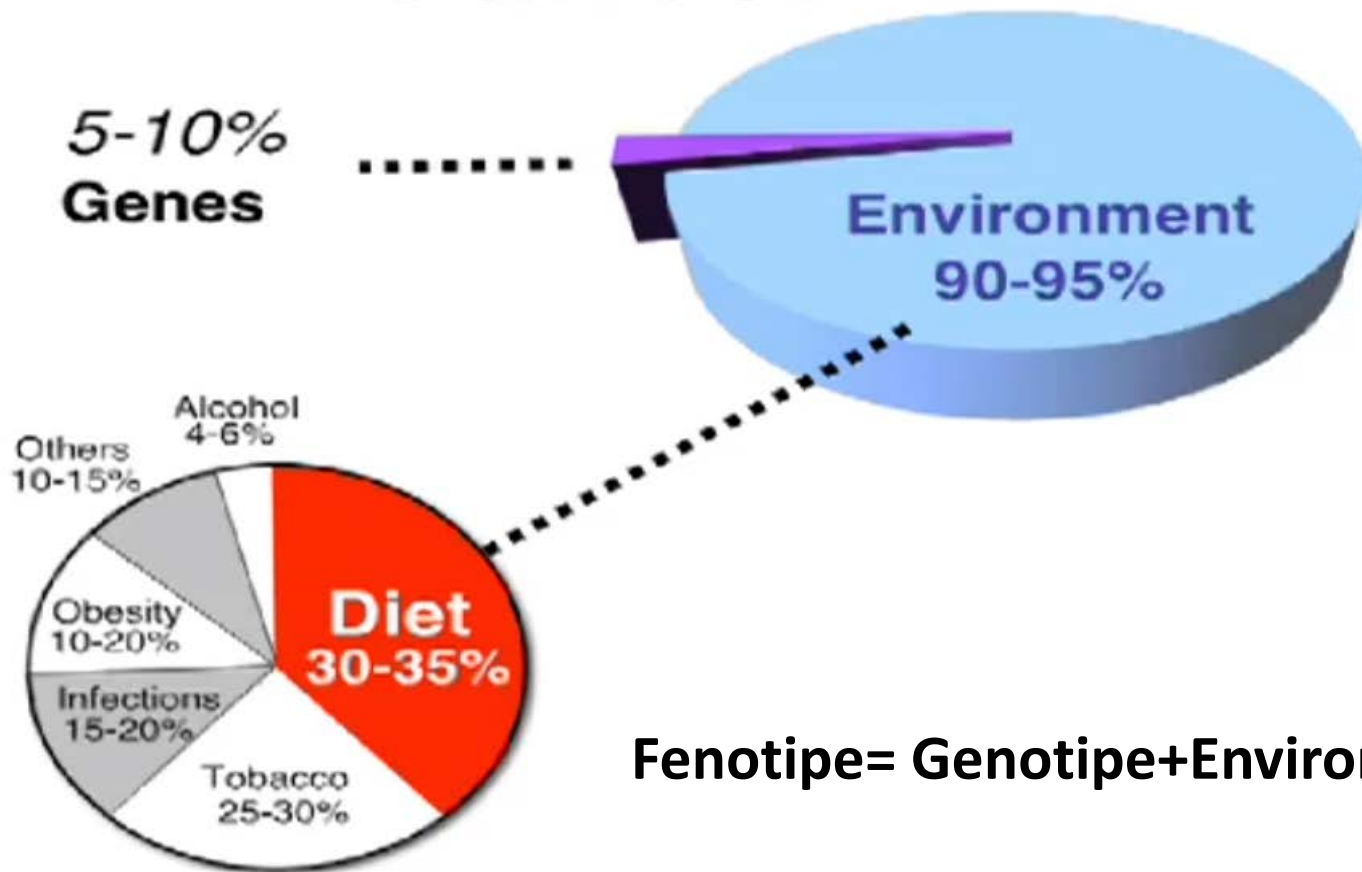


# Micro environment and cancer

Ramadhan

RS Kanker Dharmais

# Cancer



**Fenotype= Genotype+Environment**

# Breast cancer incidence vary among the country

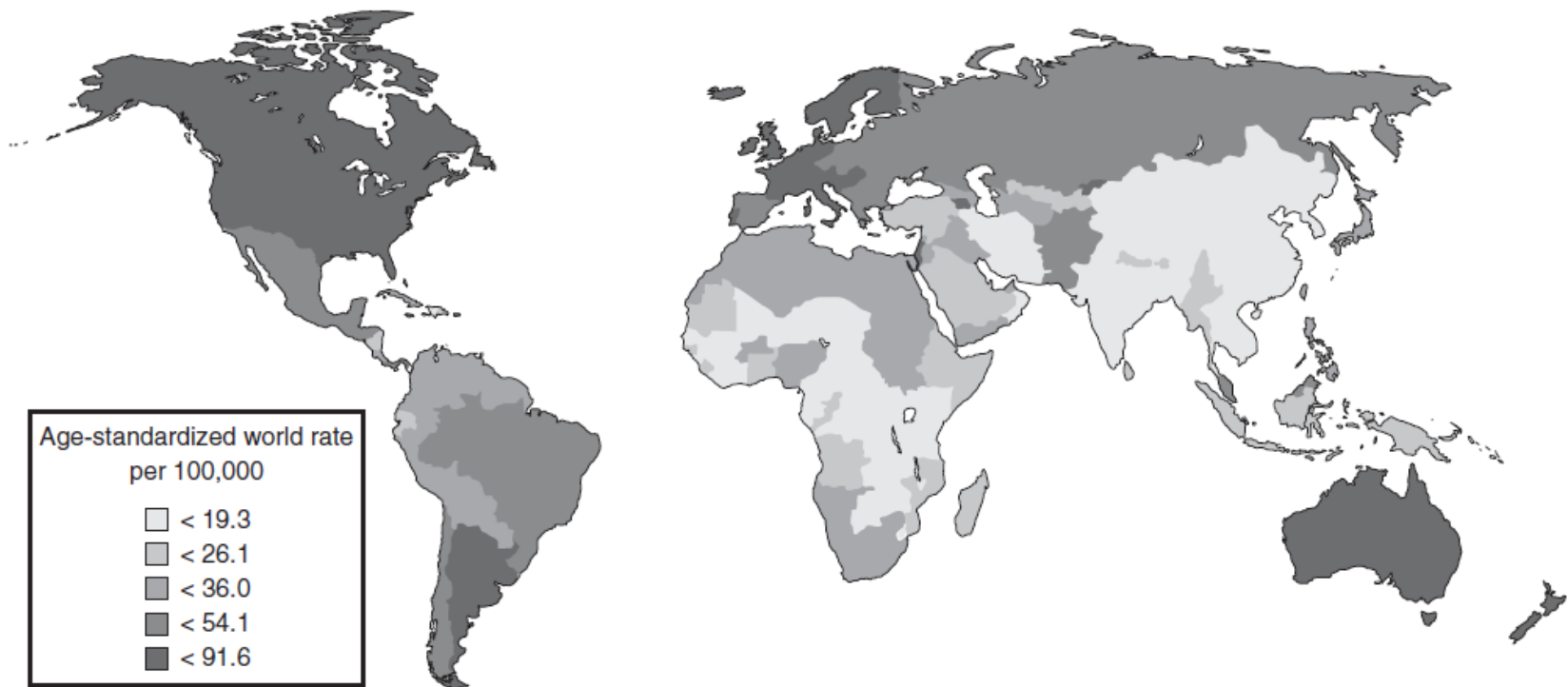
