

Systemic Treatments in Locally Advanced Non-small Cell Lung Cancer

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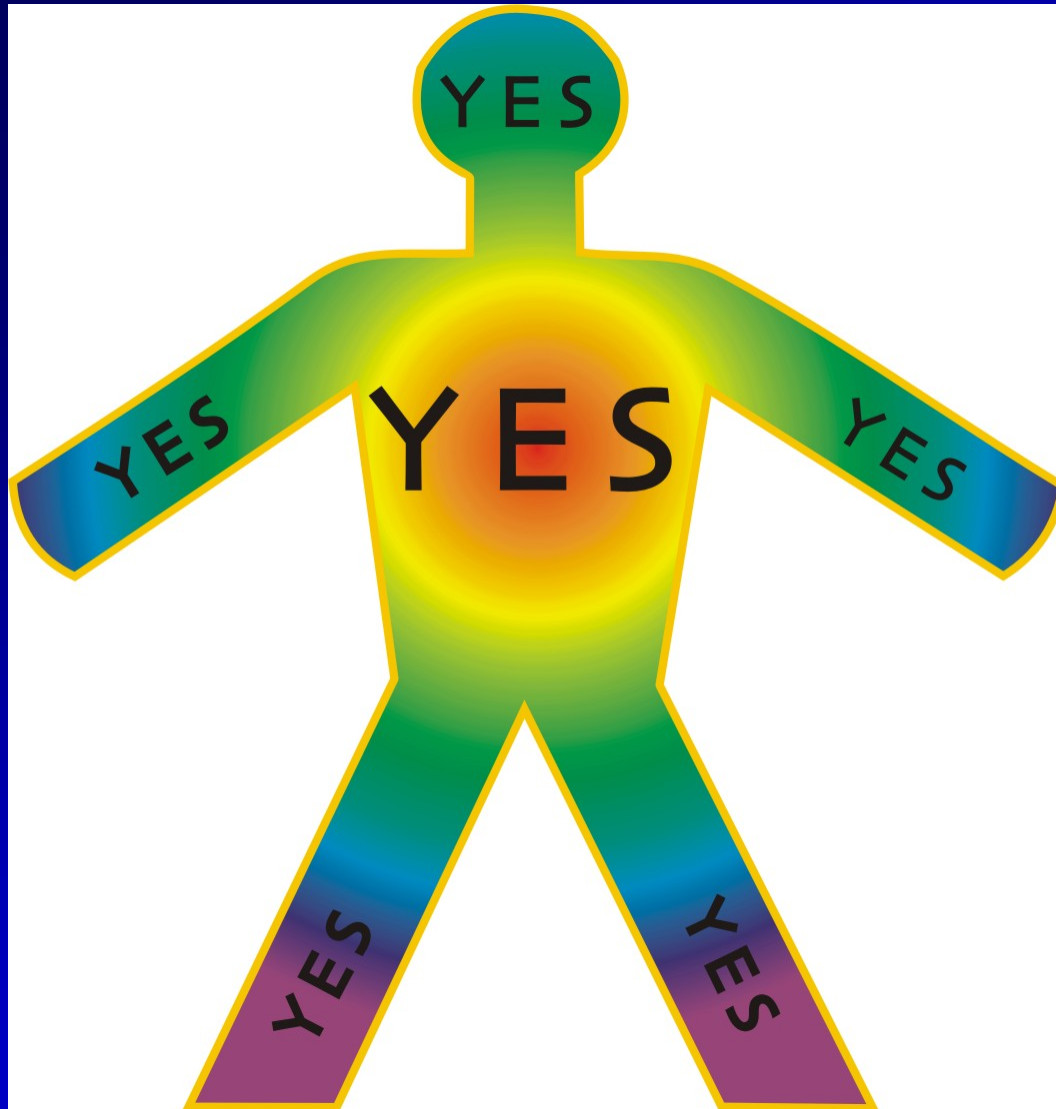


Who are all these different
doctors, and why do we need
them?

What is a Medical Oncologist?

