



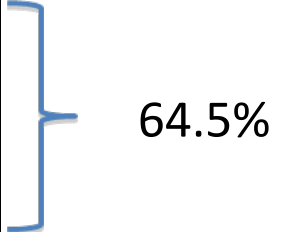
Rectal cancer – Advances in Treatment

Kenneth H. Yu

Division of Hematology/Oncology, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA

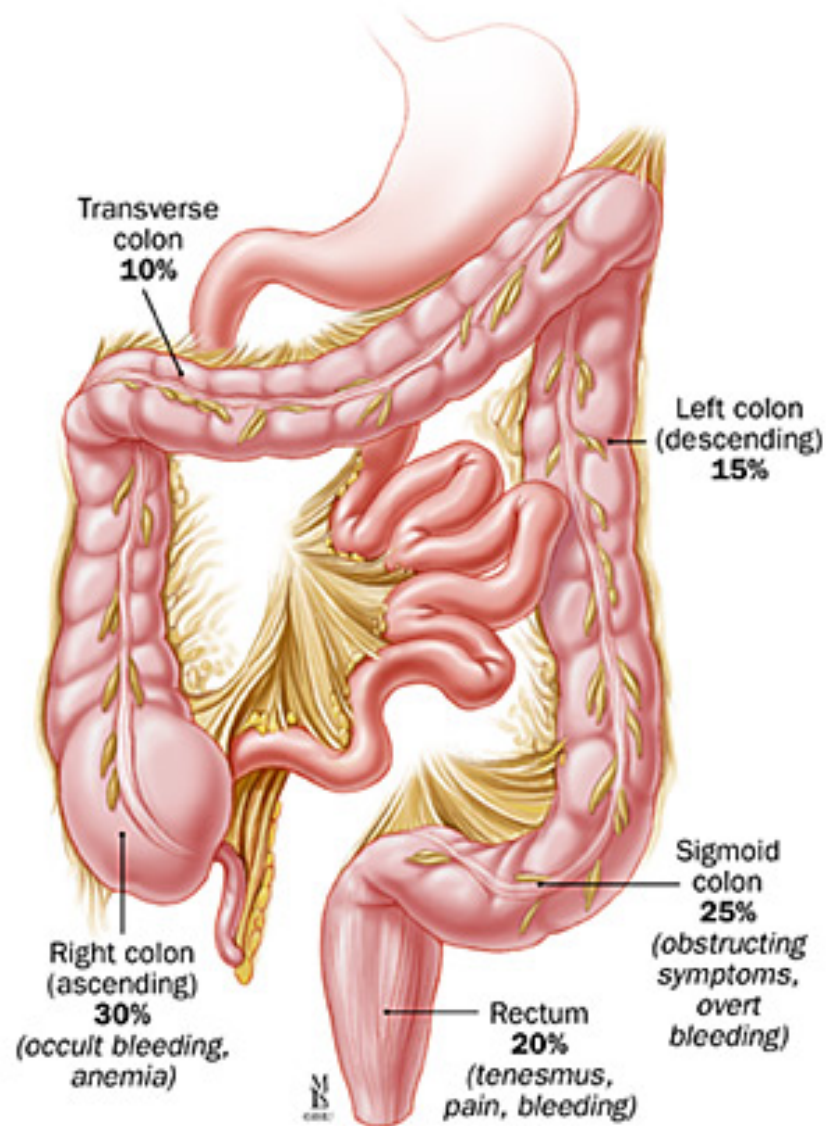
CRC Incidence by Age

	2002-2006
Median age	71
<20	0.1%
20-34	1.1%
35-44	3.8%
45-54	12.0%
55-64	18.7%
65-74	24.7%
75-84	27.7%
85+	12.1%