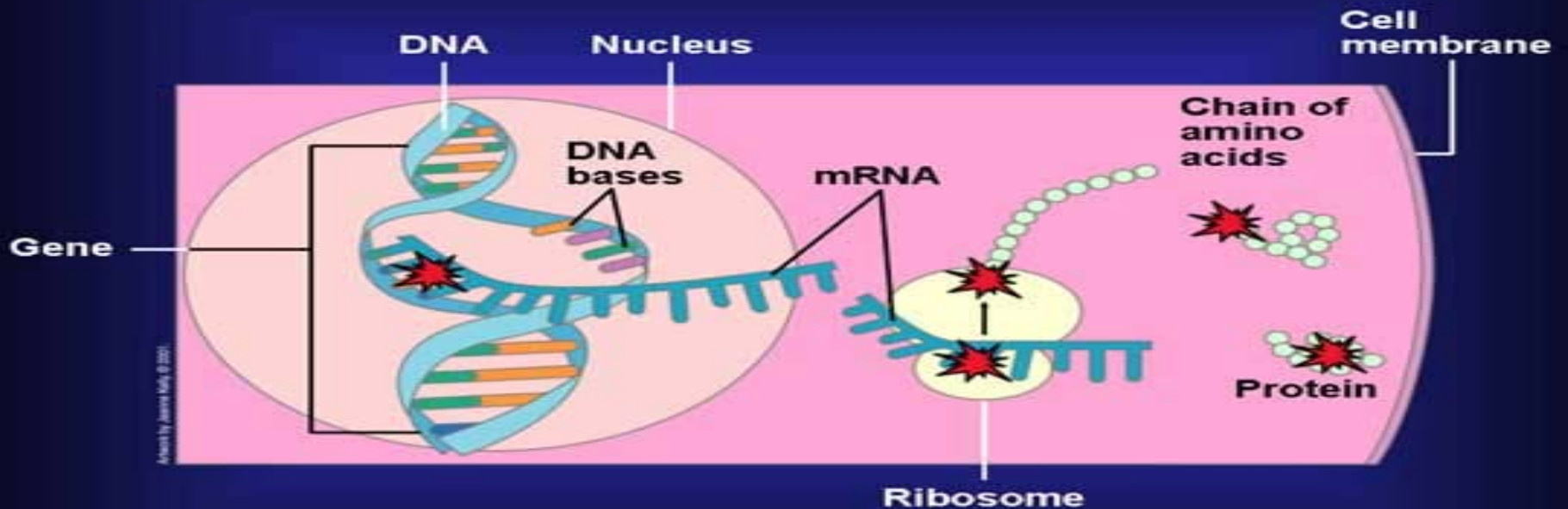


Figure 1-1 Estimated incidence by country, age-standardized by world standard population. (Data from Parkin DM. Global cancer statistics in the year 2000. *Lancet Oncol* 2001;2:533-543.)

