



המרכז הרפואי  
הלל יפה



# טיפול ביולוגי - העידן החדש בטיפול במחלה ממאירה

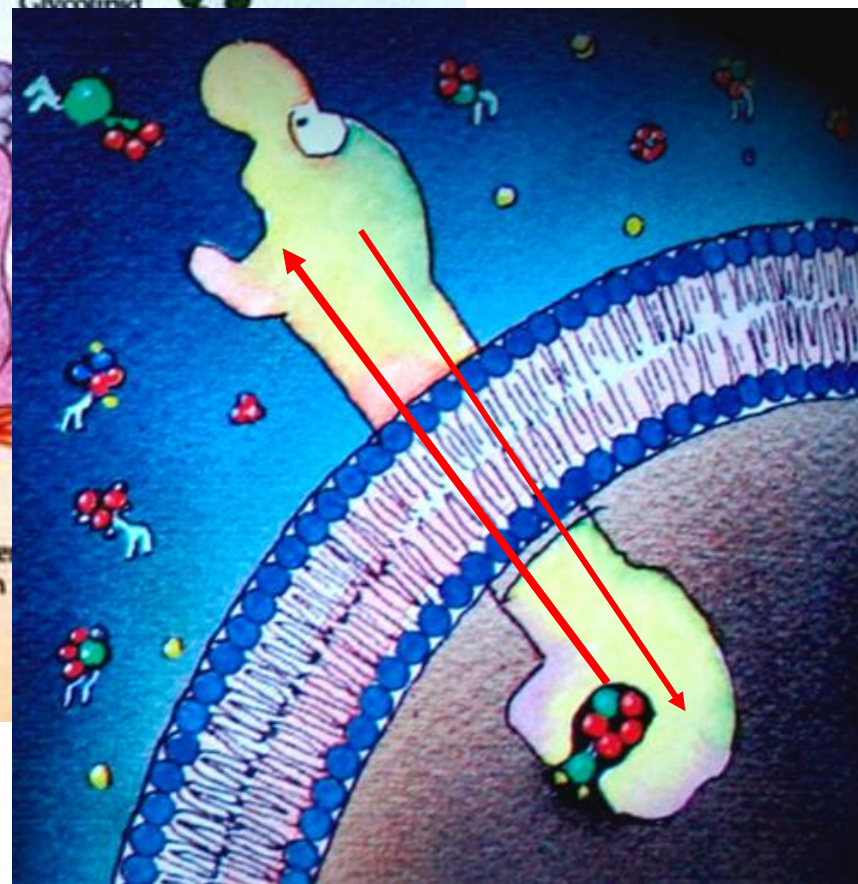
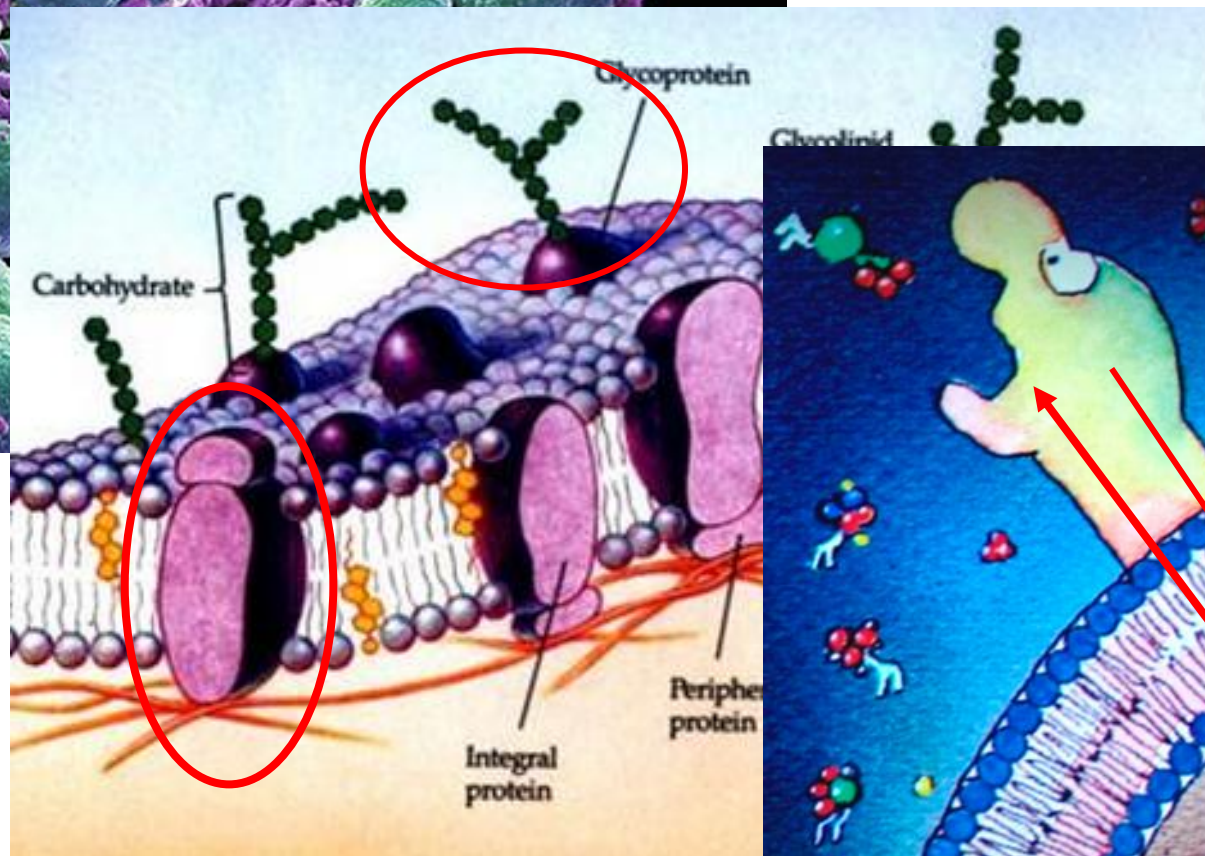
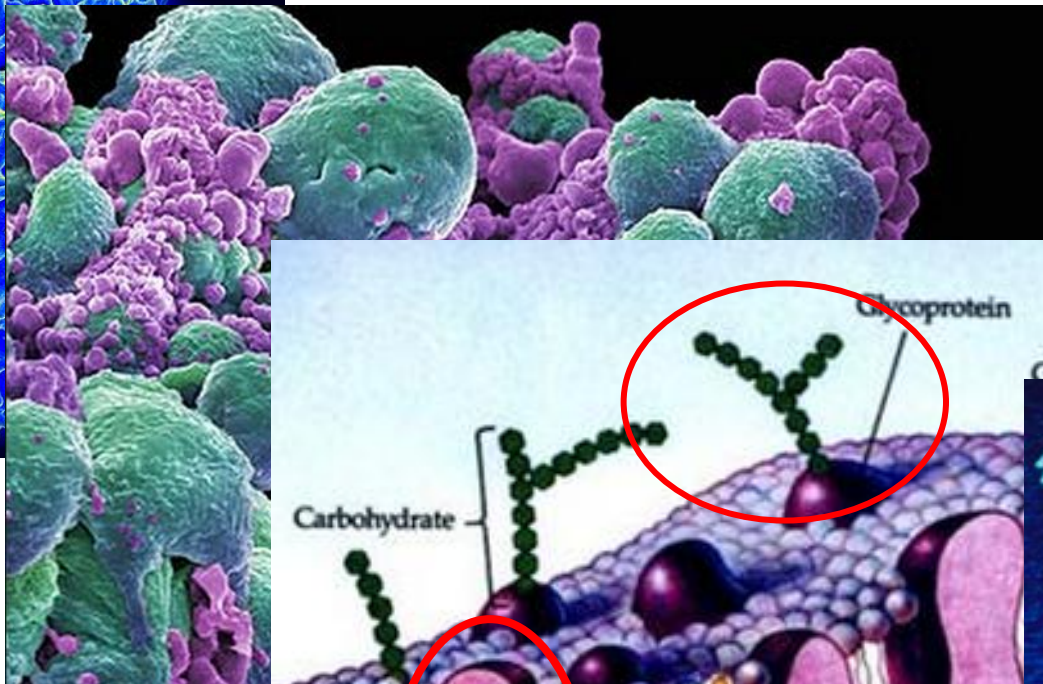
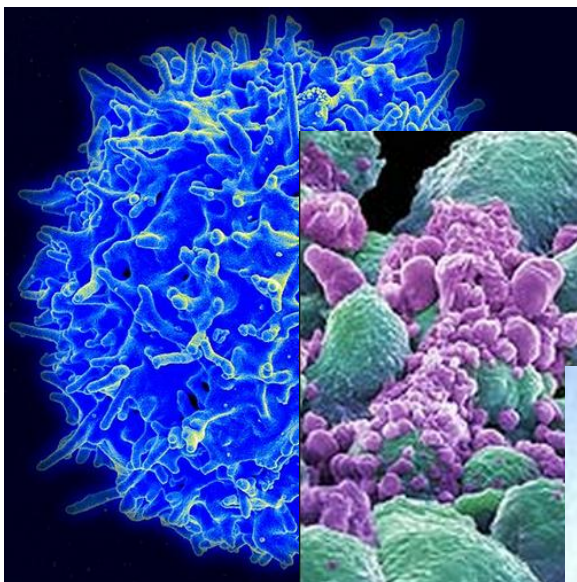
ד"ר יקטרינה שולמן