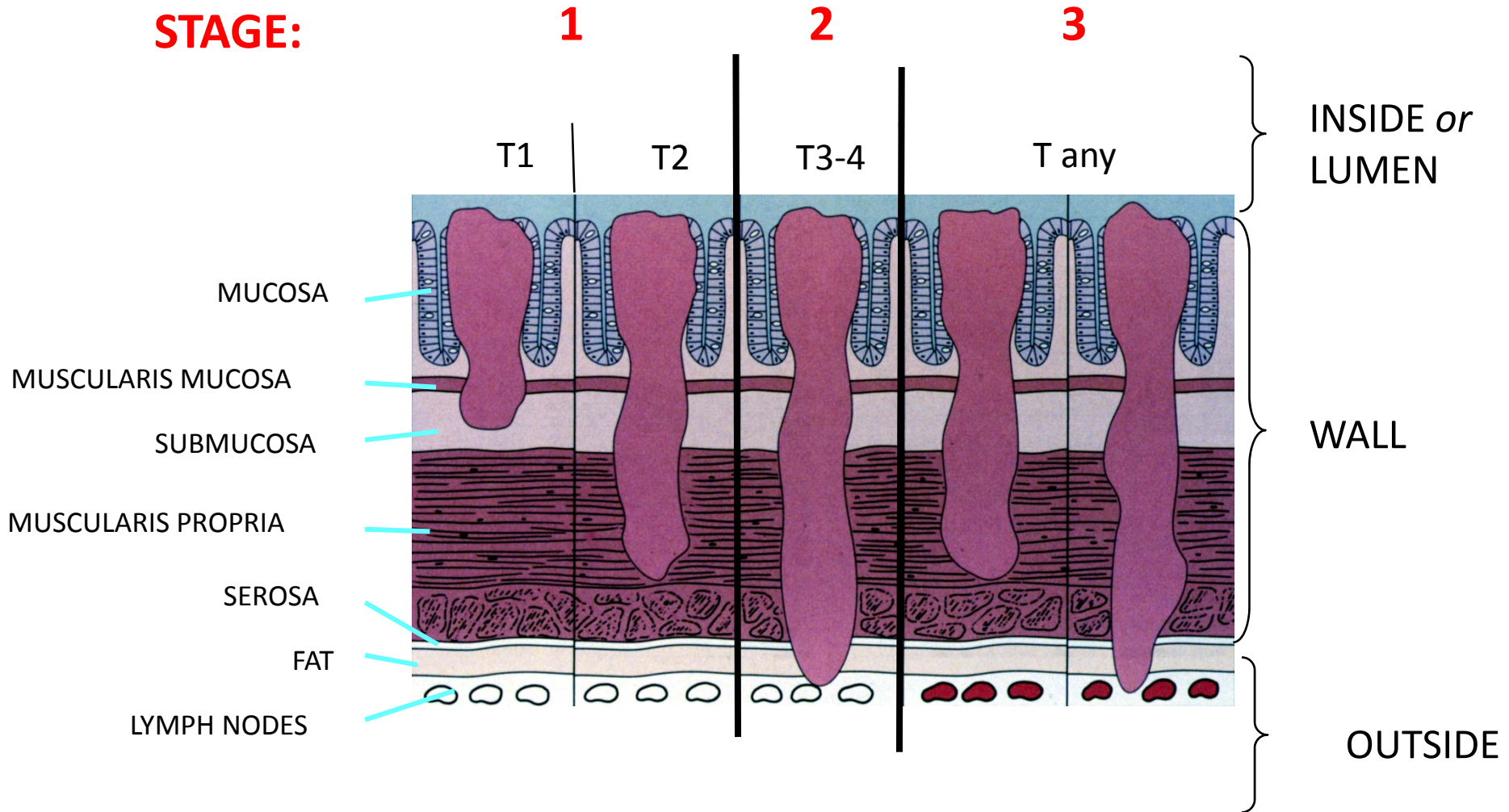
64.5%

Distribution of Cancers



Staging of Colorectal Cancer

STAGE:



Stage at Diagnosis

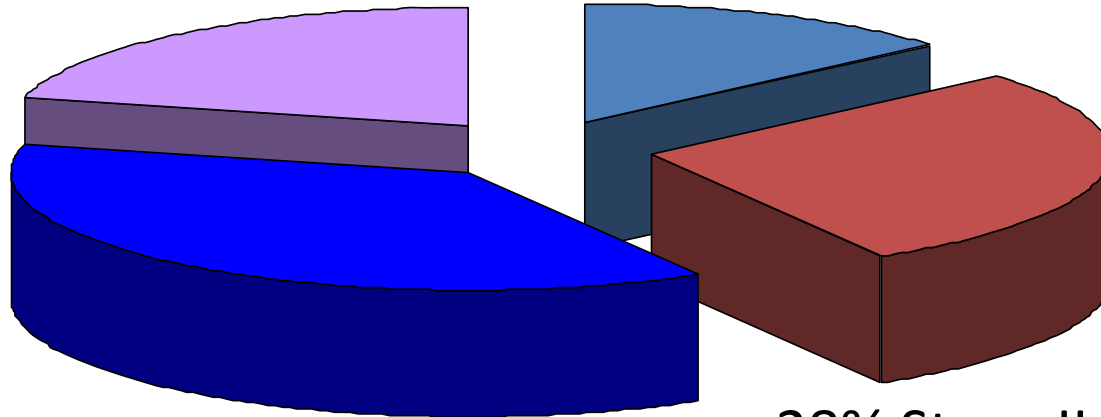
2009 new cases:

colon cancer: 106,100

rectal cancer: 40,870

21% Stage IV

14% Stage I



28% Stage II

37% Stage III

Rectal Cancer Treatment

Stage IV

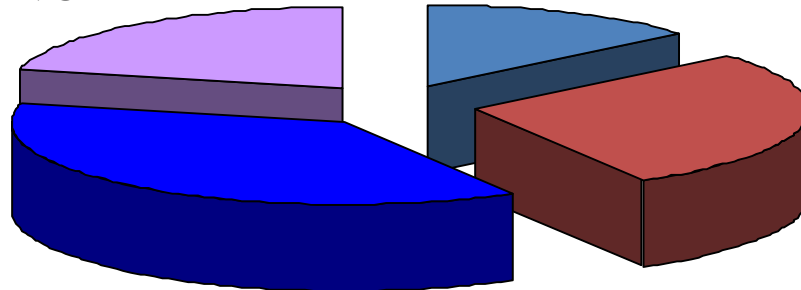
Chemotherapy +/-
Surgery +/- XRT

Stage I

Surgery → observe

Stage IV
21%

Stage I
14%



Stage II
28%

Stage III
37%

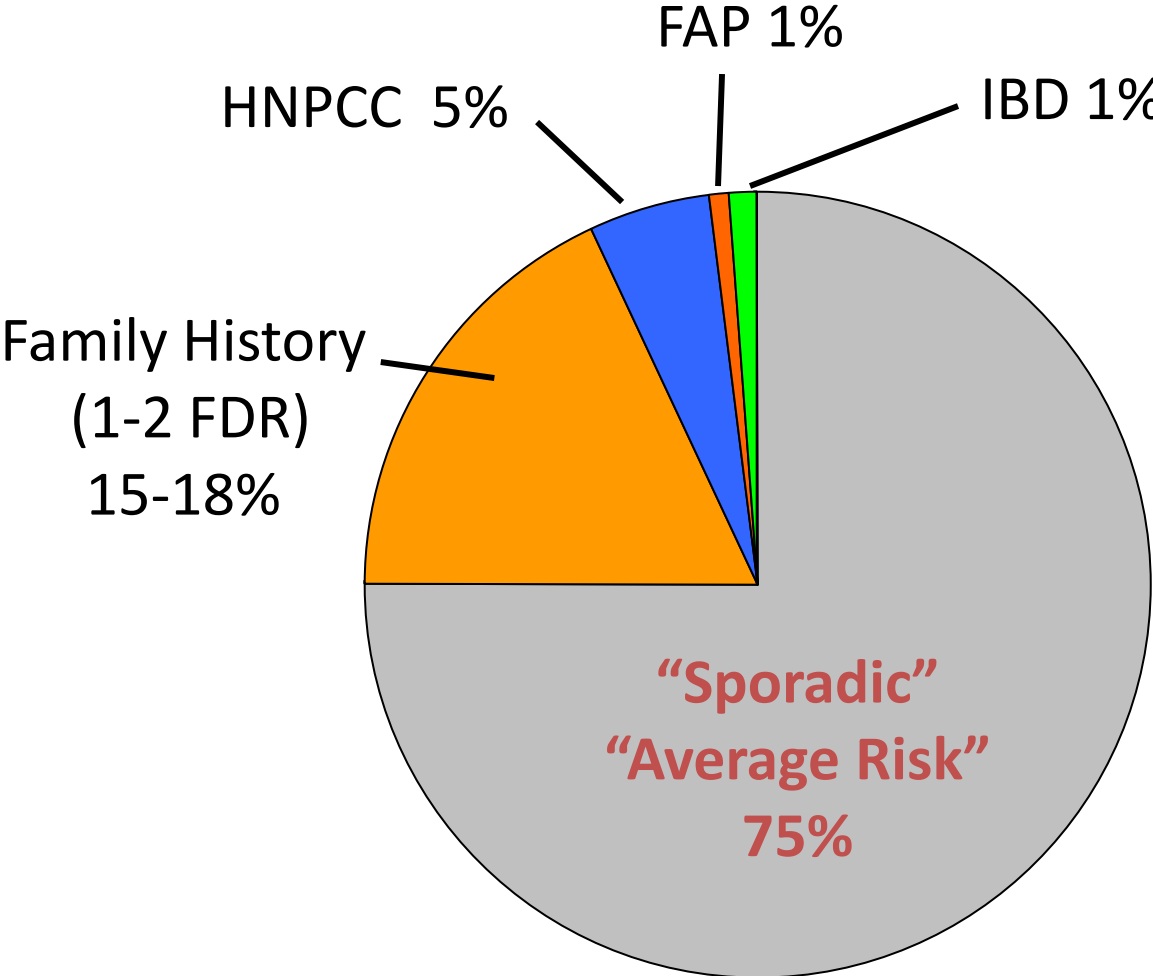
Stage III

Surgery, XRT, Chemotherapy

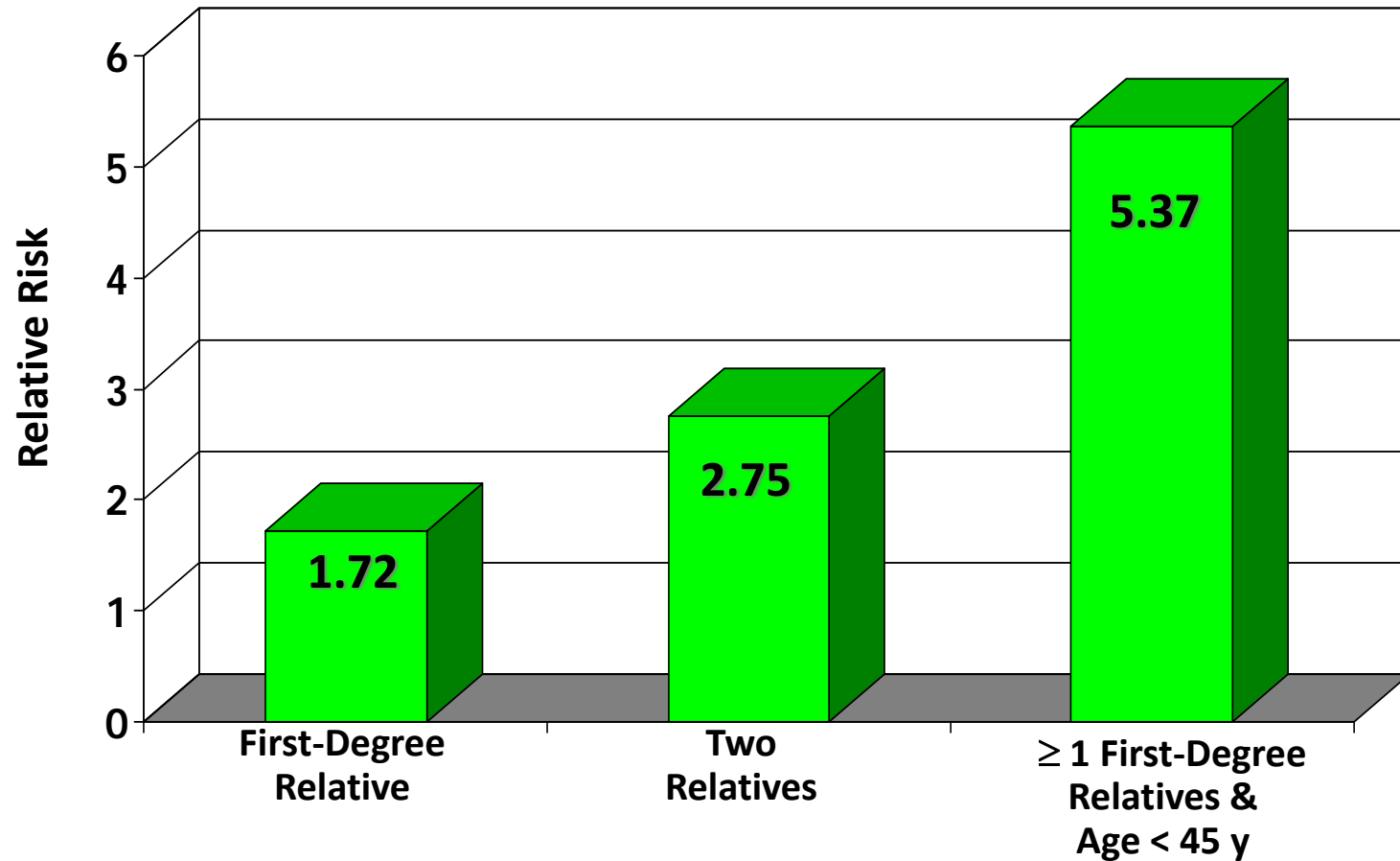
Stage II

Surgery, XRT, Chemotherapy