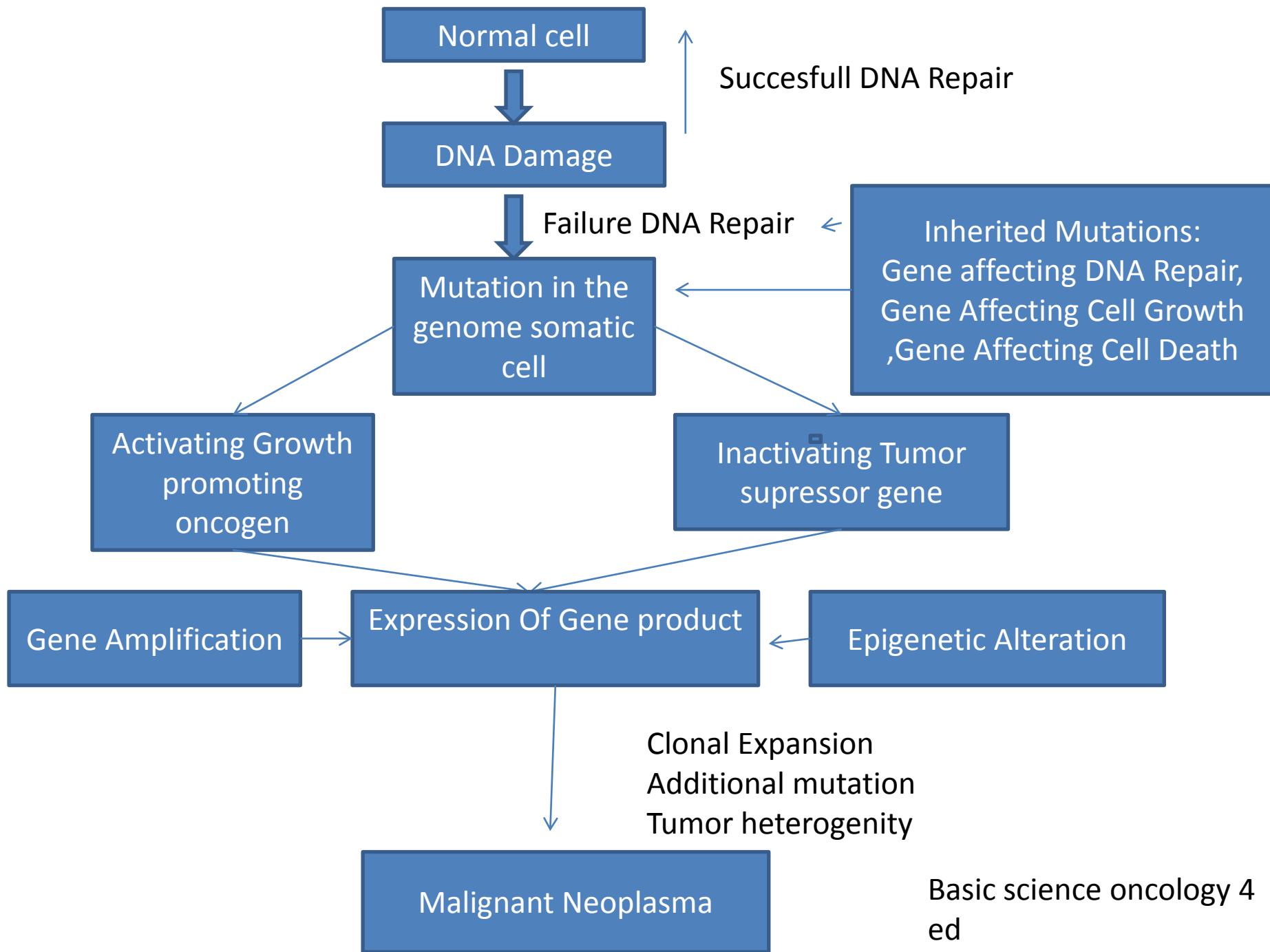
# Cancer Cell

- Cancer cells is Transform Cell : Function and Morphology

## Altered DNA->Altered Protein

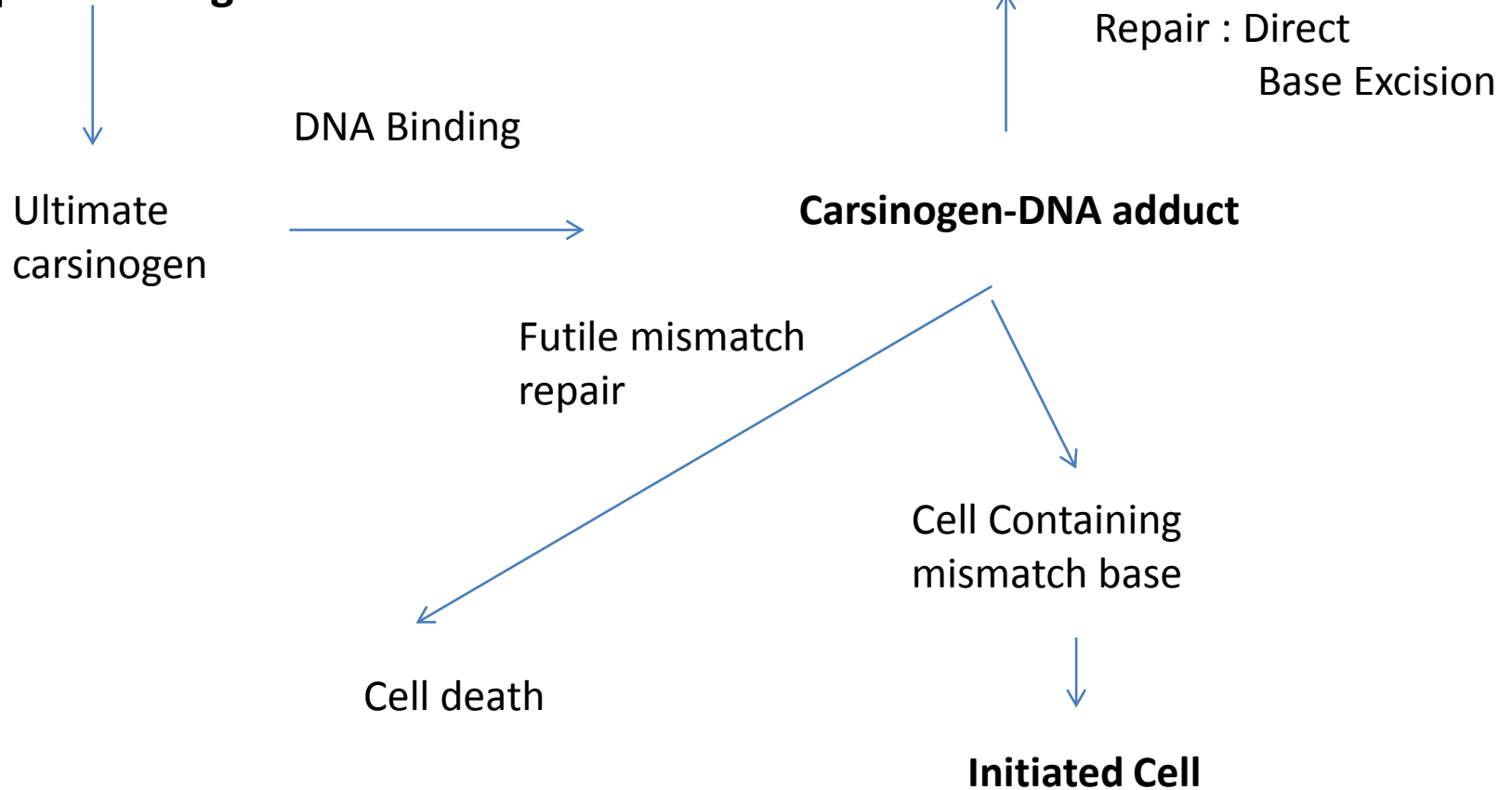


Adapted by Andrew Kelly, © 2001.