- A physician who has completed an internal medicine residency (a full-fledged internist) who then goes on to complete subspecialty training in medical oncology
- A medical oncologist specializes in the *systemic* effects of cancer (the effects of cancer on the *whole body*) AND in the treatment of cancer with *systemic (whole body)* approaches such as chemotherapy (as opposed to radiation and surgery which are *local* treatments)

Systemic Therapy=Whole Body Treatment



So why do we need the local guys?

- Thus far, local modalities (surgery and radiation) are the only treatments with any potential to *CURE* non-small cell lung cancer
- The goal of treatment in locally advanced disease is cure
- It does not have to be surgery!
(Inoperable ≠ incurable)
- BUT systemic treatments help IMPROVE THE CURE RATES OF BOTH RADIATION AND SURGERY

In Non-small cell Lung Cancer...

Everything's better with

~~Butter~~

~~Cheese~~

~~Bacon~~

~~Beer~~

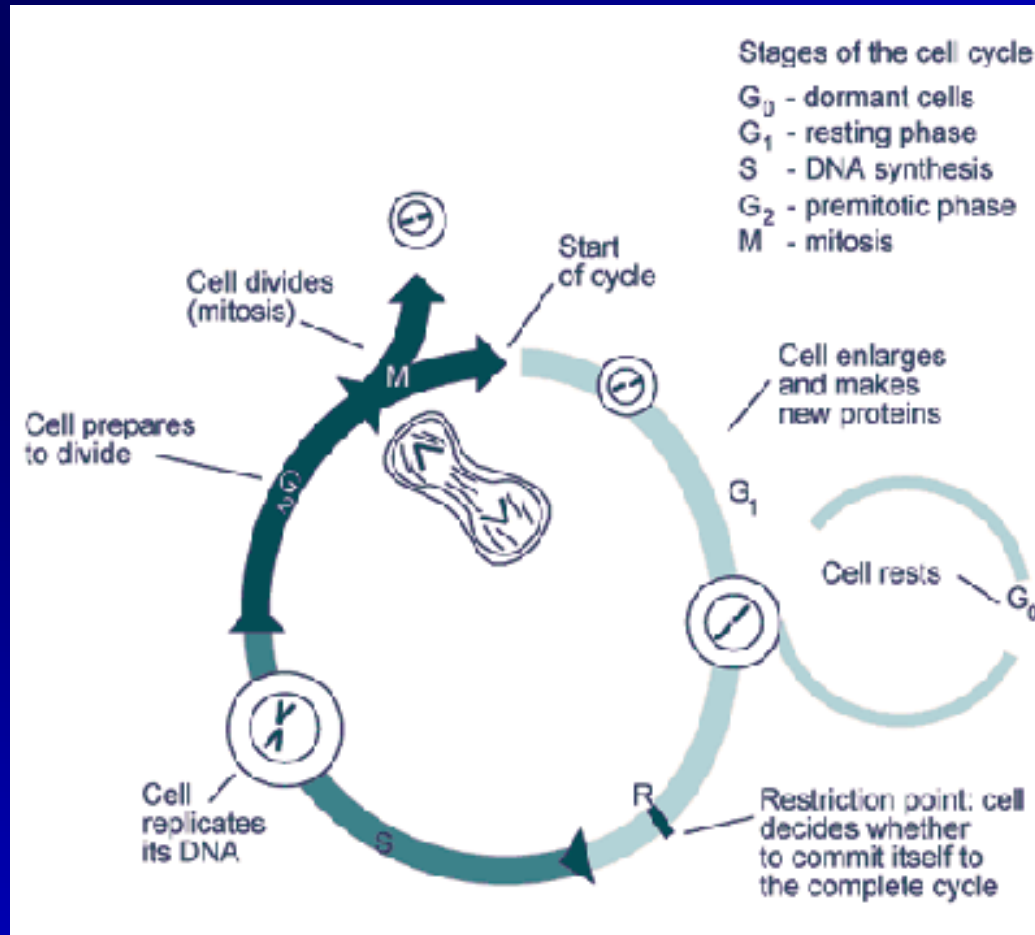
CHEMOTHERAPY!!

What are systemic cancer treatments?