יום עיון, 23 פברואר 2015

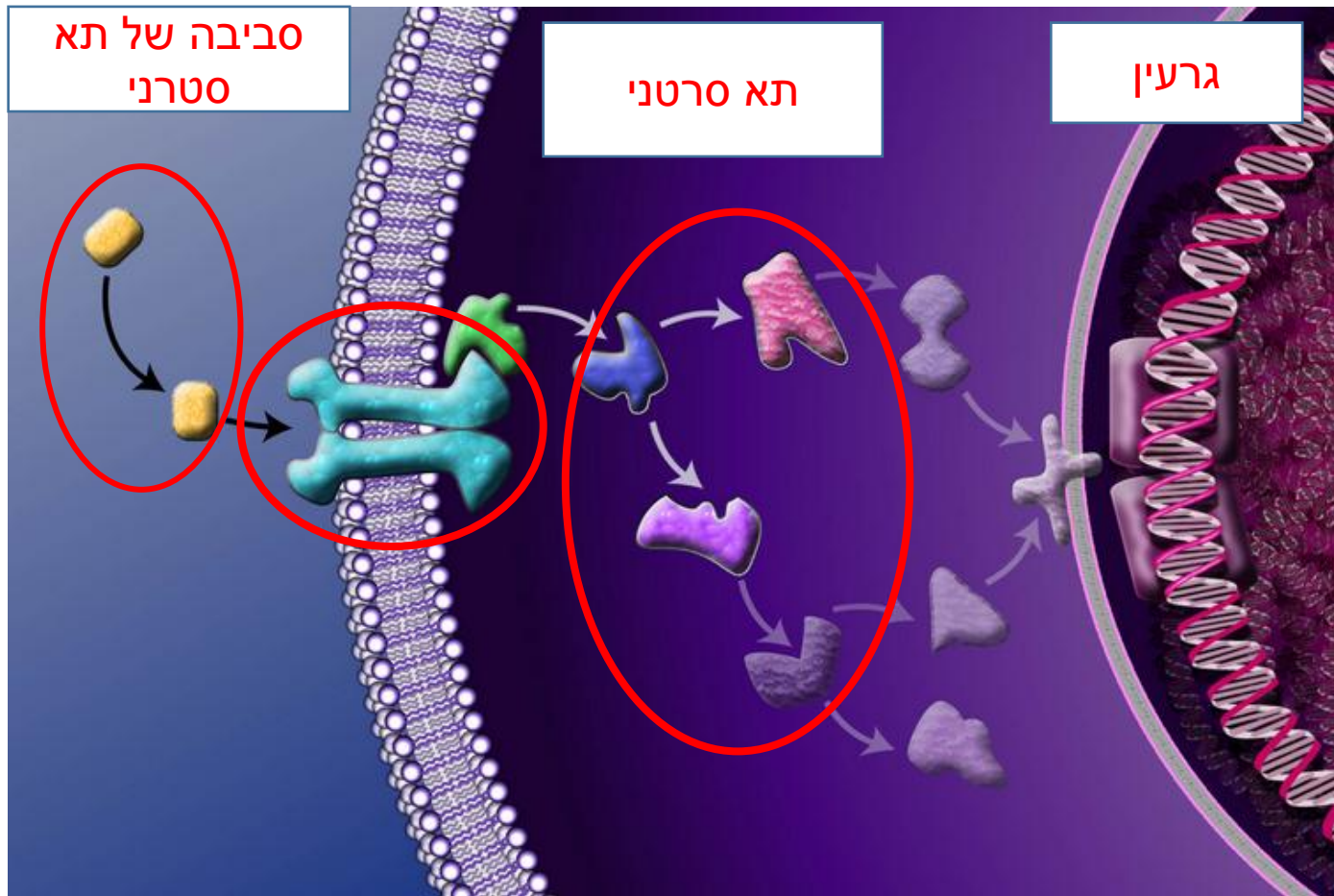
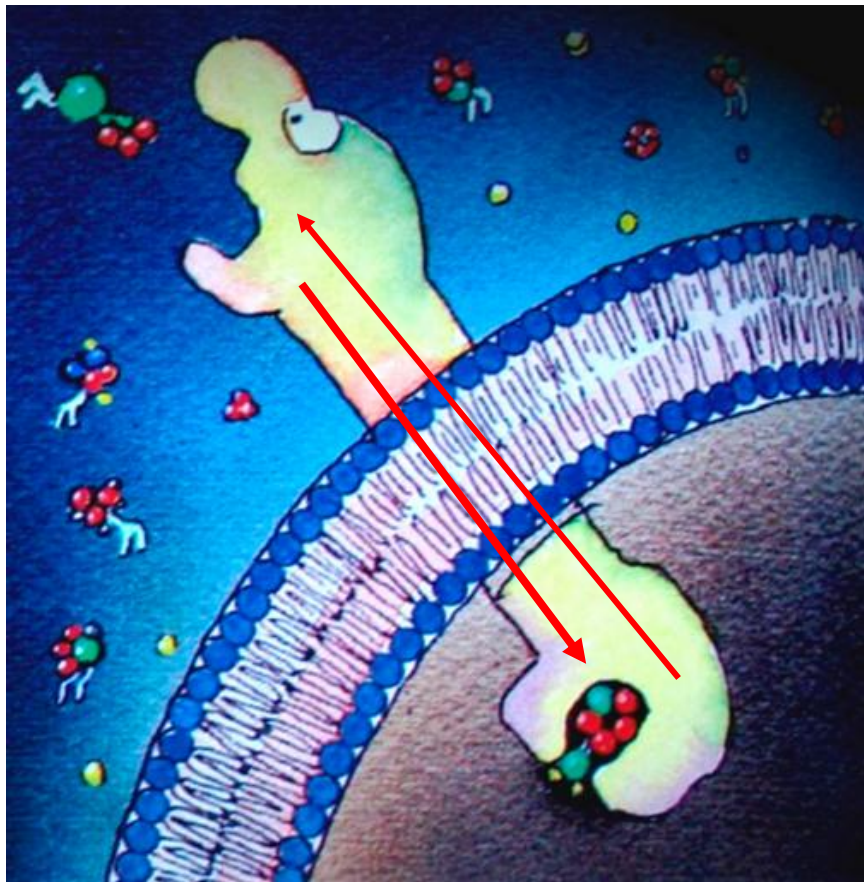
מנהלת היחידה לאונקולוגיה קלינית  
בית חולים הלל יפה