# Chemical Carcinogenesis

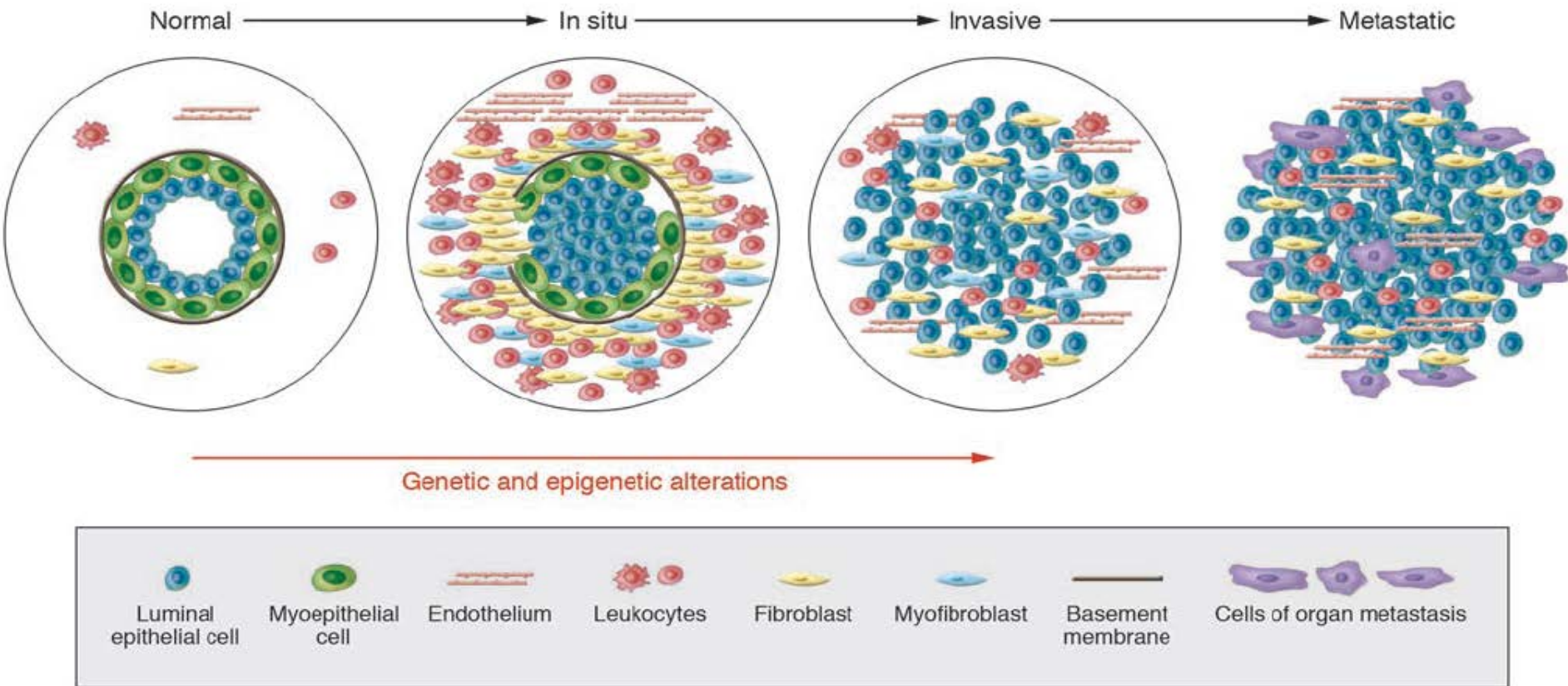
- **procarsinogen**



# Breast cancer: origins and evolution

Kornelia Polyak

Department of Medical Oncology, Dana-Farber Cancer Institute, and Department of Medicine, Harvard Medical School and Brigham and Women's Hospital, Boston, Massachusetts, USA.