Factors Associated with New Cases of Colorectal Cancer



Impact of Family History



Medical Management of Colorectal Cancer

Chemotherapy and Targeted Therapy

Key Therapeutic Agents in CRC: Historical Perspective

~1960: 5-FU

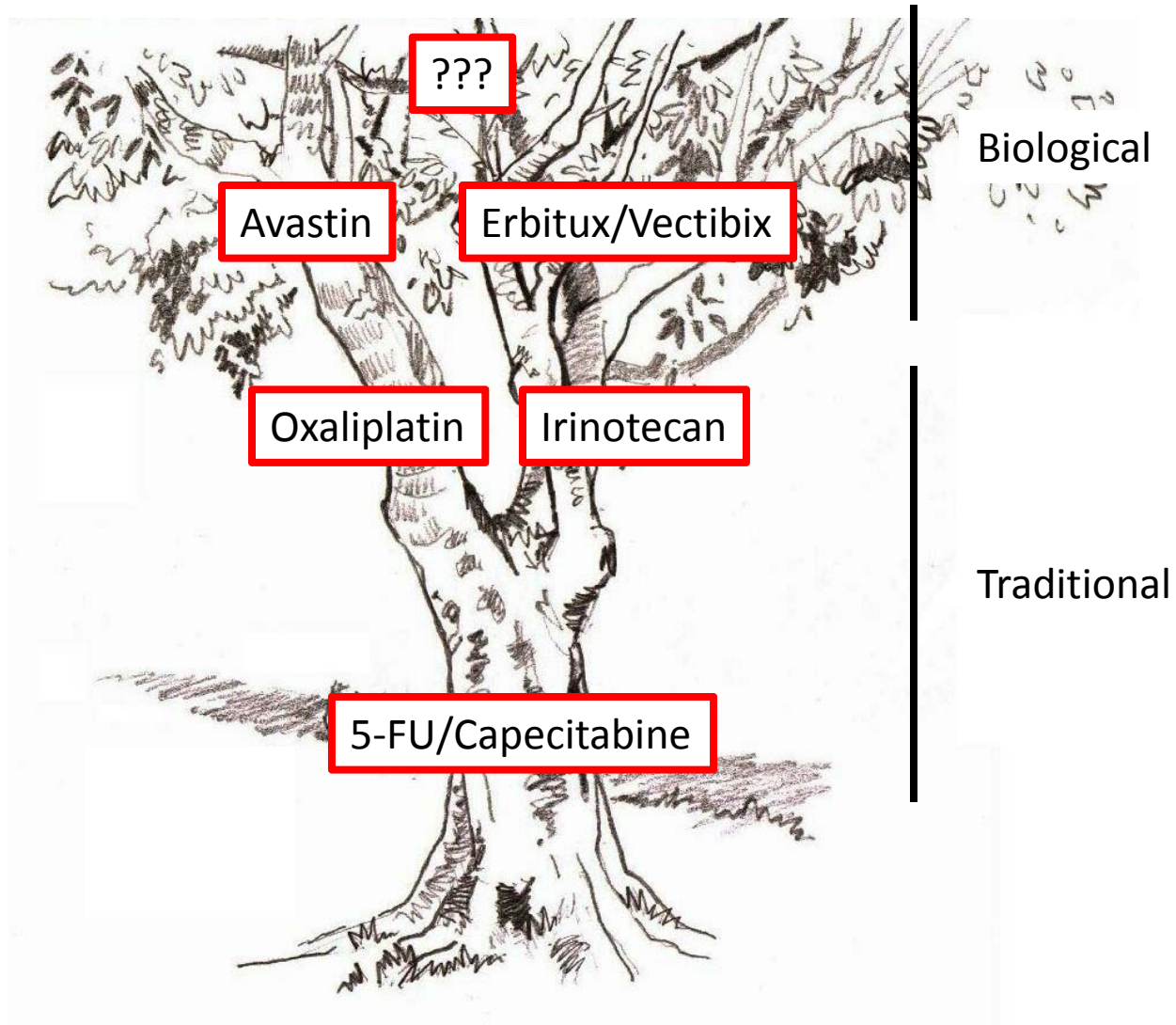


40 YEARS!

1998: IRINOTECAN
2001: CAPECITABINE
2002: OXALIPLATIN
2004: CETUXIMAB
2004: BEVACIZUMAB
2006: PANITUMUMAB

FDA approved

Therapeutic Strategy