# הקשר בין הגידול לסביבה



# הקשר בין הגידול לסביבה דרך הממברנה שת תא סרטני



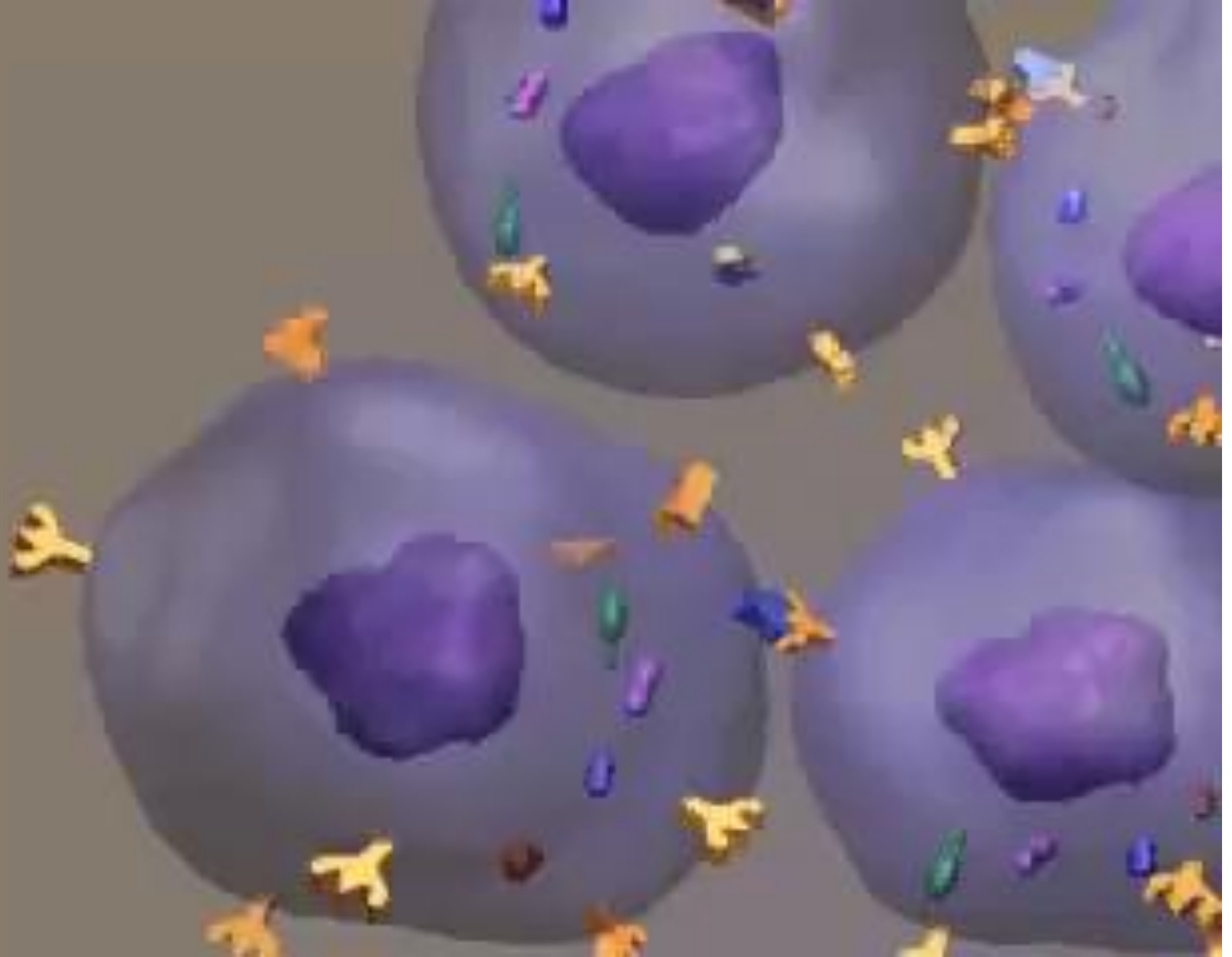
סביבה של תא סרטני

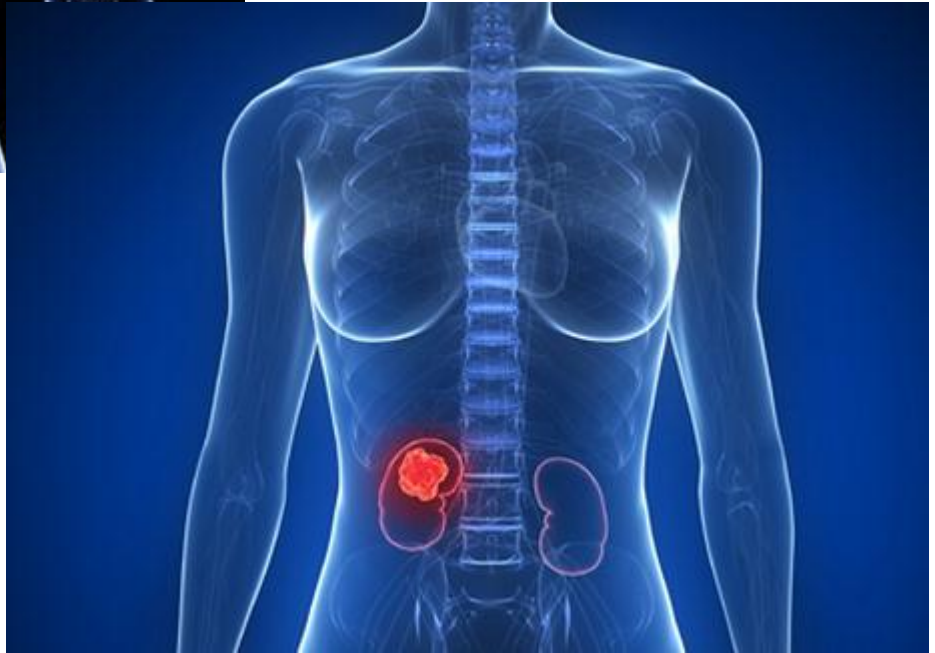
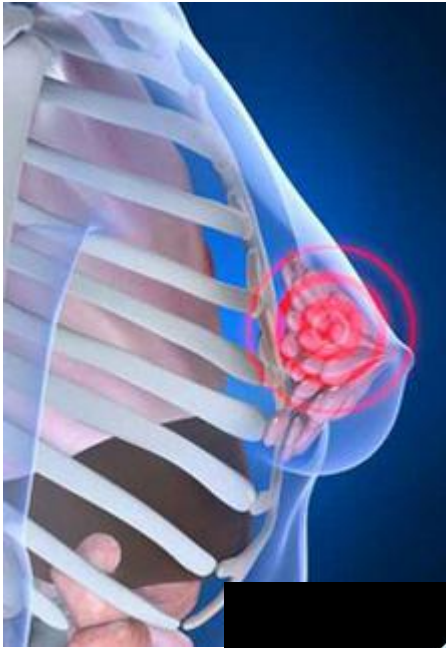
תא סרטני

גרעין

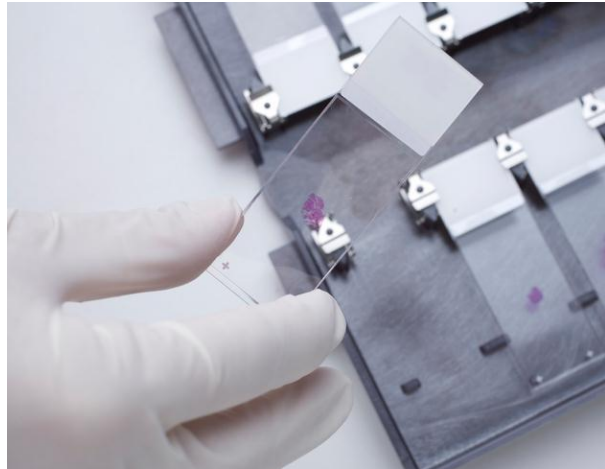
# Signal Transduction Mechanism =

הקשר בין תא  
סרטני לסביבה  
דרך ממברנה  
(קרום) של  
התא

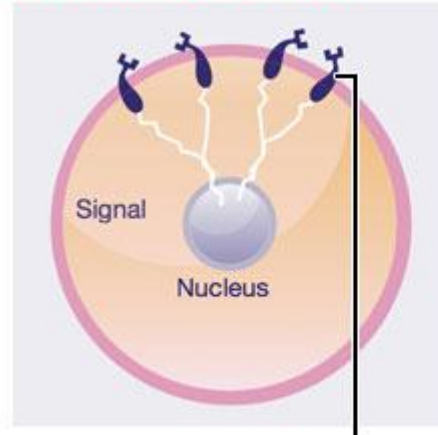




# סרטן שד – קולטן HER2NEU

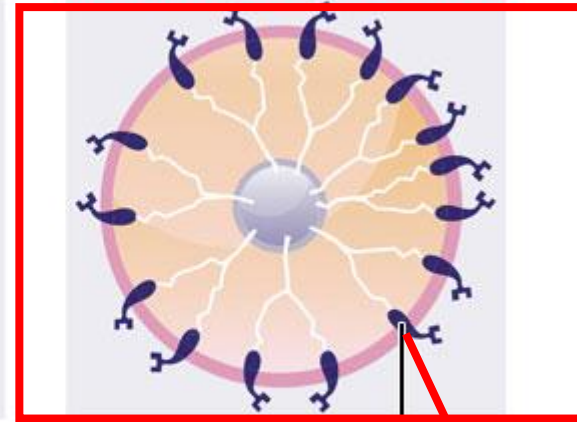


Normal breast cancer cell

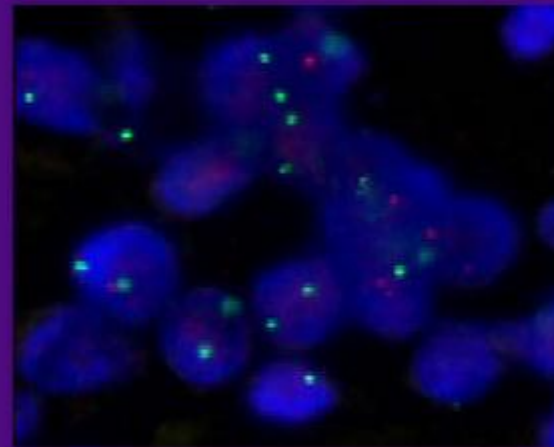
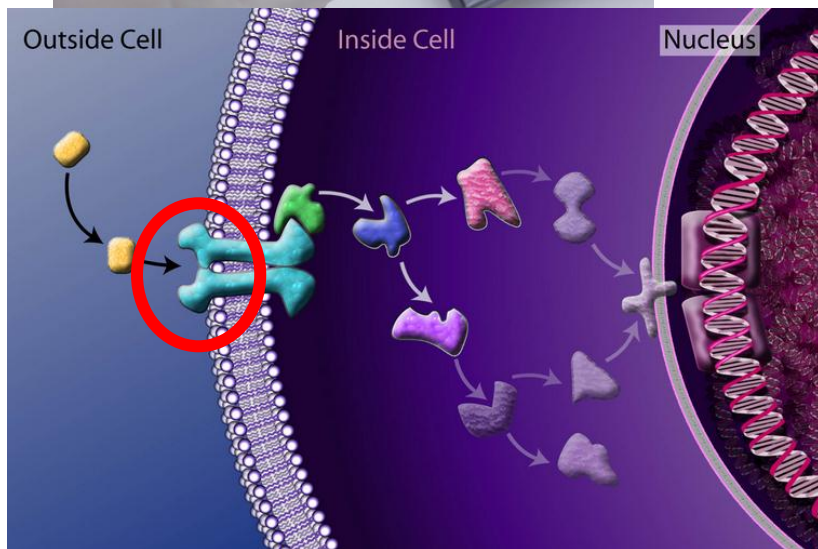