- Any anti-cancer therapies that get to every cell in the body via the bloodstream, usually via oral or intravenous administration
- Traditional cytotoxic chemotherapy targets any and all fast growing cells by inhibiting the machinery cells need to copy DNA and divide
 - Examples: cisplatin, carboplatin, etoposide, paclitaxel, docetaxel, pemetrexed, gemcitabine, vinorelbine

The Cell Cycle:

Target of Traditional Cytotoxic Chemotherapy



The Problem:

Cancer cells are not the only cells utilizing the cell cycle

Traditional Chemotherapy Side Effects

- Hair loss
 - Not all chemotherapies cause
- Nausea and vomiting
 - Aprepitant (Emend), 5HT3 antagonists (zofran, kytril, aloxi, anzemet), steroids (decadron), and ativan can help
- Bone marrow suppression
 - Low white count with decreased immune function, low red cells (anemia) with fatigue, low platelets (risk of bleeding)

Why systemic treatments when the disease appears localized?

- Chemotherapy helps the local treatments do their jobs better
 - RADIATION SENSITIZATION: chemotherapy can help radiation to work better (local control achieved with radiation better in patients who get chemotherapy at the same time)
 - NEOADJUVANT DOWNSTAGING: chemotherapy can shrink the size of tumors before surgery and “sterilize” lymph nodes affected with cancer, thereby increasing chance of complete surgical resection

Why systemic treatments when the disease appears localized?

- Chemotherapy can also address the non-localized disease we can't see
 - In lung cancer, unfortunately, disease that looks localized often isn't
 - A significant percentage of patients relapse with distant metastases after surgery, even when the surgeon "got it all", because of microscopic metastatic disease
 - Chemotherapy CAN cure MICRO metastatic disease!

How do we know that?

- Because CURE rates are increased in patients with locally advanced disease who get chemotherapy in addition to their radiation and surgery and chance of developing distant metastases is less (Induction chemotherapy or concurrent chemoradiotherapy)
- Cure rates also higher in patients who get adjuvant chemotherapy after surgery in locally advanced disease

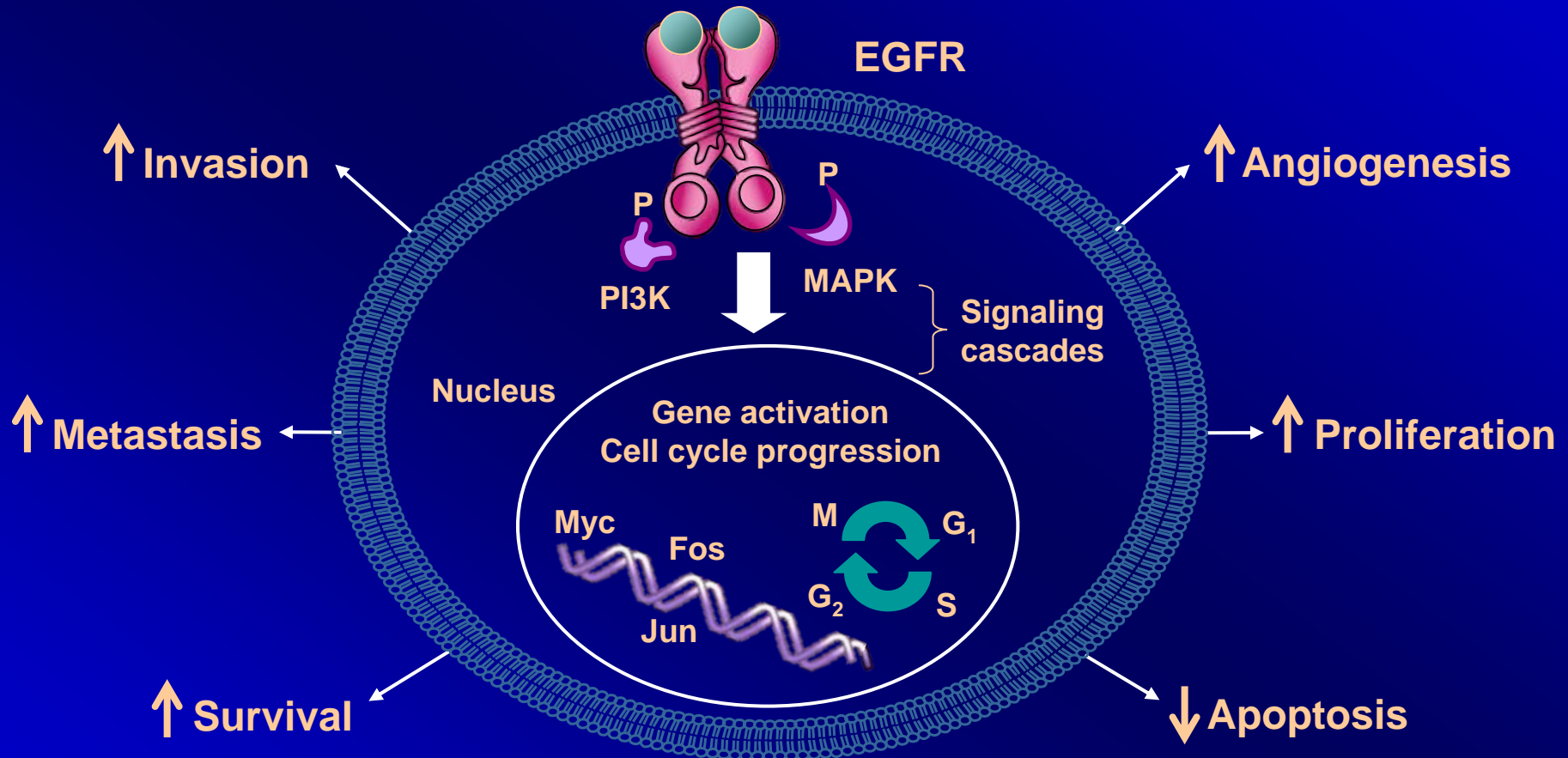
Sequencing of Chemotherapy in Locally Advanced Disease