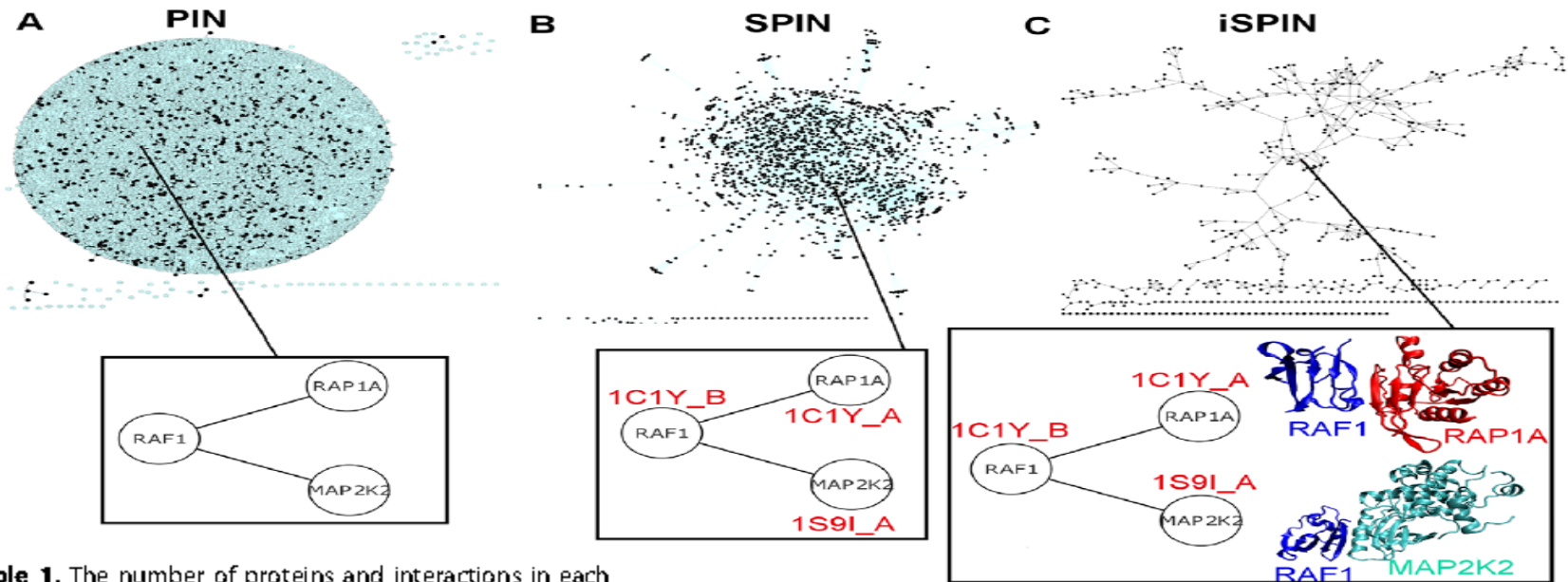




# Human Cancer Protein-Protein Interaction Network: A Structural Perspective

Gozde Kar, Attila Gursoy, Ozlem Keskin\*

Center for Computational Biology and Bioinformatics and College of Engineering, Koc University, Rumeli Feneri Yolu, Sariyer Istanbul, Turkey



**Table 1.** The number of proteins and interactions in each network.

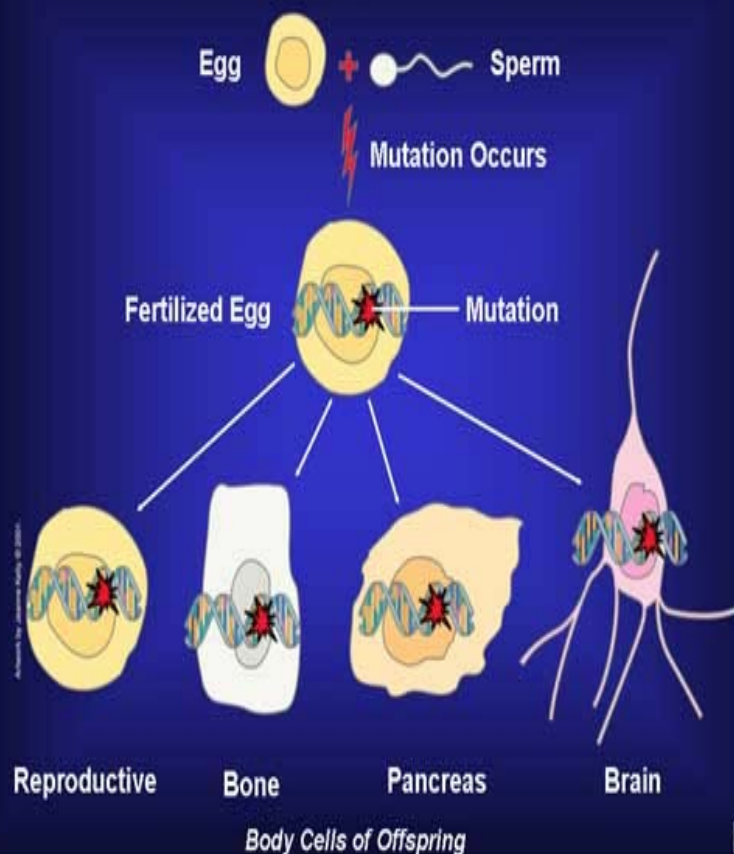
Network name	Protein	Interaction	Known complex in PDB
PIN	13584	85083	206
cPIN	8990	27413	149
SPIN	1702	5312	206
cSPIN	1303	3221	149
iSPIN	534	549	206
ciSPIN	381	363	149

Cancer proteins have smaller, more planar, less tightly packed and less hydrophobic binding sites compared to non-cancer proteins