Normal amount of HER2 receptors send signals telling cells to grow and divide.<sup>1</sup>

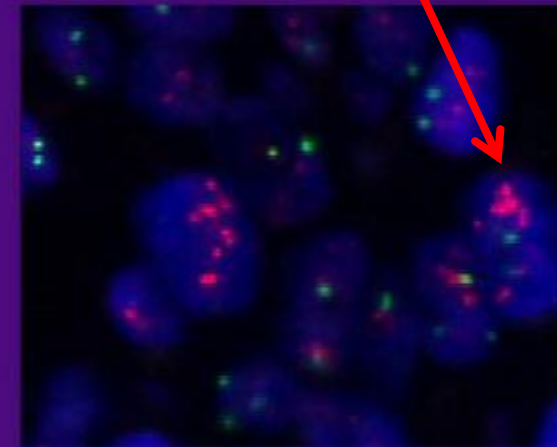
Abnormal HER2+ breast cancer cell



Too many HER2 receptors send more signals, causing cells to grow too quickly.<sup>1</sup>



HER2 Negative



HER2 Positive

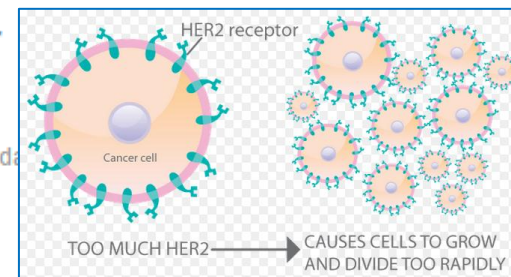


# Perjeta Boosts Overall Survival in HER2-Positive Metastatic Breast Cancer

Save as Favorite

Sign in to receive recommendations

Published on **September 30, 2014** at 10:30 AM



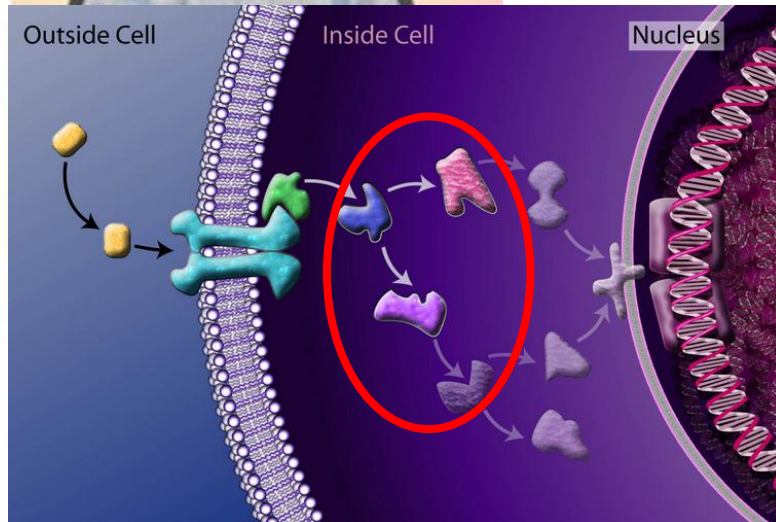
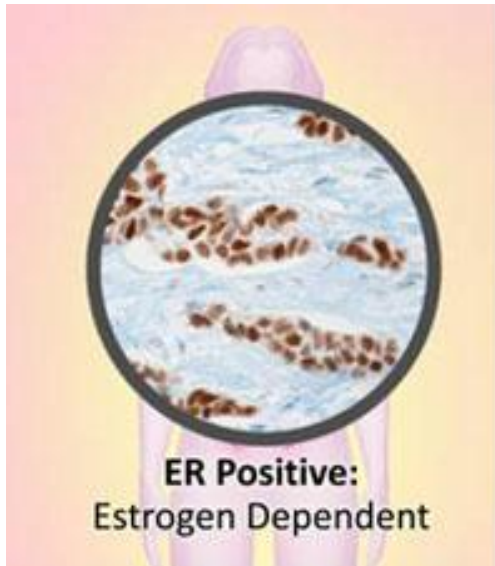
**TOPIC:** *Diagnosis, Chemotherapy, and Targeted Therapy*

**TAGS:** *Metastatic/Advanced-stage: Stage IV, HER2 Enriched Breast Cancer, Invasive or Infiltrating Ductal Carcinoma, Invasive or Infiltrating Lobular Carcinoma, Luminal B Breast Cancer, Planning/Considering Targeted Therapy, Targeted Therapy for Metastatic Cancer, HER2/neu Positive Cancer, Taxotere (chemical name: docetaxel), Herceptin (chemical name: trastuzumab), and Perjeta (chemical name: pertuzumab; aka Omnitarg)*

On Sept. 28, 2014, final results from the CLEOPATRA study showed that women who got Perjeta, Herceptin, and Taxotere lived about 1.5 years longer than women who got only Herceptin and Taxotere.