- Chemotherapy given simultaneously with radiation works better than given before or after radiation, but the combination is more toxic
 - More fatigue, esophagitis, risk of pneumonitis
- When used with surgery, not clear if should be given before or after surgery or simultaneous with radiation

Newer Approaches in Systemic Treatments

- “Targeted” agents: go after a unique aspect of the cancer that makes the cancer cells different from other normal cells
 - Usually a protein expressed/overexpressed only on cancer cells, or a mechanism for growth used by cancer cells but not normal cells
 - Examples
 - hormonal therapy (breast and prostate cancer)
 - In lung, anti-EGFR treatments (erlotinib, gefitinib, cetuximab)

The Epidermal Growth Factor Receptor (EGFR) Pathway in Cancers

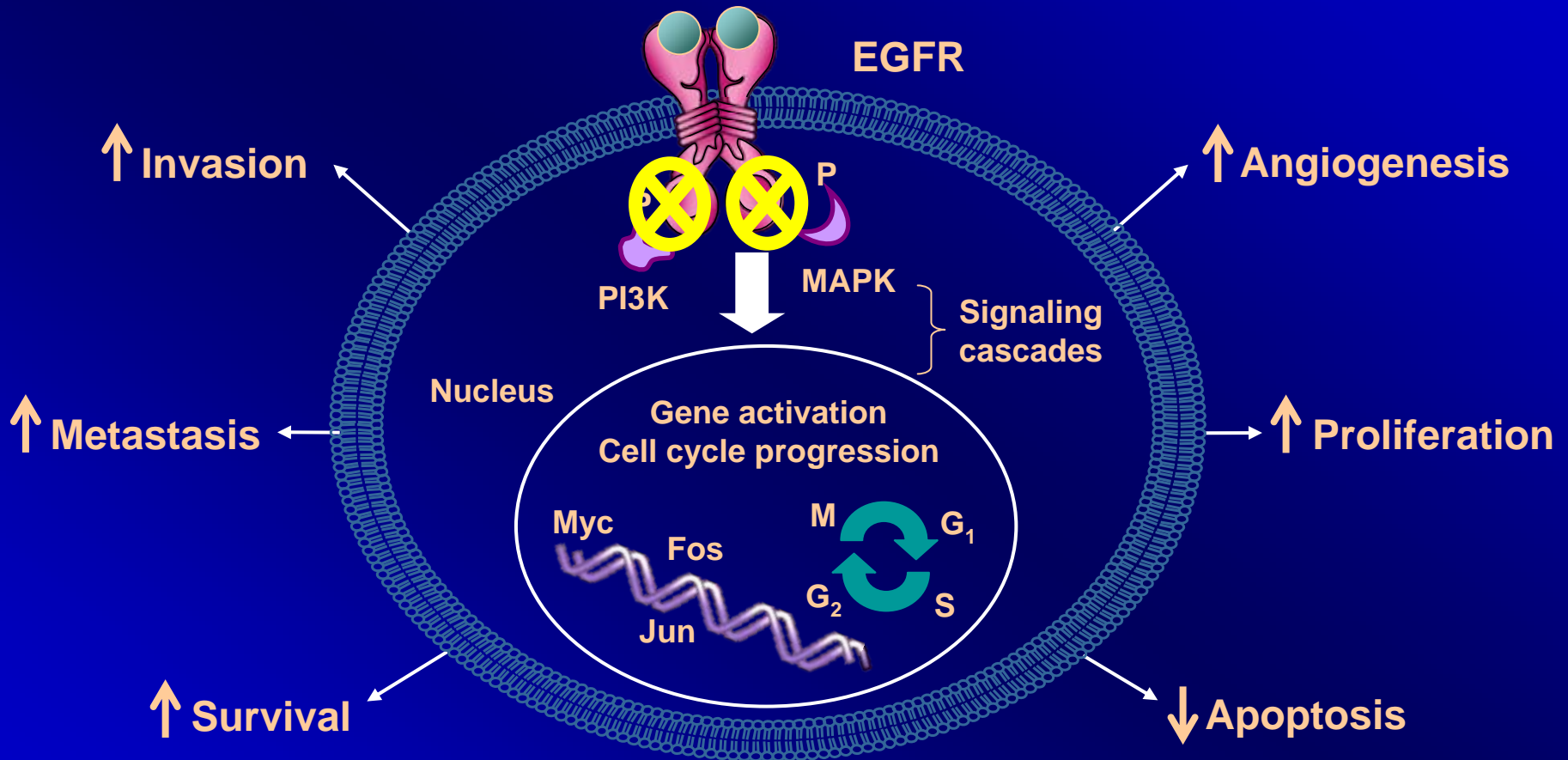


MAPK = mitogen-activated protein kinase.

Roskoski. *Biochem Biophys Res Commun.* 2004;319:1.

Rowinsky. *Annu Rev Med.* 2004;55:433.

Erlotinib (Tarceva)/Gefitinib (Iressa)