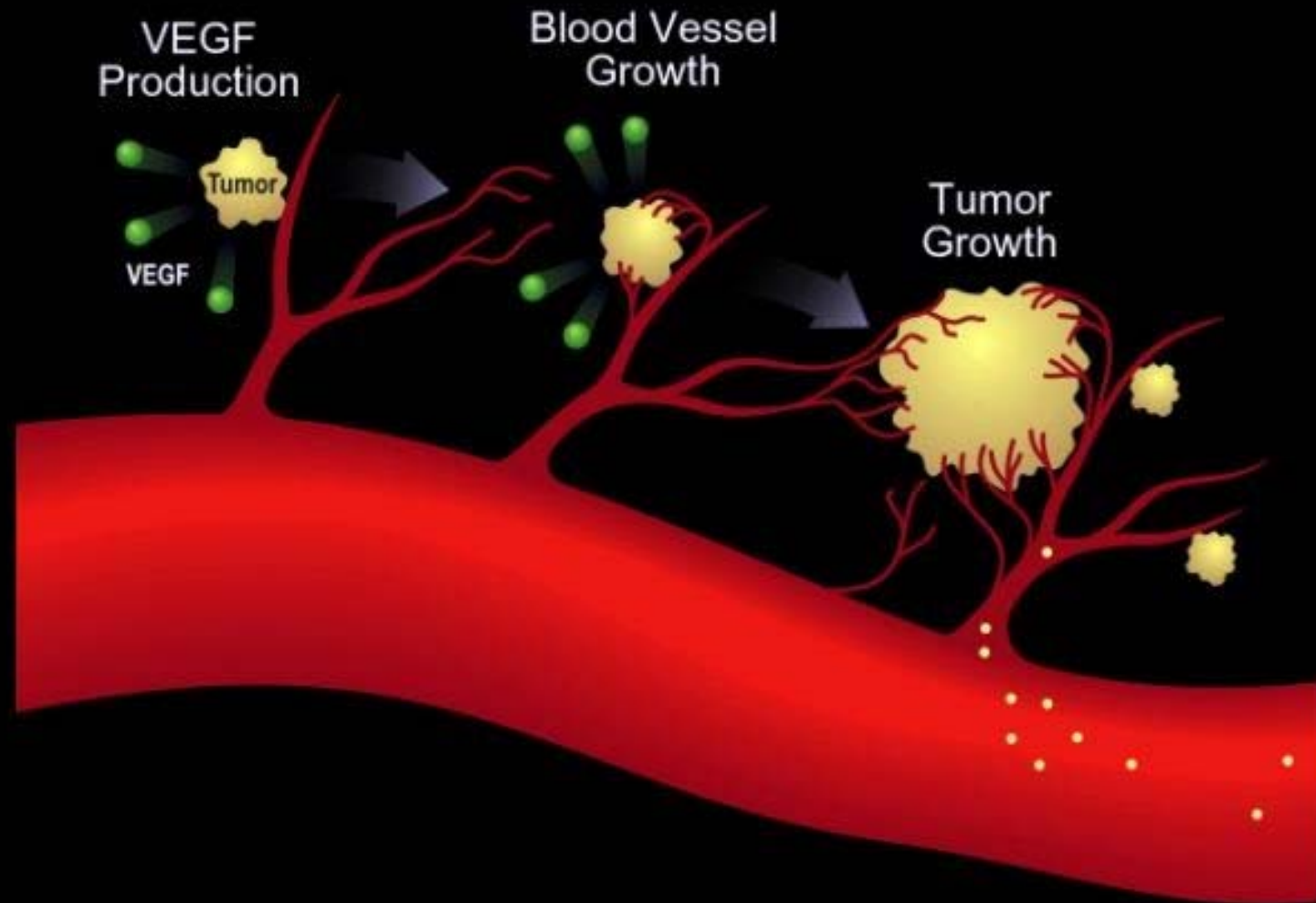
Biological targeting

- Treatments directed against cancer specific targets
- More efficacious
- Less toxic

Vascular Endothelial Growth Factor

- VEGF
 - potent mediator of angiogenesis
 - expressed in 40-60% colorectal tumors
 - associated with recurrence and prognosis
- Preclinical evaluation of anti-VEGF MAb
 - A4.6.1 causes dose-dependent growth inhibition of VEGF expressing human CRC xenografts in mice.