# סרטן שד – קולטנים הורמונליים



↓

טיפול הורמונלי

→

התפתחות  
עמידות לטיפול  
הורמונלי

→

28 Tablets      NDC 0078-0567-51  
Carton contains 4 individual blister cards of 7 tablets      Rx only

30 comprimés enrobés  
**AROMASINE®**  
25 mg  
exemestane  
Voie orale

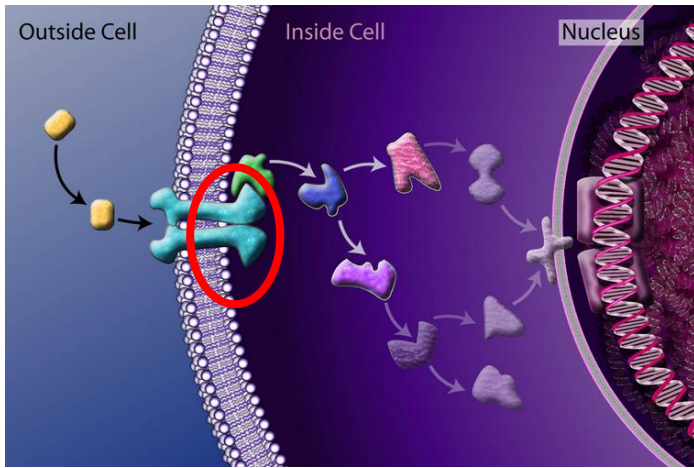
**+**

**AFINITOR®**  
(everolimus) tablets  
Each tablet contains  
**10 mg**  
everolimus  
NOVARTIS

החזרת  
רגישות לטיפול הורמונלי  
ע"י שילוב של טיפול הורמונלי  
וטיפול ביולוגי

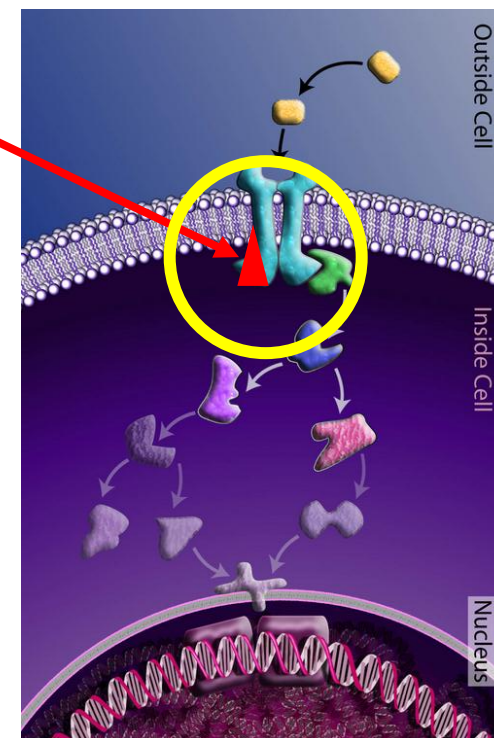
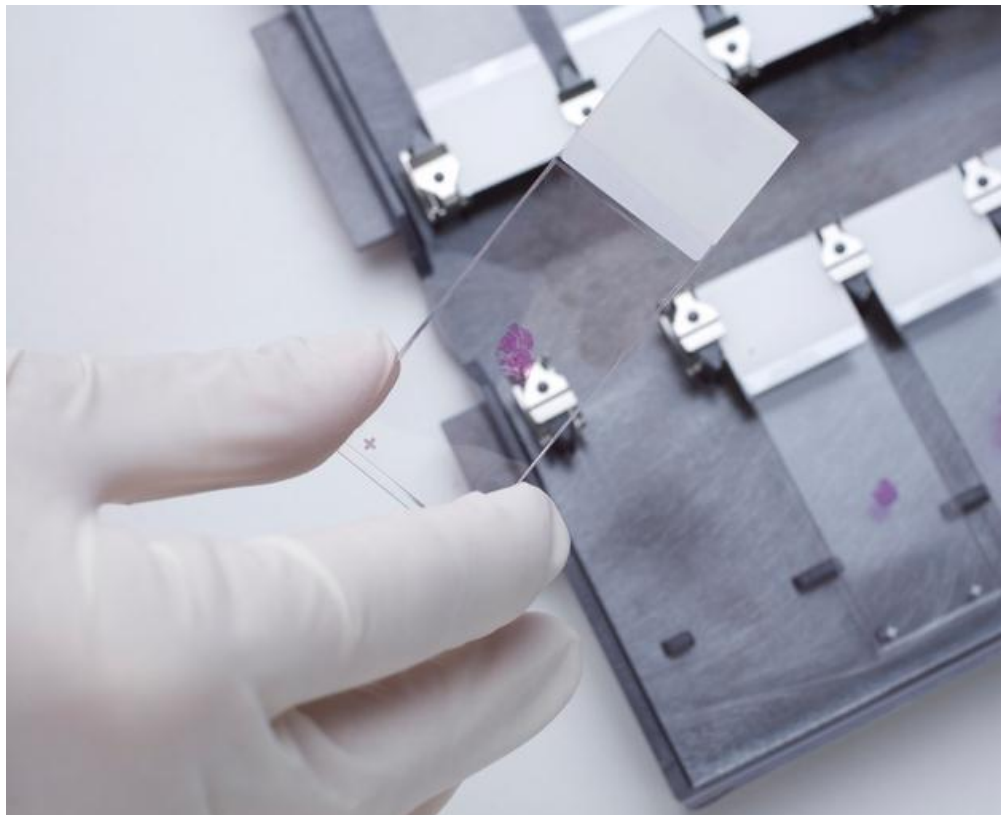
ממאירות ריאה –

# Non-Small Cell Lung Carcinoma



# EGFR, ALK – LUNG cancer

## מוטציה והתאמת טיפול



ניתן למצוא את המוטציה בכ-20% מגידולי הריאה

# בדיקות התאמה בין גידול לטיפול ביולוגי



# Crizotinib Highly Active in *ROS1*-Mutated Lung Cancer

Megan Brooks

November 19, 2014

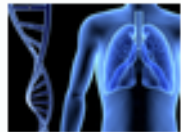


Comment



Print

## EDITORS' RECOMMENDATIONS



ASCO: Molecular Testing for All Lung Adenocarcinomas



Drugs to Avoid in Patients on Tyrosine Kinase Inhibitors

Crizotinib Beats Chemo in ALK-Positive Advanced NSCLC

## Topic Alert

Receive an email from Medscape whenever new articles on this topic are

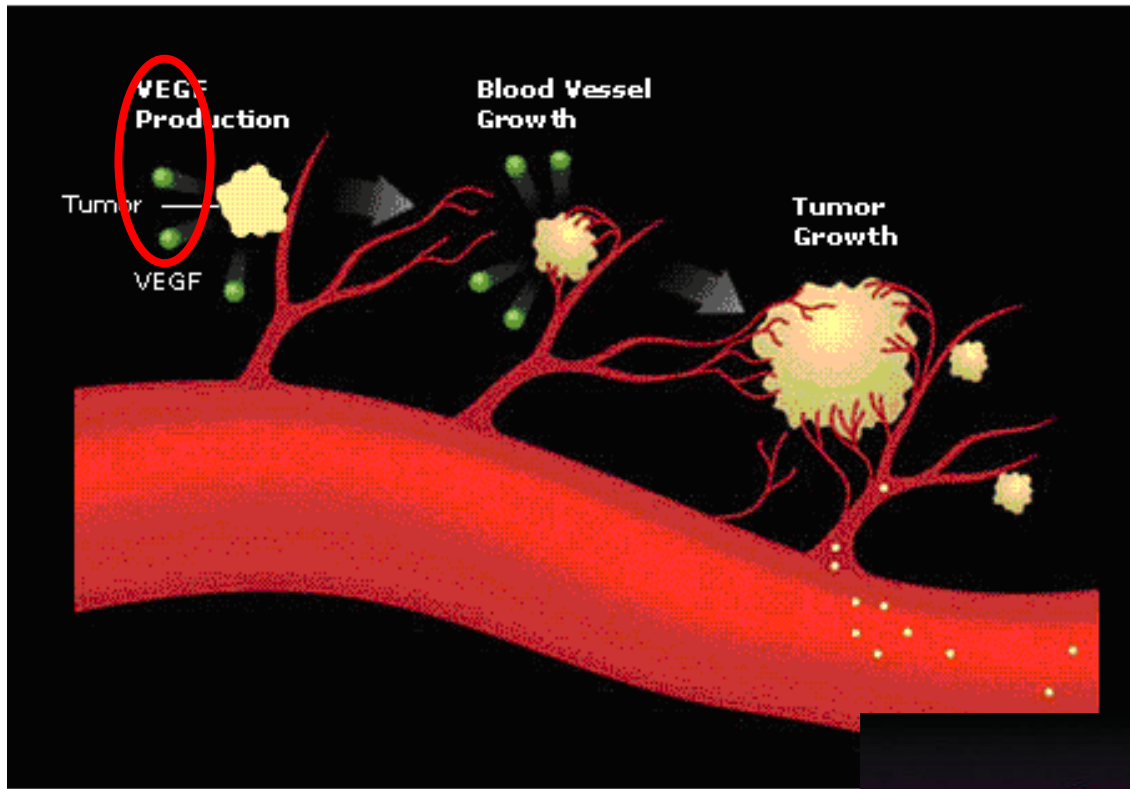
Crizotinib (*Xalkori*, Pfizer Inc) has shown potent antitumor activity in a second subgroup of patients with non–small cell lung cancer (NSCLC) — those with advanced *ROS1* proto-oncogene receptor tyrosine kinase (*ROS1*)–rearranged tumors, which are found in about 1% of NSCLC patients.

Crizotinib is already marketed for late-stage NSCLC with anaplastic lymphoma kinase (*ALK*) gene rearrangement, which is found in about 4% to 5% of NSCLC patients.

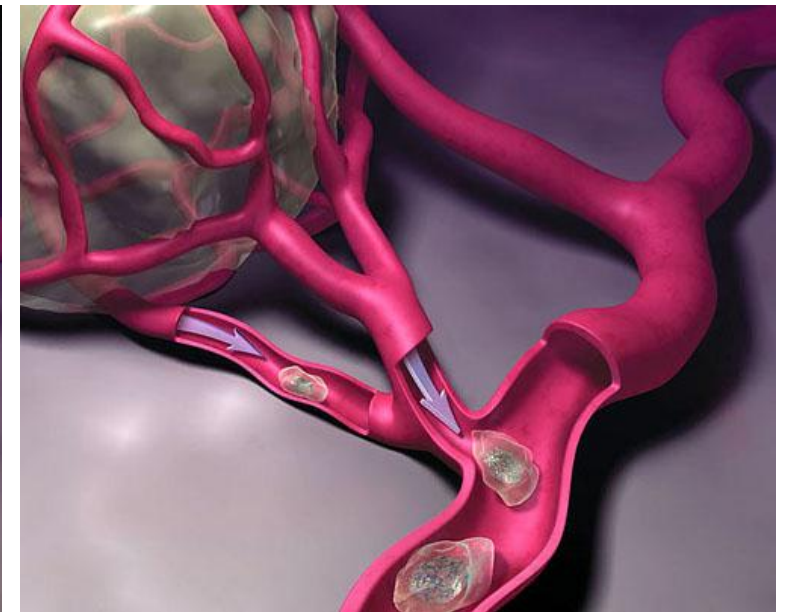
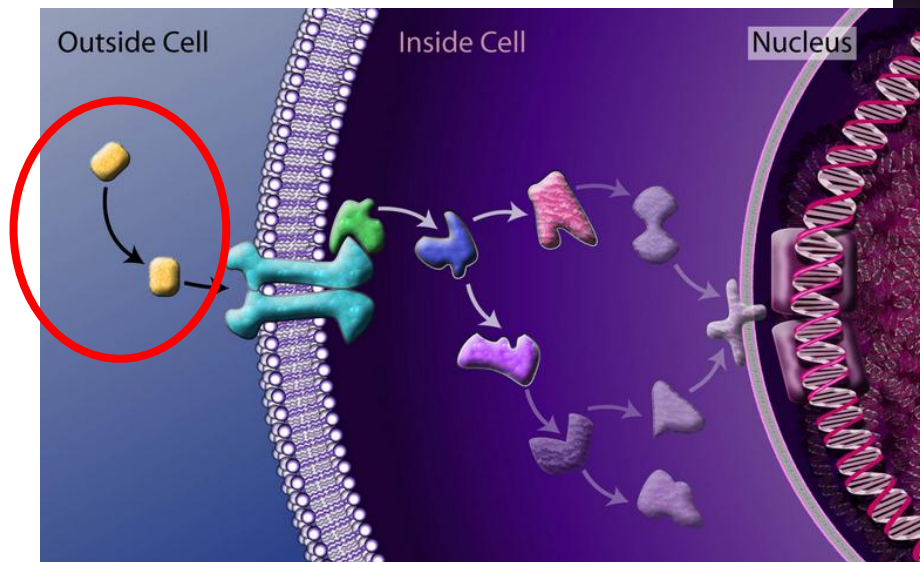
### Better Than Expected

"*ROS1* rearrangement defines a second molecular subgroup of NSCLC for which crizotinib is highly active," says Alice T. Shaw, PhD, of Massachusetts General Hospital Cancer Center in Boston, who reports clinical results in this patient population in the *New England Journal of Medicine*.