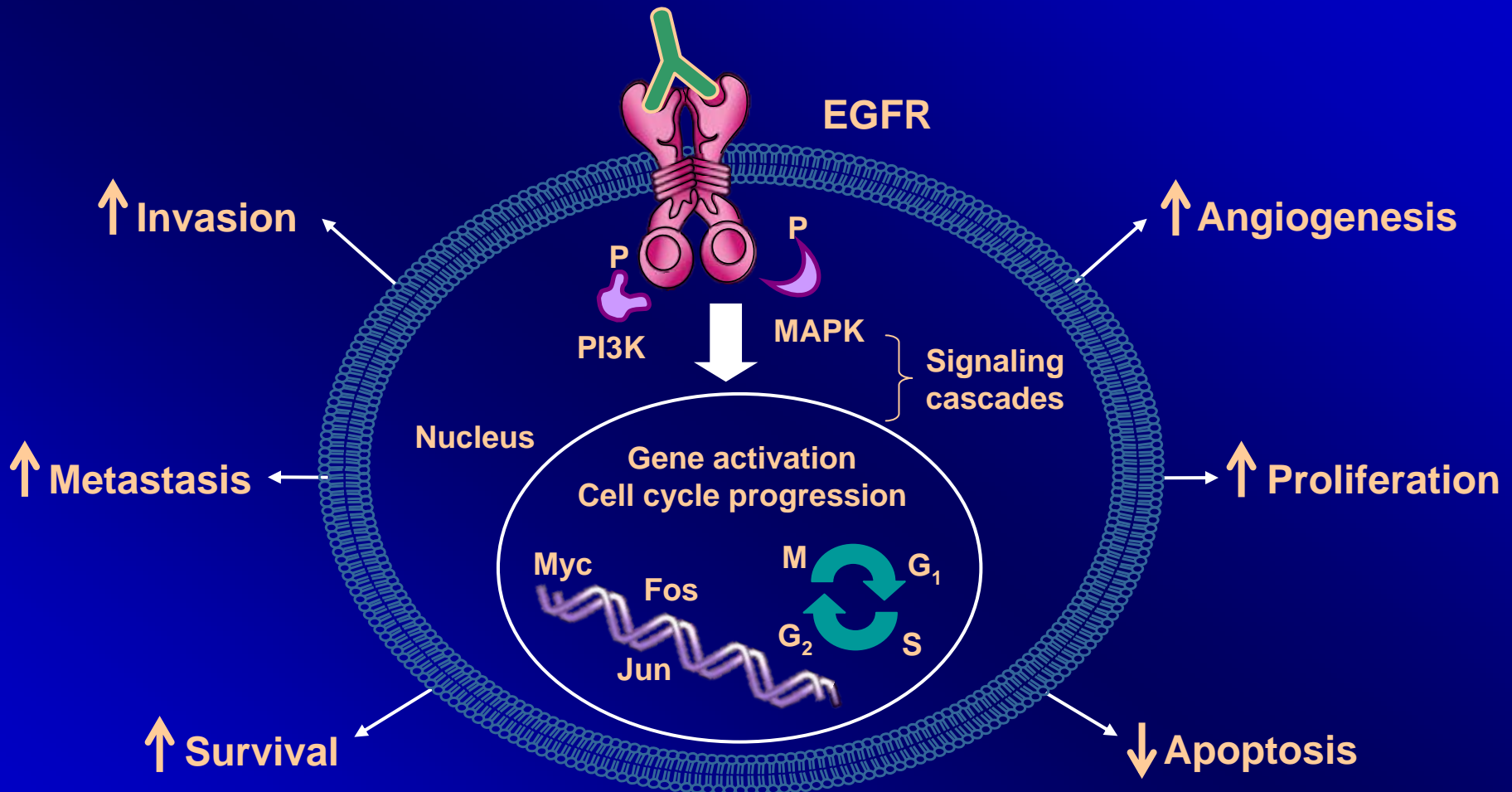


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Cetuximab (Erbitux)



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Yet another approach: Anti-angiogenic Agents

- Do not target the cancer cells directly. Rather, target the cells and processes necessary for the formation of blood vessels which are required for tumors to grow. However, the blood vessels are made up of “normal” cells which may be easier to target than cancer cells, and (with some notable exceptions), new blood vessel formation not usually necessary for non-cancer cells
- Example: Bevacizumab (Avastin)

The Problem with the New Stuff

- Erlotinib, cetuximab, and bevacizumab have all improved patient outcomes in stage IV disease
- Thus far, we have not figured out how to incorporate these agents in the treatment of locally advanced disease
 - Bevacizumab with radiation has caused dangerous side effects
 - Patients who received gefitinib after chemoradiation did worse than patients who received placebo

Clinical Trials for Locally Advanced Disease at Abramson Cancer Center: Because we **MUST** do better

- Is erlotinib after surgery better in patients specially selected based on **molecular characteristics** of their tumors? (2 studies)
- Does the addition of bevacizumab to chemotherapy after surgery improve outcomes?
- Does the addition of cetuximab to chemoradiation improve outcomes?
- Is pemetrexed a better chemotherapy to use with radiation than the prior standard?
- Will tumor vaccines after surgery or chemoradiation improve outcomes? (3 studies: MUC1, MAGE, telomerase)

NIH Research Funding per Death in 2008

Breast Cancer	\$23,754
Prostate Cancer	\$11,959
Lung Cancer	\$1,414

Lung Cancer Activists





Philadelphia, PA - November 1, 2009

This is the fourth annual Free to Breathe® Lung Cancer 5K. The event provides an opportunity for lung cancer advocates, survivors and the community to come together to raise awareness and support to fight this disease. All proceeds from this event will benefit the National Lung Cancer Partnership's research, education and awareness programs

www.freetobreathe.com

7:30am - Opening Anthem & Rally

8:30am - 5K Race Begins; Walks Begin Immediately Following

Where:

Carousel House

Belmont Avenue & N. Concourse Drive

West Fairmount Park

Philadelphia, PA 19131

(across from the Please Touch Museum/Memorial Hall)

