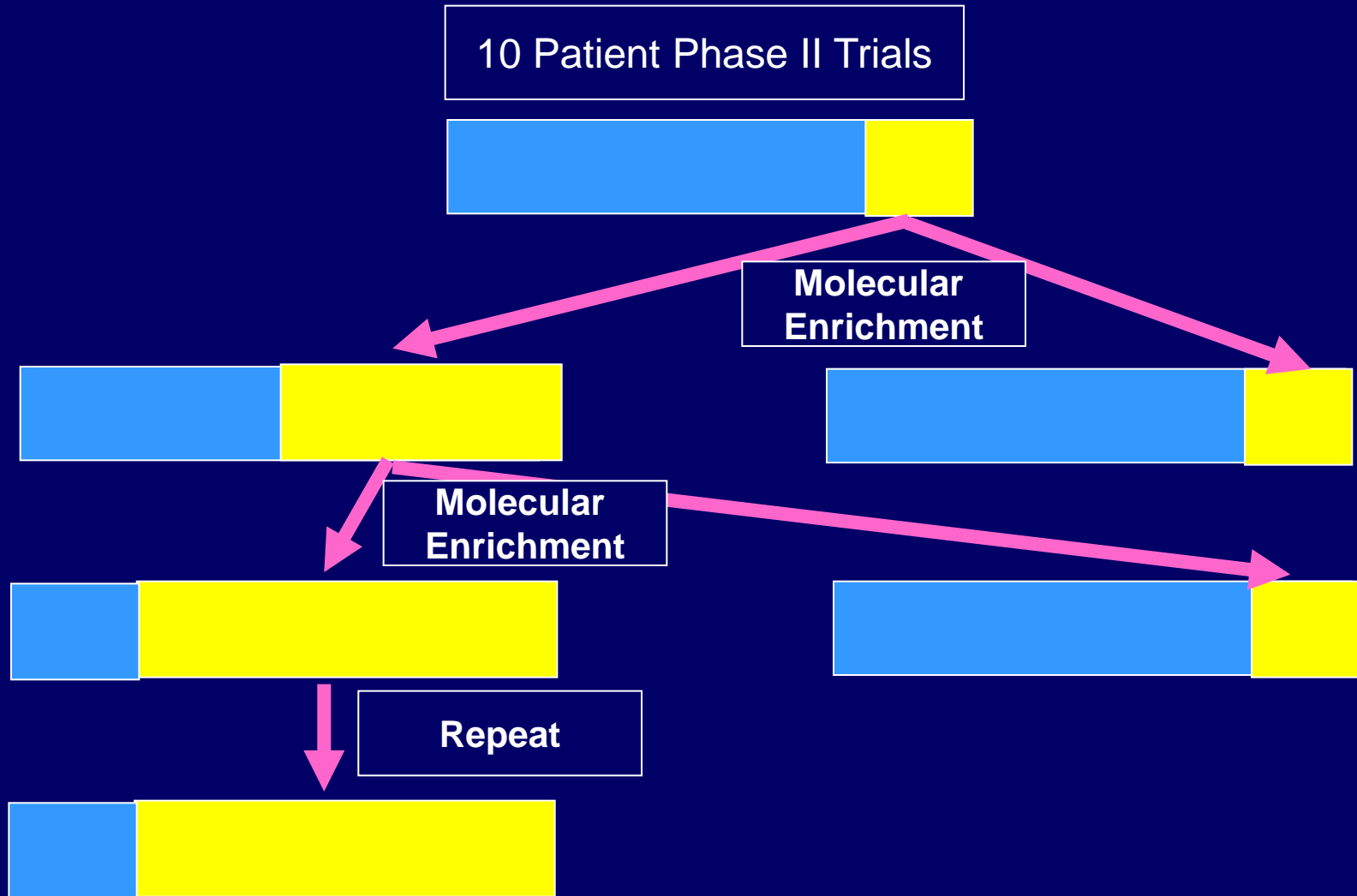
- Adjuvant therapy fails most of the time.
  - Only a small percentage are cured with treatment
- Phase III trials are designed to detect small differences
  - When PFS became acceptable, we decided we were not going to cure cancer
- Clinical trial accrual in the US is at an all time low.
  - We now “off shore” this to the lowest bidder, most in need?
- Cancer treatment adds relatively little to survival
  - If you had to pay for it, would you?
- Cancer as a chronic disease is not the same as other chronic diseases
- The cost of colon cancer therapy now exceeds the cost of dialysis
- Many Pipeline drugs- not enough money, not enough patients?