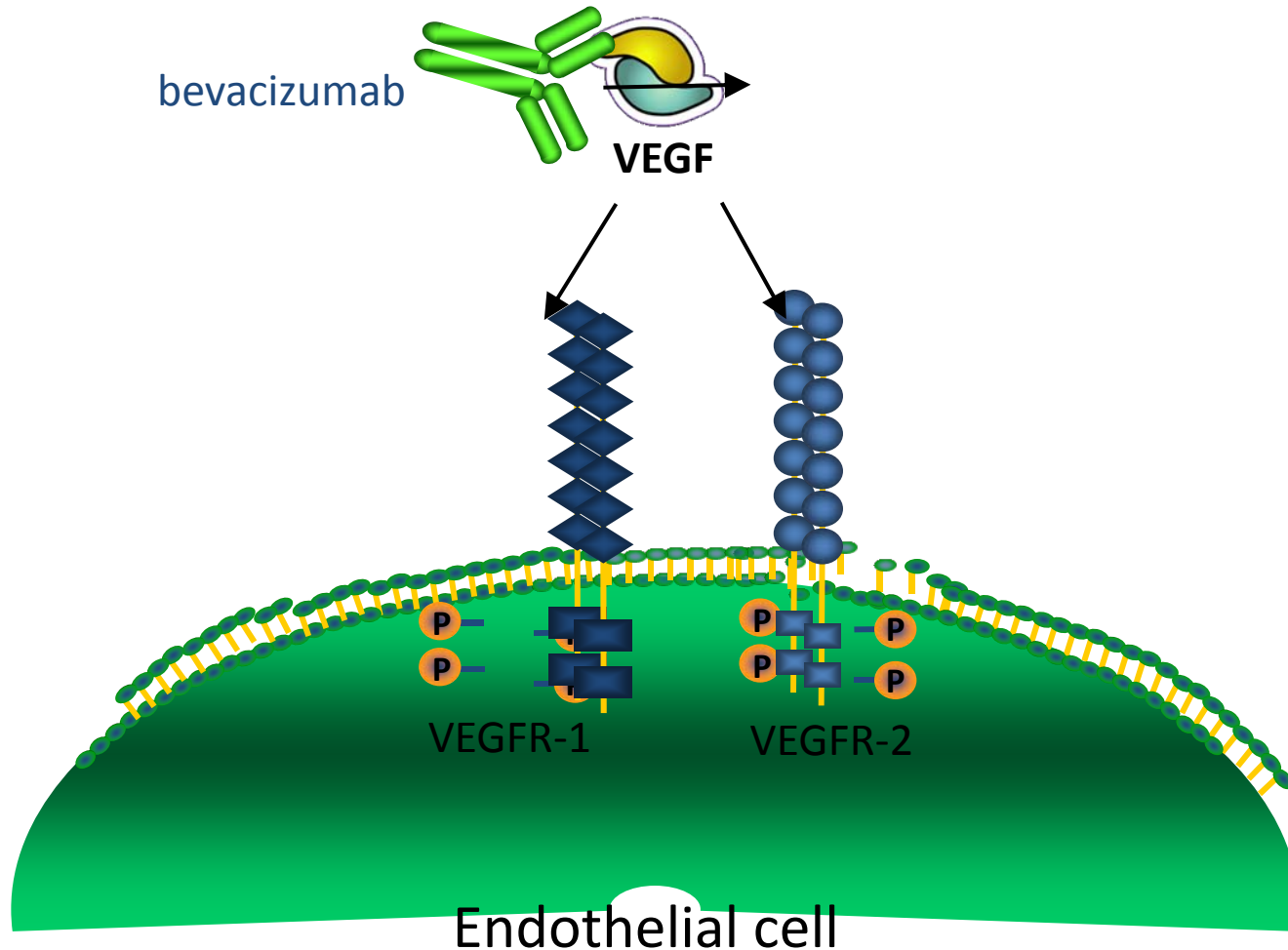
Angiogenesis



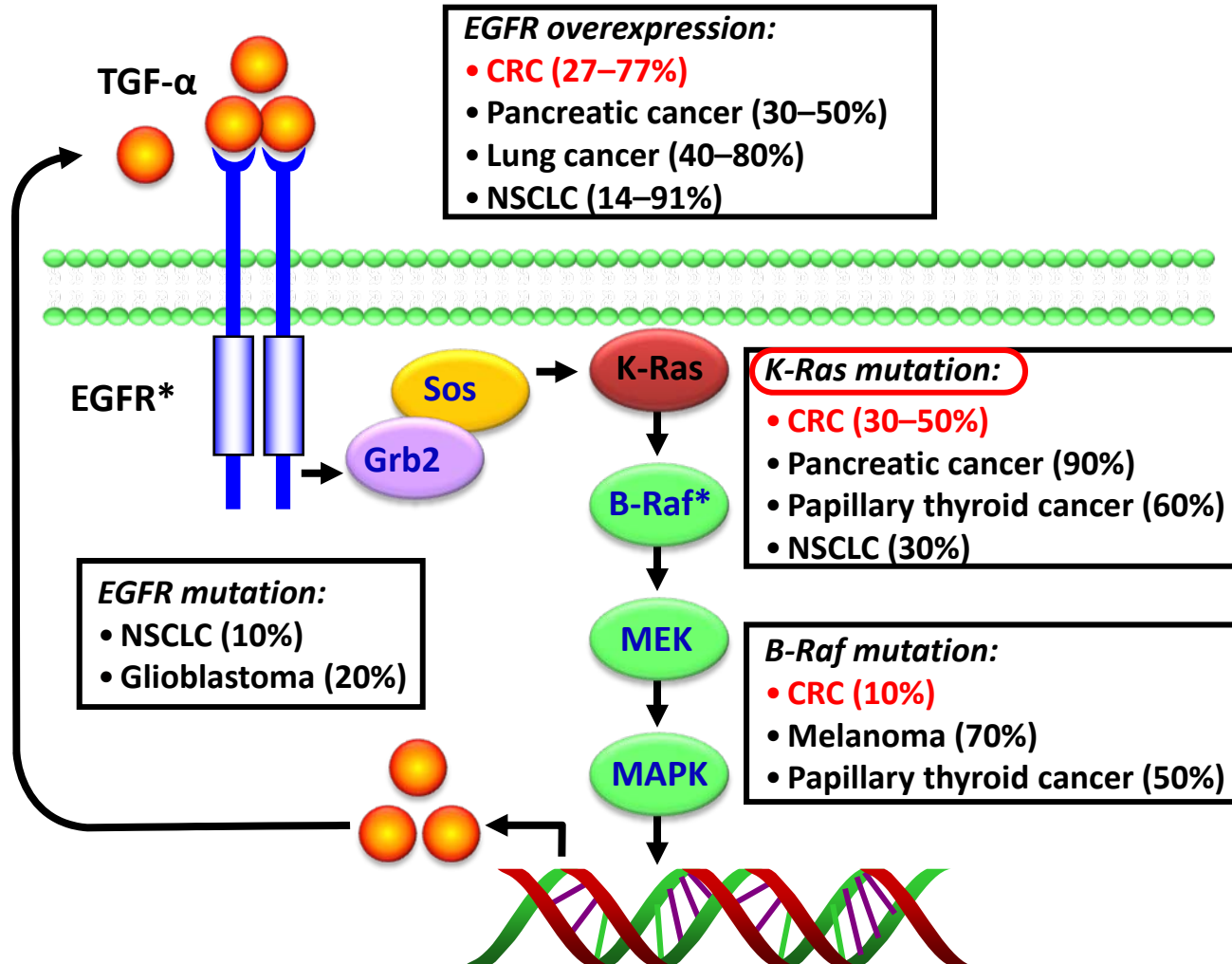
Avastin (Bevacizumab, rhuMAb-VEGF)



Agents Targeting the VEGF Pathway



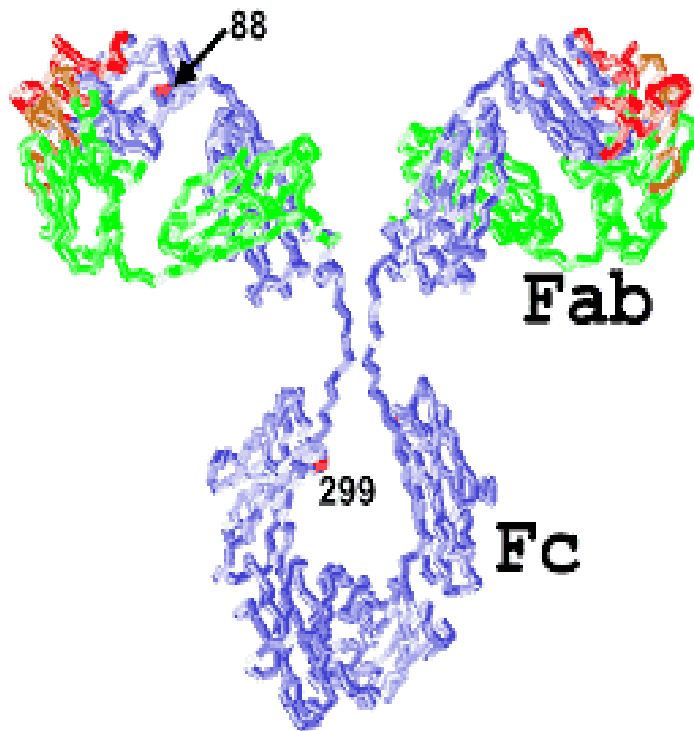
Targeting the EGFR pathway: *K-Ras* mutations