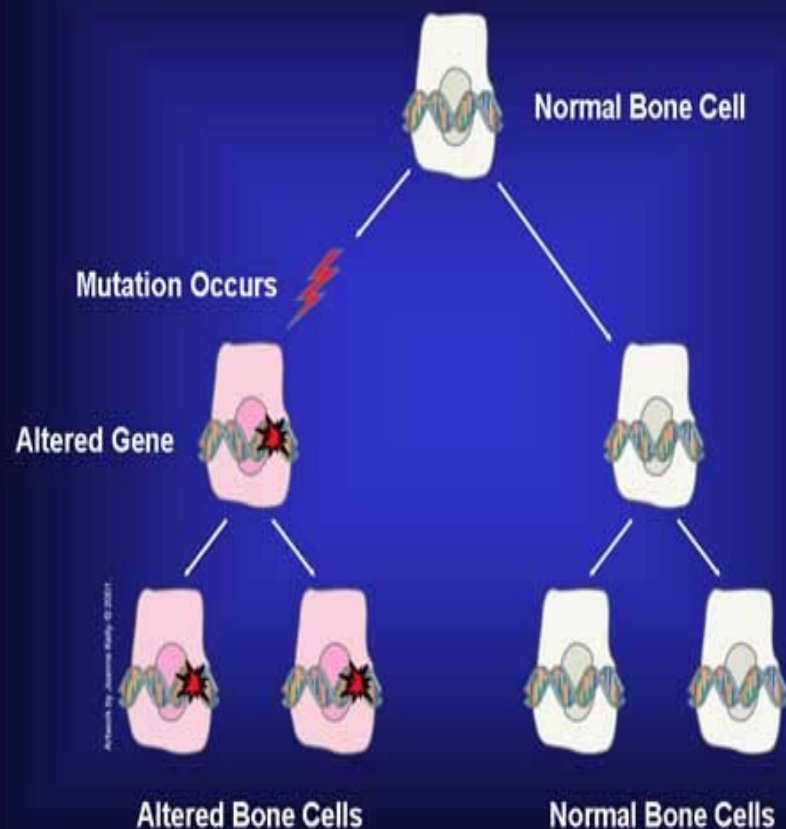
# Gene alteration and tissue specific

## Hereditary Mutations



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## Acquired Mutations

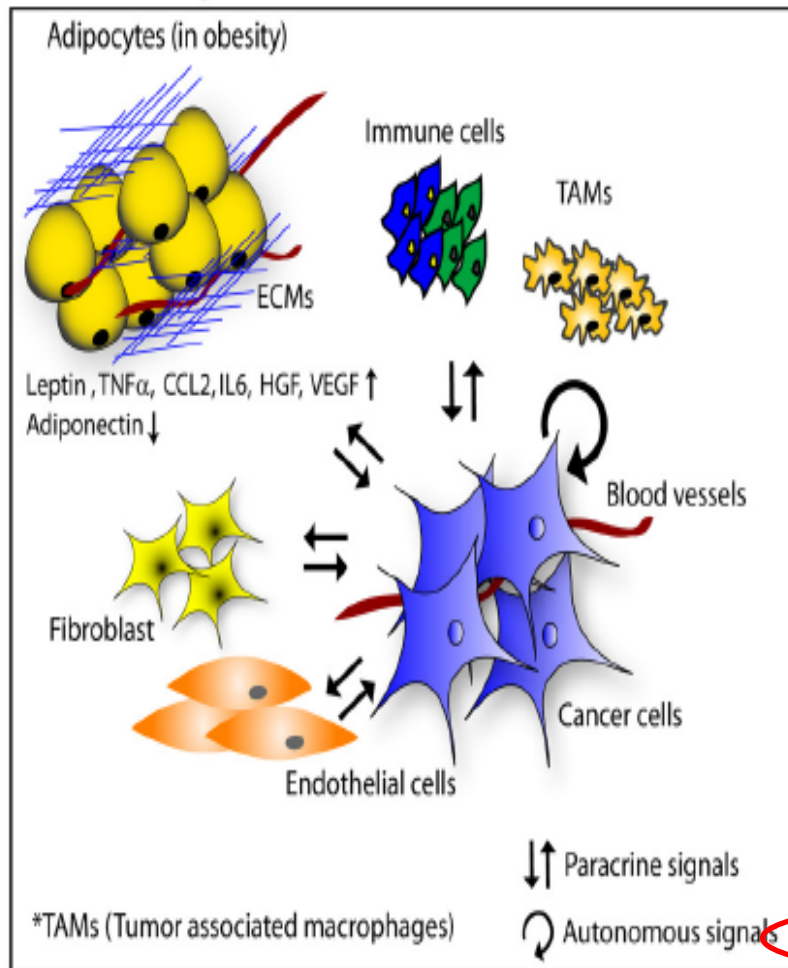


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INSTITUTE

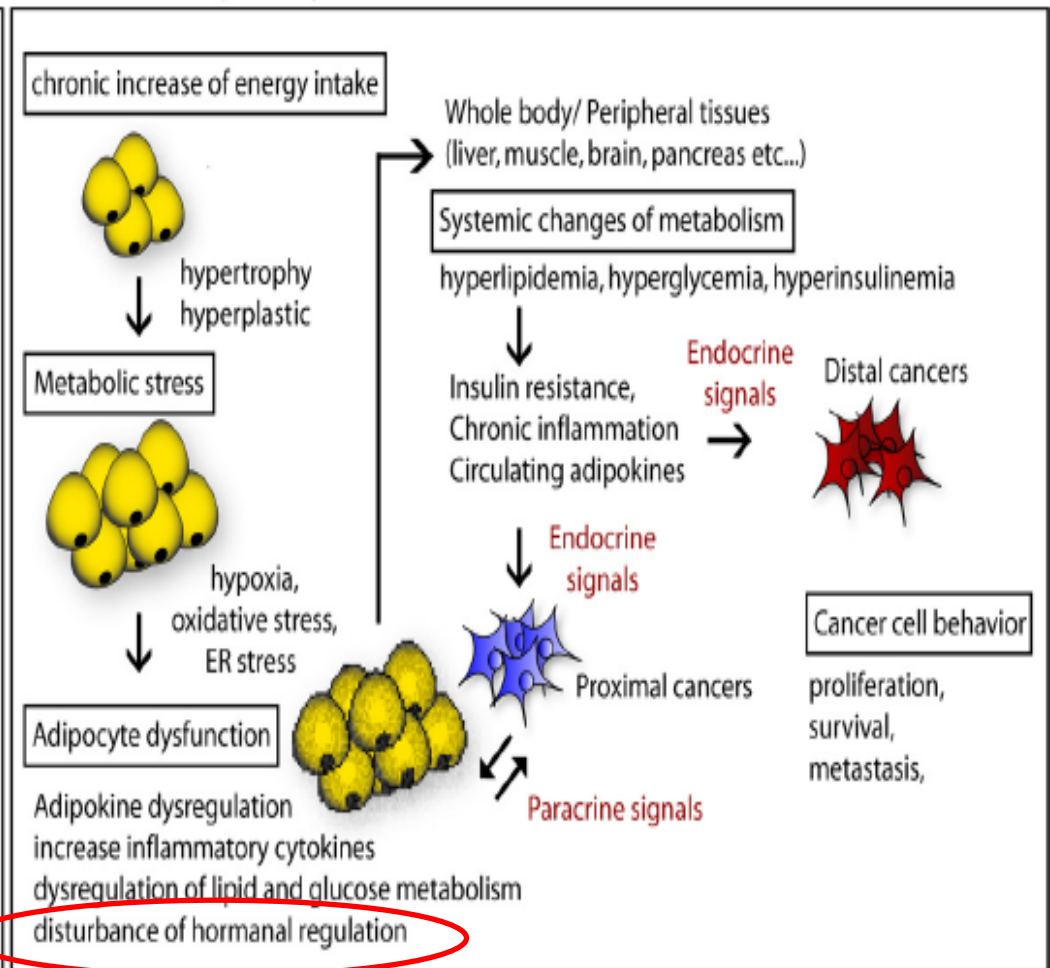
# Paracrine and Endocrine Effects of Adipose Tissue on Cancer Development and Progression