# חשיבות תהליך הספקת דם להתפתחות הגידול

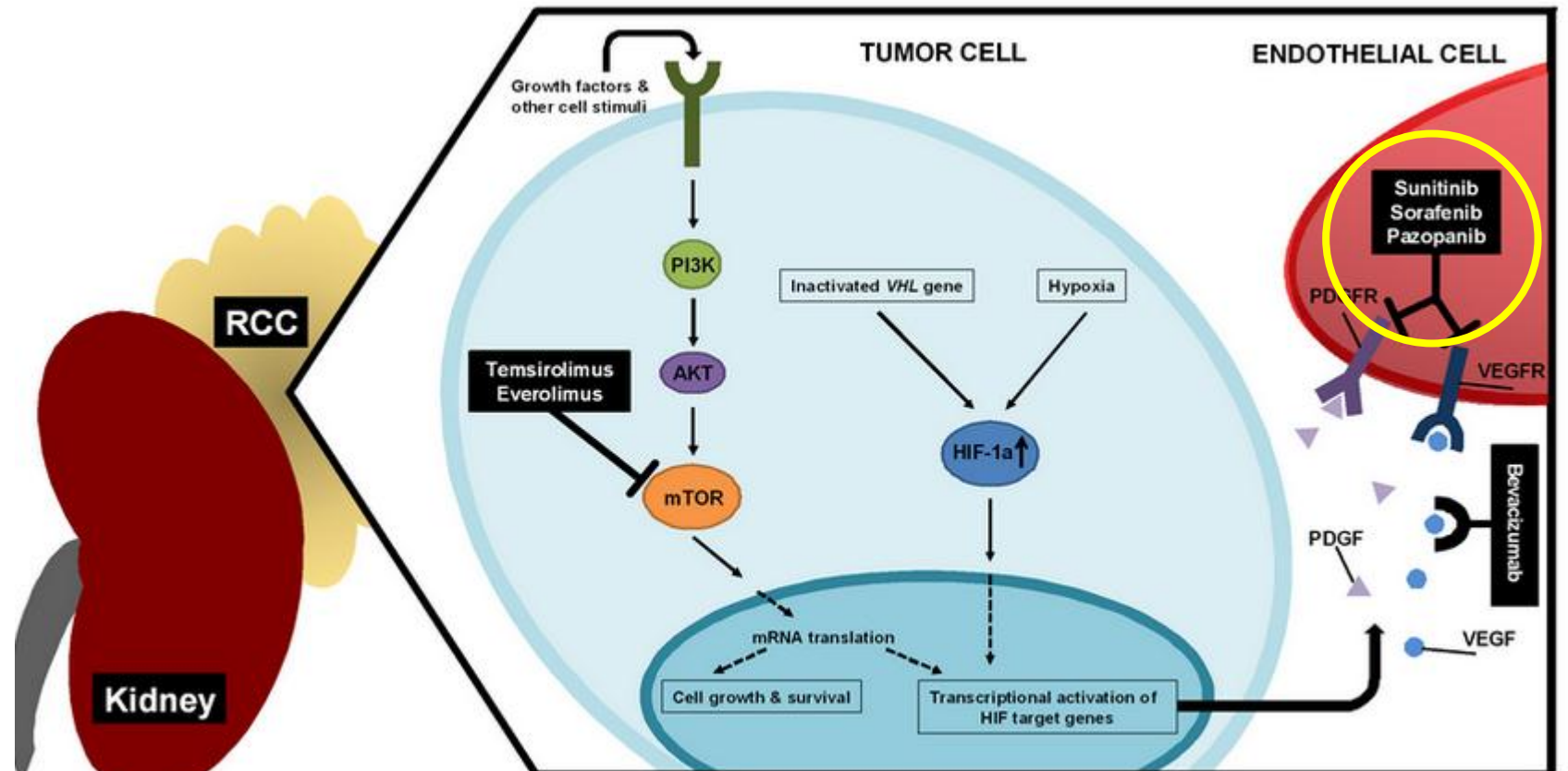
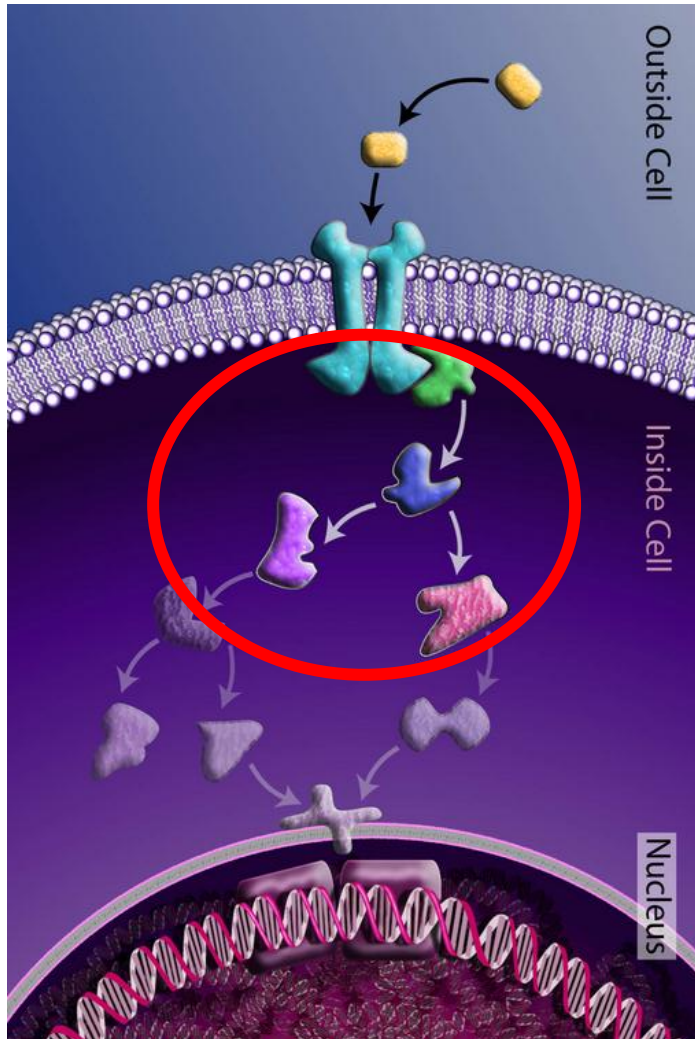


Source: Genentech.