TGF = transforming growth factor

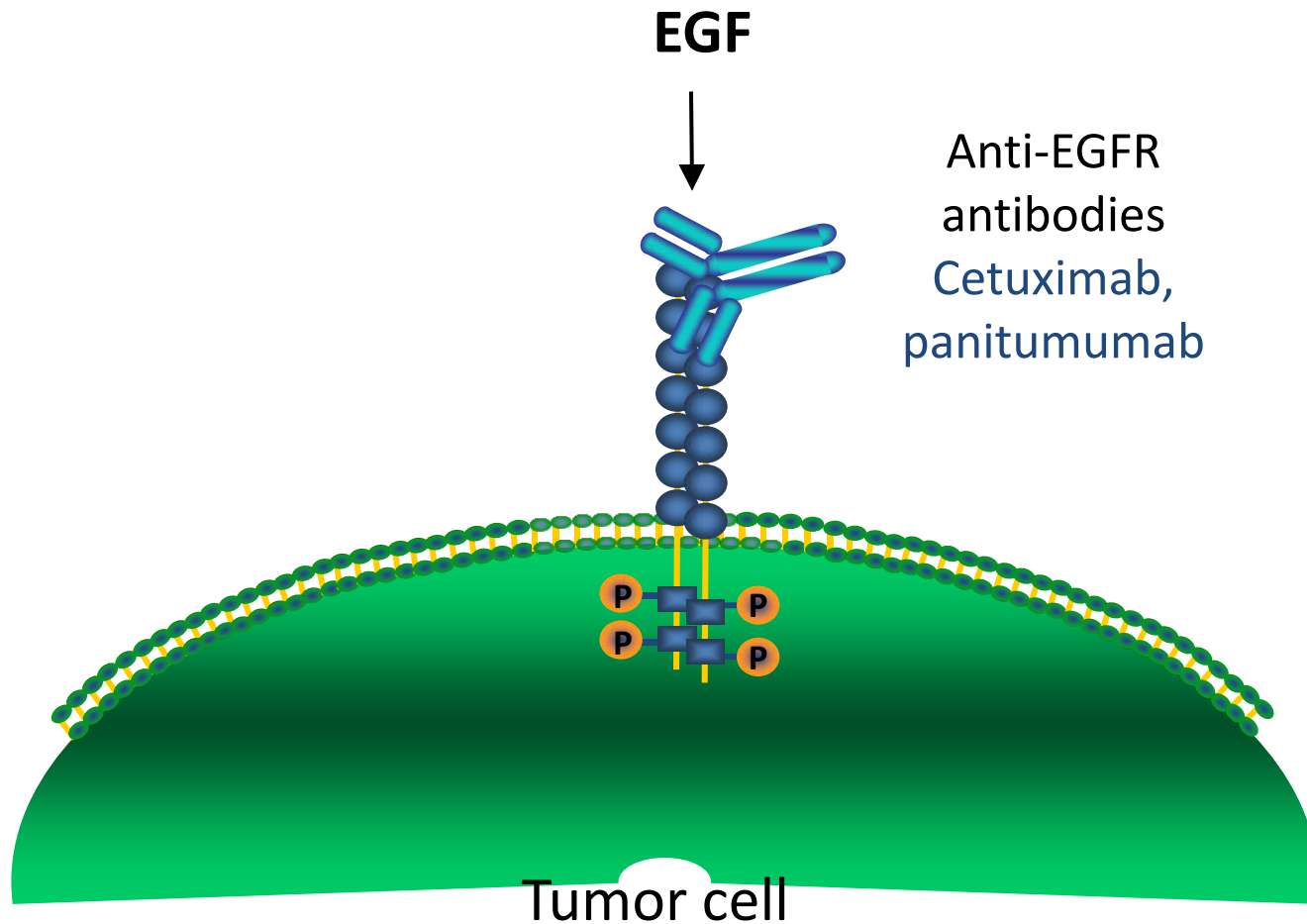
Adapted from Roberts Der. Oncogene 2007

Cetuximab

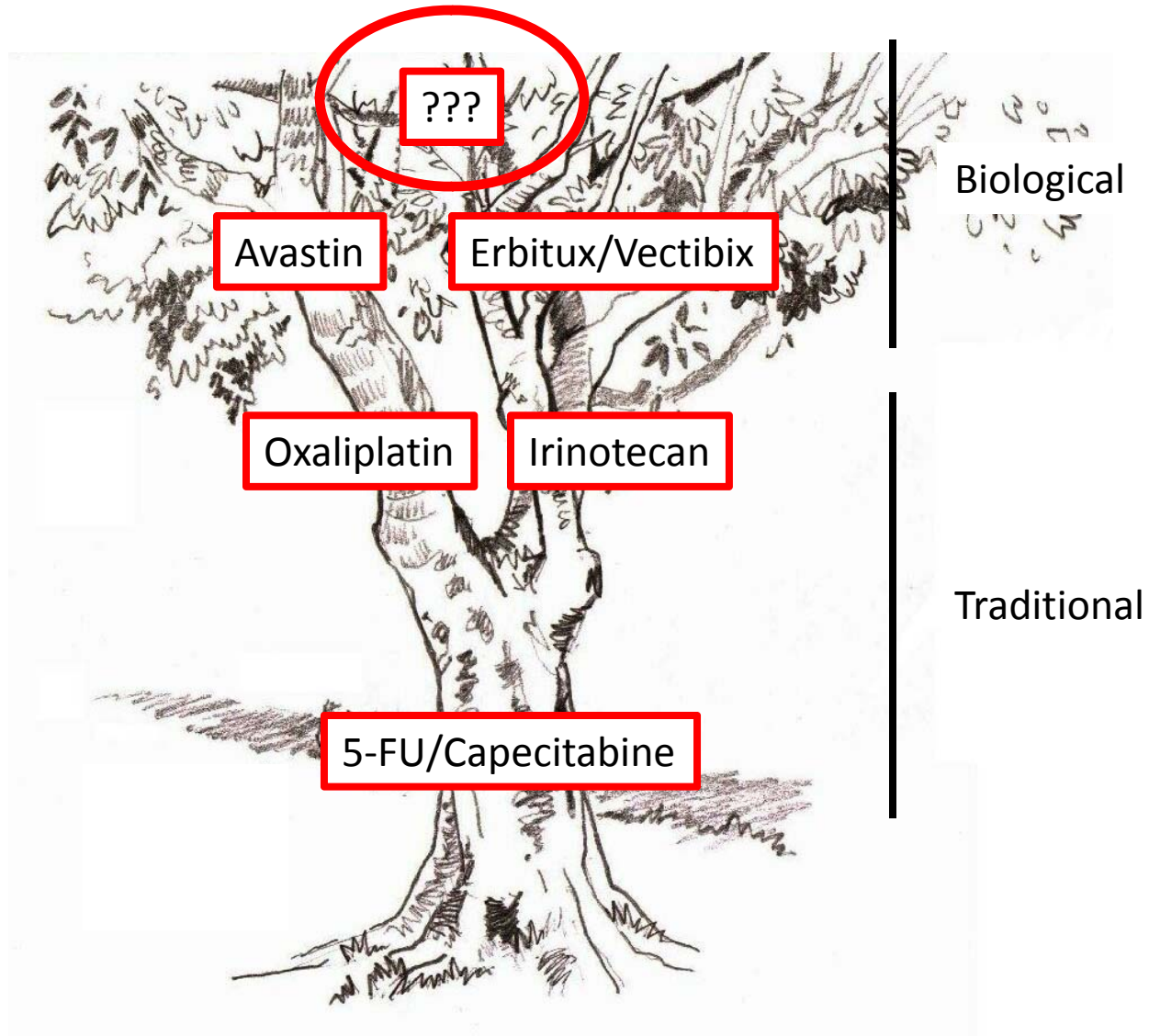


- Chimeric monoclonal antibody
 - EGFR & heterodimers
- Approved 02/2004

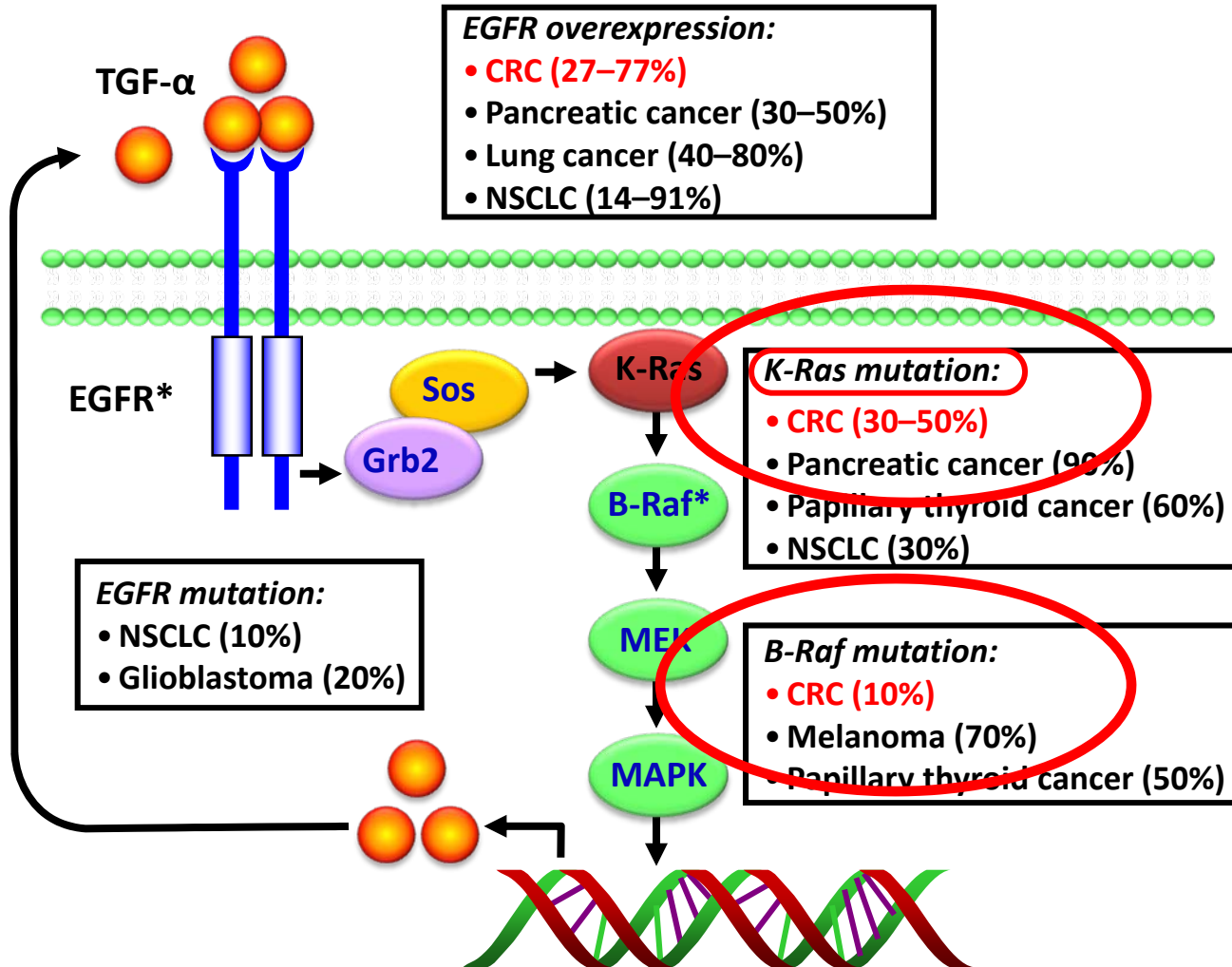
Agents Targeting the Epidermal Growth Factor Pathway



Therapeutic Strategy



???



TGF = transforming growth factor

Adapted from Roberts Der. Oncogene 2007

Targeting B-Raf

- Mutated in 10% of colorectal cancers
- Phase I trial of Sorafenib and Irinotecan
- Most common B-Raf mutation also found in melanoma

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TARGET CANCER

A Roller Coaster Chase for a Cure

By AMY HARMON

Published: February 21, 2010

PHILADELPHIA — His patient, a spunky Italian-American woman in her 60s, was waiting in an exam room down the hall for the answer: Was the experimental drug stopping her deadly [skin cancer](#)?

[Enlarge This Image](#)


But as Dr. Keith Flaherty read out the measurements of her [tumors](#) from the latest [CT scan](#), he could not keep the distress from his voice.

“She’s worse,” he said to the clinical trial nurse at the [University of Pennsylvania’s melanoma clinic](#).

Like the 17 other patients on the drug trial — the corporate lawyer, the receptionist with young children, the Philadelphia philanthropist — the woman known in the trial as Patient 18 was going to die, most likely within

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What does the future hold