Jiyoung Park, David M. Euhus, and Philipp E. Scherer

## A Paracrine signals (tumor microenvironment)



## B Endocrine signals (systemic effects)



# Change the environment VS Chemotherapy

## Chemotherapy VS Ovarian suppression

Study	Treatment		Result
Scottish (6)	CMF	versus Surgery	No Difference
Scandinavian(8)	CMF	versus Xrt	No Difference
Zebra (12)	CMF	versus OS	No Difference
IBSG VIII	CMF	versus OS	No Difference
GROCTA 02(47)	CMF	versus OS + Tam	No Difference
<b>ABCSG (11)</b>	<b>CMF</b>	<b>versus OS+Tam</b>	<b>Better RFS fo OS+ Tam</b>
French	CMF	versus OS+Tam	No Difference
FASG 08(48)	FEC	Versus OS+ Tam	No Difference
GABG (14)	CMF	versus Goserilie	No Difference
Wallwiener and co workers(15)	CMF	versus Leuproline	No Difference

# Breast Cancer Risk Factor

- Age >40
- Related to hormonal activity:
  - 1. Early menarche
  - 2. Nulli para
  - 3. Contraception pill/HRT
  - 4. Physical activity
  - 5. Family history
- Demography

# Estrogen level japanese and america white

**Table II** Serum oestrogen and sex hormone binding globulin (SHBG) concentration of Japanese and American white subjects<sup>a</sup>

<i>Variable</i>	<i>Japanese</i>	<i>American whites</i>	<i>% difference<sup>b</sup></i>	<i>P-value<sup>c</sup></i>
Oestrone (pmol l <sup>-1</sup> )	83.2 (78.0, 88.4)	122.4 (109.5, 136.5)	47%	<0.0001
Oestradiol <sup>d</sup> (pmol l <sup>-1</sup> )	17.4 (16.3, 18.6)	23.8 (21.4, 26.6)	36%	<0.0001
Oestradiol <sup>e</sup> (pmol l <sup>-1</sup> )	22.4 (21.0, 23.9)	26.8 (23.7, 30.4)	20%	0.012
SHBG (nmol l <sup>-1</sup> )	58.6 (53.4, 64.1)	55.1 (45.8, 66.2)	- 6%	0.54

**Table III** Serum oestrogen and sex hormone binding globulin (SHBG) concentration of Japanese and American white subjects<sup>a</sup> adjusted for weight

<i>Variable</i>	<i>Japanese</i>	<i>American whites</i>	<i>% difference<sup>b</sup></i>	<i>P-value<sup>c</sup></i>
Oestrone (pmol l <sup>-1</sup> )	82.8	118.7	43%	<0.0001
Oestradiol <sup>d</sup> (pmol l <sup>-1</sup> )	17.8	22.6	27%	0.0009
Oestradiol <sup>e</sup> (pmol l <sup>-1</sup> )	22.7	26.3	16%	0.024
SHBG (nmol l <sup>-1</sup> )	56.9	59.3	+ 4%	0.64