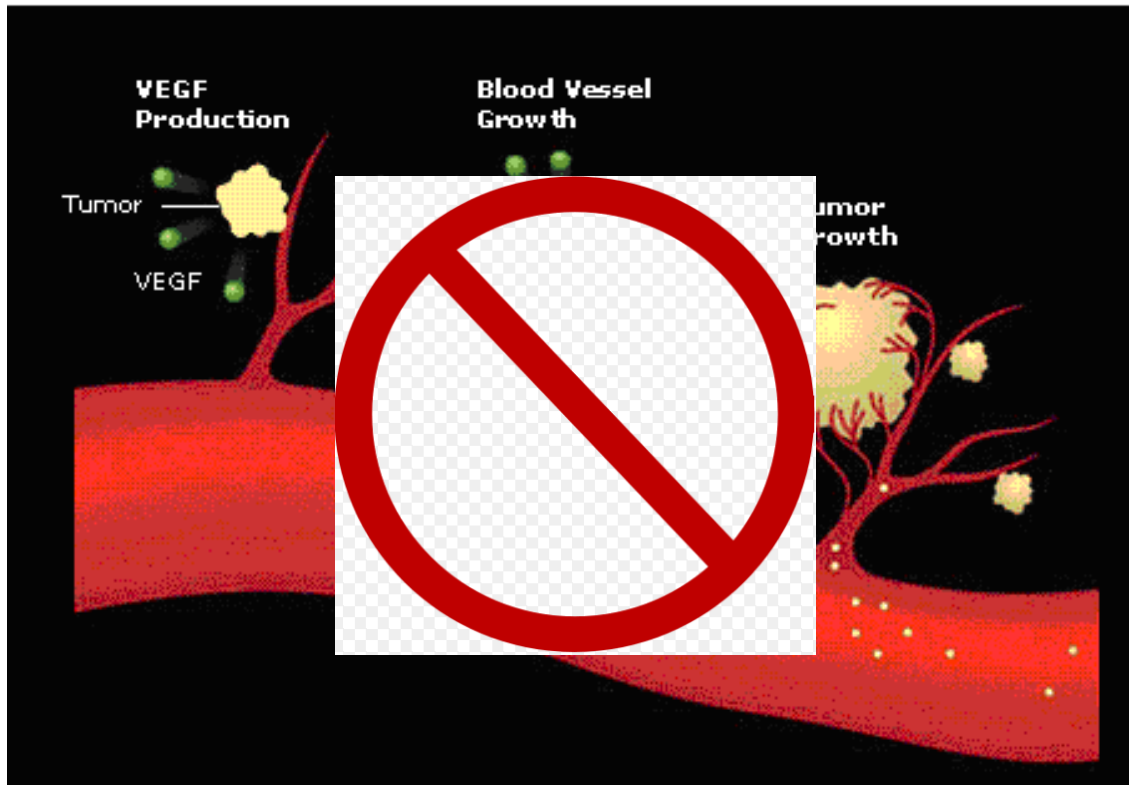


# גידול בכליה renal cell carcinoma

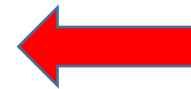
- גידול עמיד לכימותרפיה וקרינה
- טיפול ביולוגי יעיל אך לא סלקטיבי



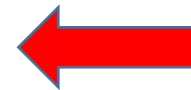
# ממאירות מעי הגס



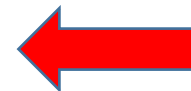
Source: Genentech.



Avastin (bevacizumab)



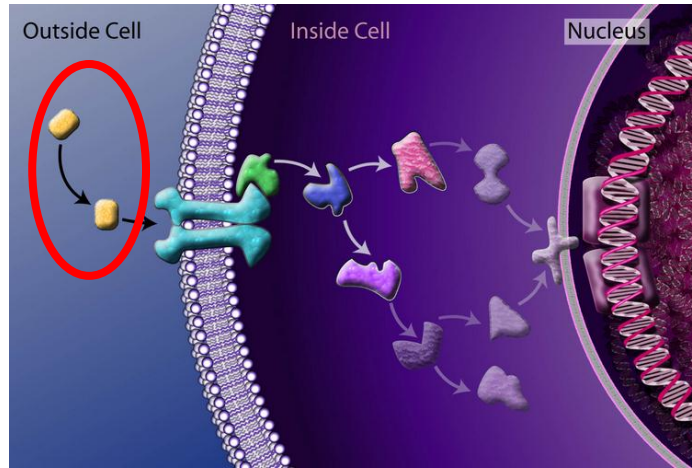
Zaltrap (aflibercept)



Stivarga (regorafenib)



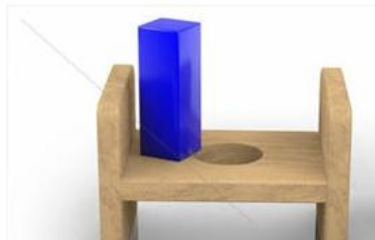
# ממאירות מעי הגס – בחירת חולים לטיפול anti-EGFR



Erbix (cetuximab) ✓

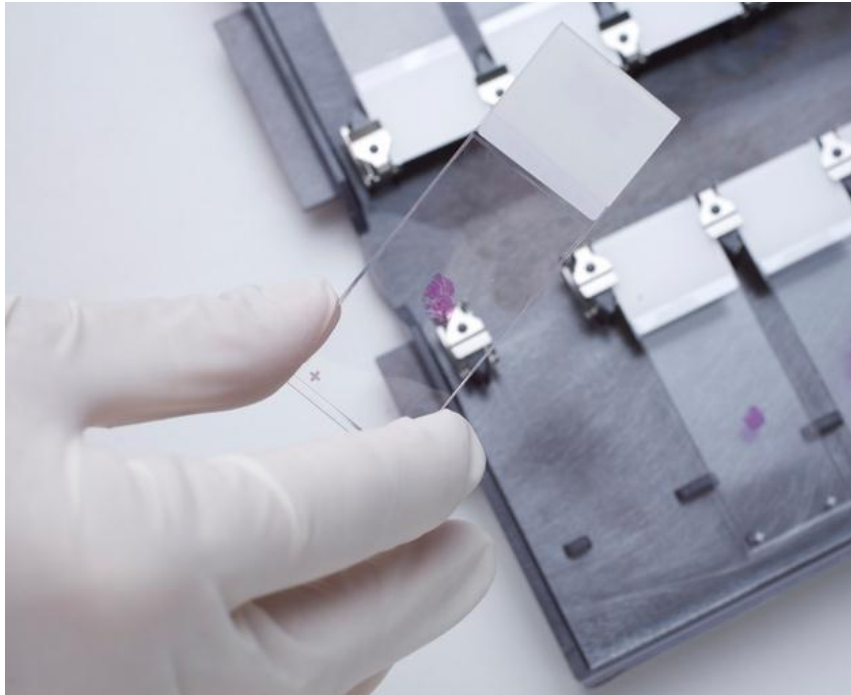
Vectibix (panitumumab) ✓

מוטציה ב- RAS (גן) בכ-50% מגידולי מעי גס



חסר יעילות של טיפול ביולוגי

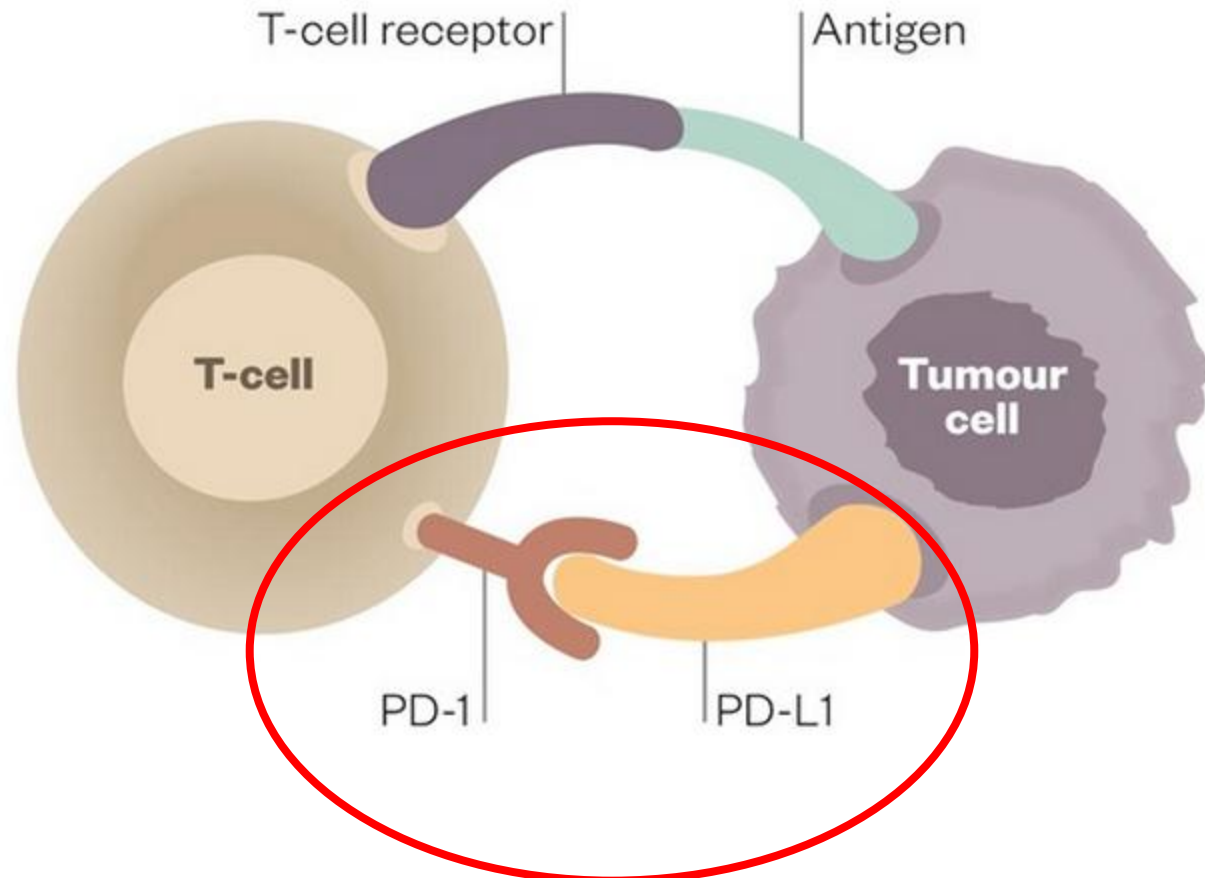
# רק גידולי מעי גם ללא מוטציה מגיבים לטיפול ב- Cetuximab or Panitumumab