# We are in a time of change

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- We now acknowledge the errors of the past
- We have better technology to support the war
  - A new kind of war
- We know that success will require work, collaboration and sacrifice
- The rewards are unimaginable
- Are our hearts in this? Do we have the stomach for it?

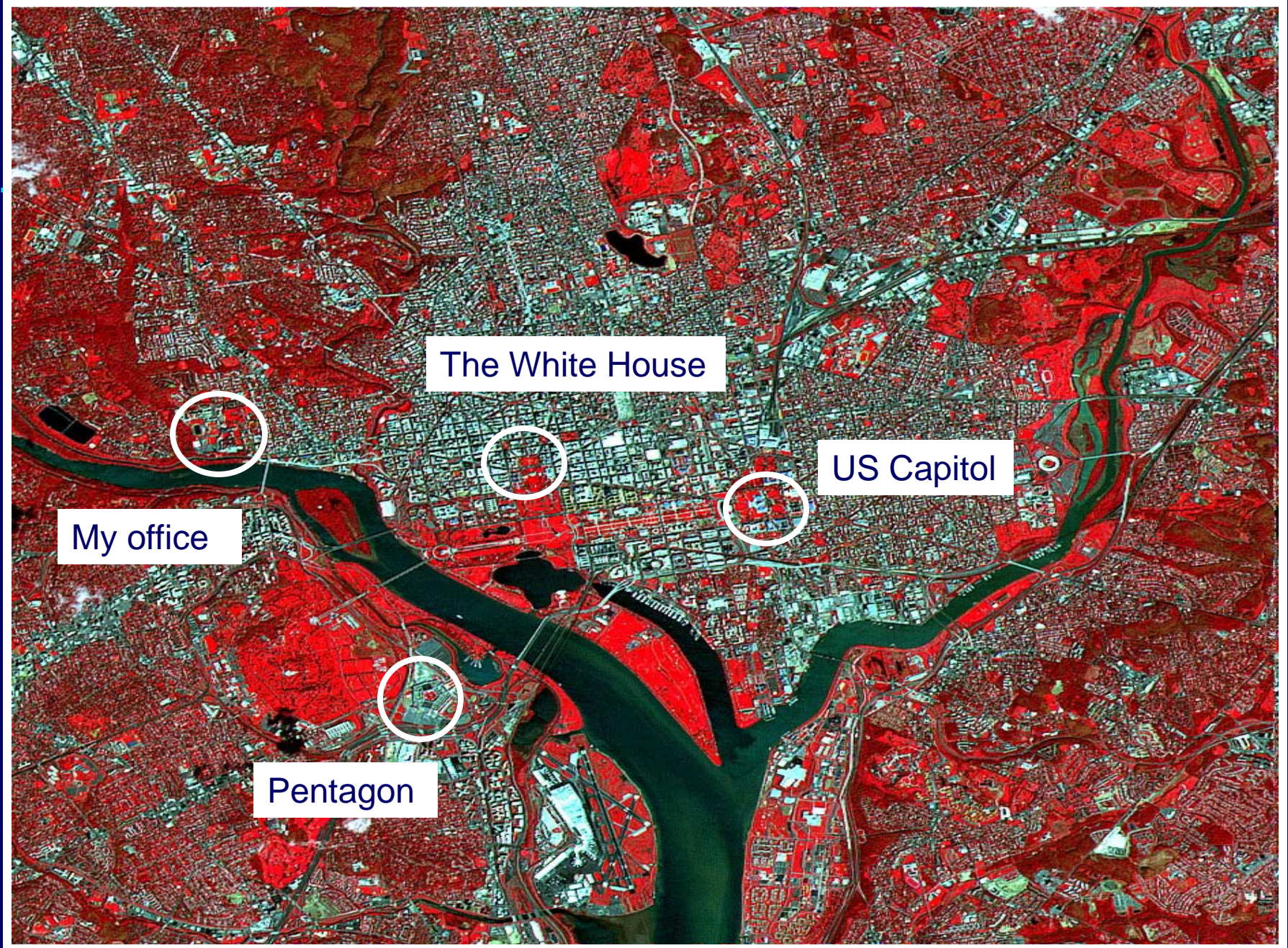
# A Proposal for New Drug Development in Cancer





<b>Where we are</b>	<b>Where we need to be</b>
Safety and Efficacy	Value
Cancers are the same	Cancers are different
Defining cancers by site of origin	Defining cancers by molecular profile
Phase III trials with PFS as endpoint	Phase II trials with response rate as endpoint
Only watching the tumor	Watching the tumor and the host response





The White House

US Capitol

My office

Pentagon





SIPRESS

*“My approach is nontraditional, but from a uniquely Western perspective.”*