<u>Test</u>	<u>Nucleotide Change</u>	<u>Amino Acid Change</u>	<u>Negative</u>	<u>Positive</u>
KRAS_CODON12	GGT>GTT	Gly12Val	x	
KRAS_CODON12	GGT>GAT	Gly12Asp	x	
KRAS_CODON12	GGT>TGT	Gly12Cys	x	
KRAS_CODON12	GGT>AGT	Gly12Ser	x	
KRAS_CODON12	GGT>GCT	Gly12Ala	x	
KRAS_CODON12	GGT>CGT	Gly12Arg	x	
KRAS_CODON13	GGC>AGC	Gly13Ser	x	
KRAS_CODON13	GGC>TGC	Gly13Cys	x	
KRAS_CODON13	GGC>CGC	Gly13Arg	x	
KRAS_CODON13	GGC>GTC	Gly13Val	x	
KRAS_CODON13	GGC>GAC	Gly13Asp	x	
KRAS_CODON13	GGC>GCC	Gly13Ala	x	
KRAS_CODON61	CAA>CAT	Gln61His	x	
KRAS_CODON61	CAA>CAC	Gln61His	x	
KRAS_CODON117	AAA>CAA	Lys117Gln	x	
KRAS_CODON117	AAA>GAA	Lys117Glu	x	
KRAS_CODON117	AAA>TAA	Lys117X	x	
KRAS_CODON117	AAA>ACA	Lys117Thr	x	
KRAS_CODON117	AAA>AGA	Lys117Arg	x	
KRAS_CODON117	AAA>ATA	Lys117Ile	x	
KRAS_CODON117	AAA>AAC	Lys117Asn	x	
KRAS_CODON117	AAA>AAG	Lys117Lys	x	
KRAS_CODON117	AAA>AAT	Lys117Asn	x	
KRAS_CODON146	GCA>ACA	Ala146Thr	x	
KRAS_CODON146	GCA>CCA	Ala146Pro	x	
KRAS_CODON146	GCA>TCA	Ala146Ser	x	

# חשיבות הפעילות התקינה של המערכת האימונית

- דרך מנגנון PD-L1 תאי גידול "משתיקים" את התגובה של מערכת החיסון של הגוף



התרופות הראשונות לחסימת 1L-PD יעילות לטיפול במלנומה ונמצאות בשלבי מחקר שונים בגידולים רבים אחרים



**OPDIVO™**  
(nivolumab)  
INJECTION FOR INTRAVENOUS USE 10 mg/mL

## Opdivo Shows Promise Against Lung Cancer

By Zosia Chustecka

Medscape Medical News

Reviewed by Brunilda Nazario, MD

Jan. 13, 2015 -- Drug-maker Bristol-Myers Squibb says a trial of nivolumab (Opdivo) has been stopped early because the drug improves how long people with a type of advanced lung cancer live compared to chemotherapy.

Conferen

# 2015 Gastrointestinal Cancers Symposium DAILY NEWS

## KEYNOTE-012 Sheds Light on Pembrolizumab Activity in Gastric Cancer

JAN 15, 2015

## FDA Approves Keytruda for Advanced Melanoma Based on Phase 1b Study

James Radke

Published Online: Friday, Sep 05, 2014

The screenshot shows the top of the FDA website. On the left is the FDA logo. To its right is the text "U.S. Food and Drug Administration" and "Protecting and Promoting Your Health". On the far right, there is a search bar with the text "A to Z Index" above it and "Search F" inside. Below this is a horizontal navigation menu with buttons for "Home", "Food", "Drugs", "Medical Devices", "Radiation-Emitting Products", "Vaccines, Blood & Biologics", and "Animal & Vet".

### News & Events

Home > News & Events > Newsroom > Press Announcements

### FDA News Release

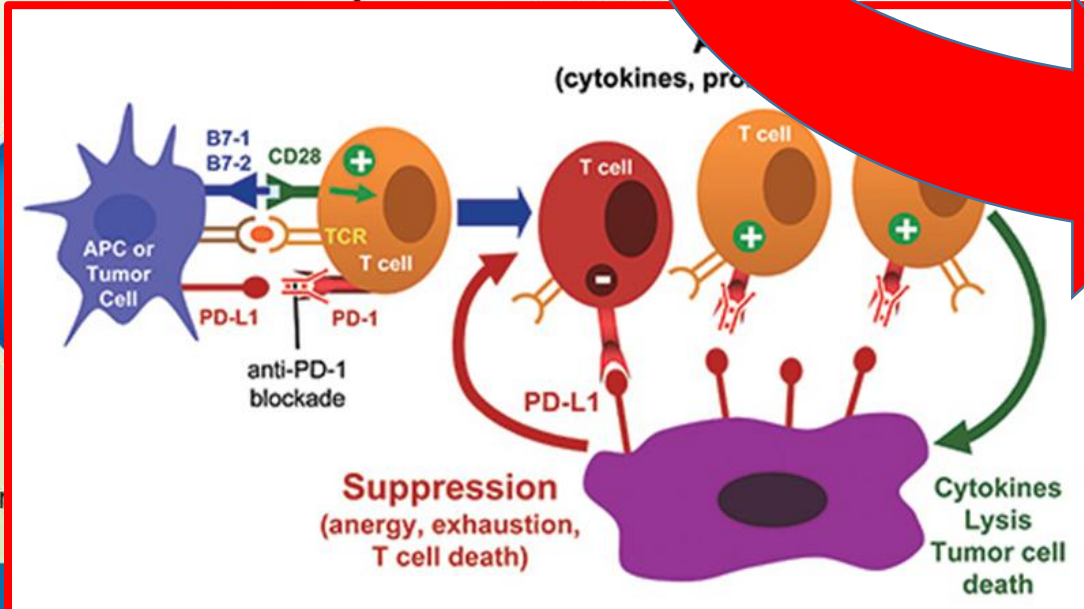
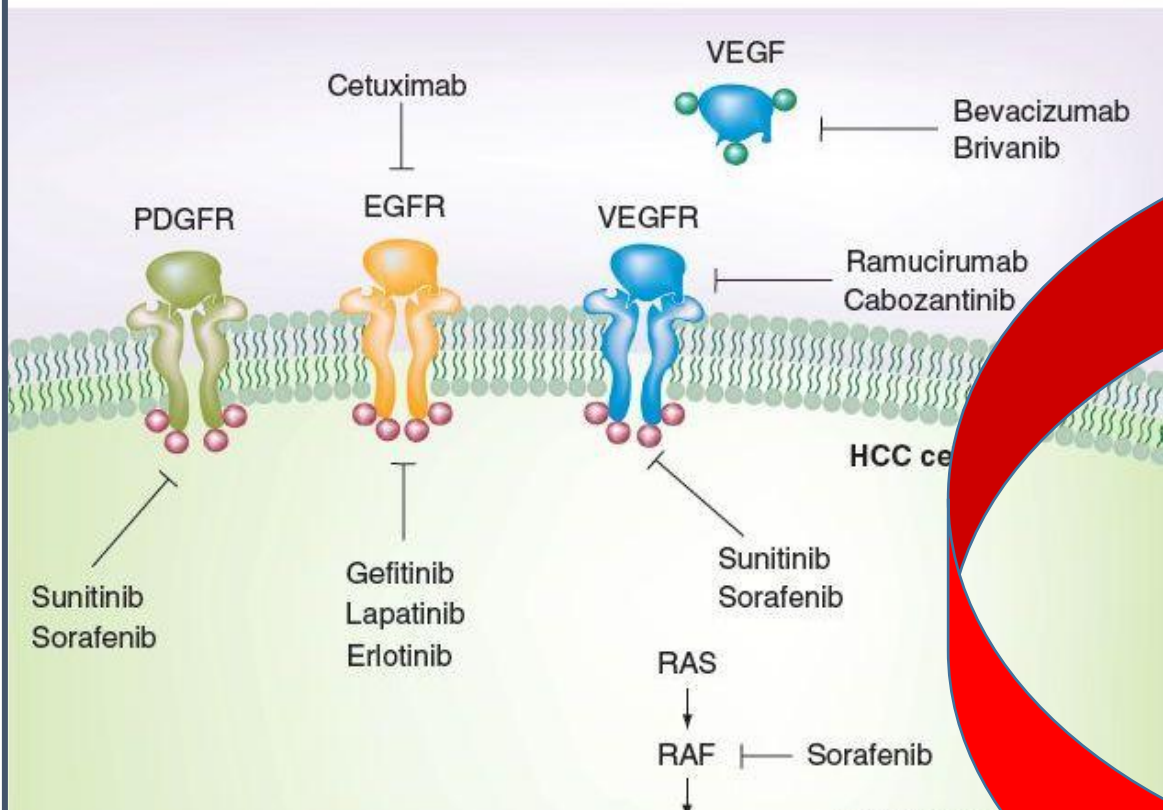
## FDA approves Opdivo for advanced melanoma

For Immediate Release

December 22, 2014

# Pembrolizumab Appears Promising in Treatment of Non-Small Cell Lung Cancer





Survival  
↓ Apoptosis

Ap

FOTORESEARCH®

# תודה רבה !