# Breast cancer incidence vary among the country

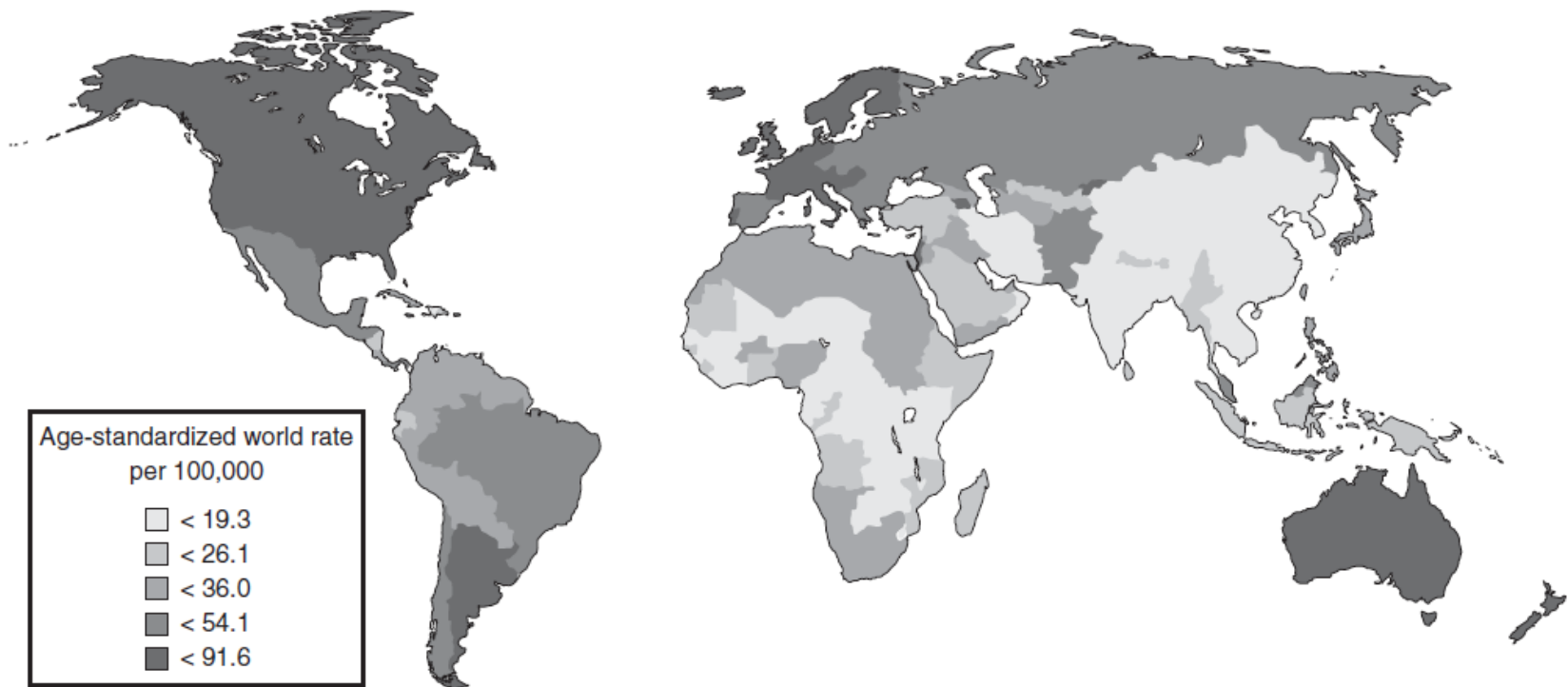
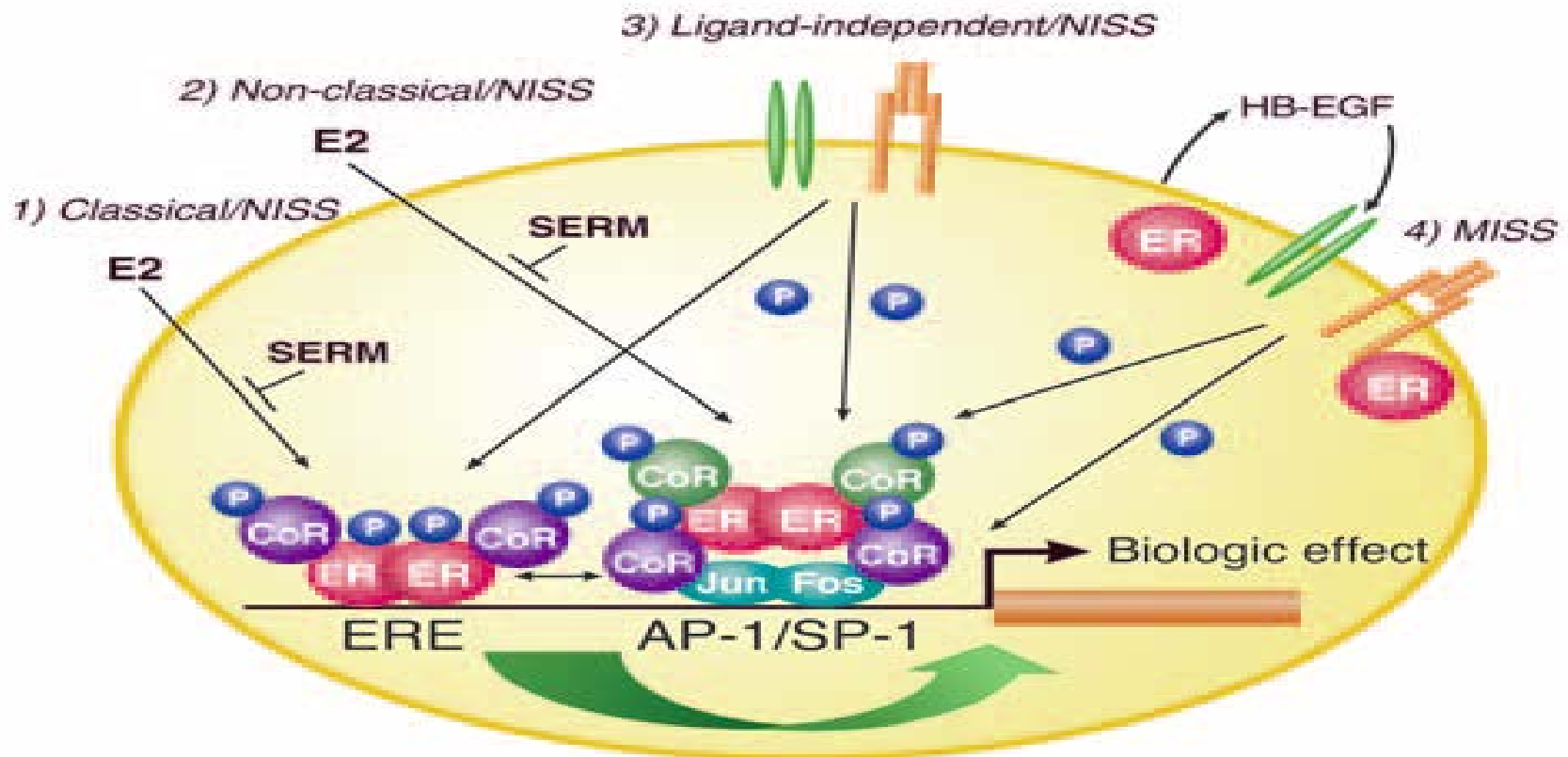


Figure 1-1 Estimated incidence by country, age-standardized by world standard population. (Data from Parkin DM. Global cancer statistics in the year 2000. *Lancet Oncol* 2001;2:533-543.)

# Estrogen and breast cancer progression

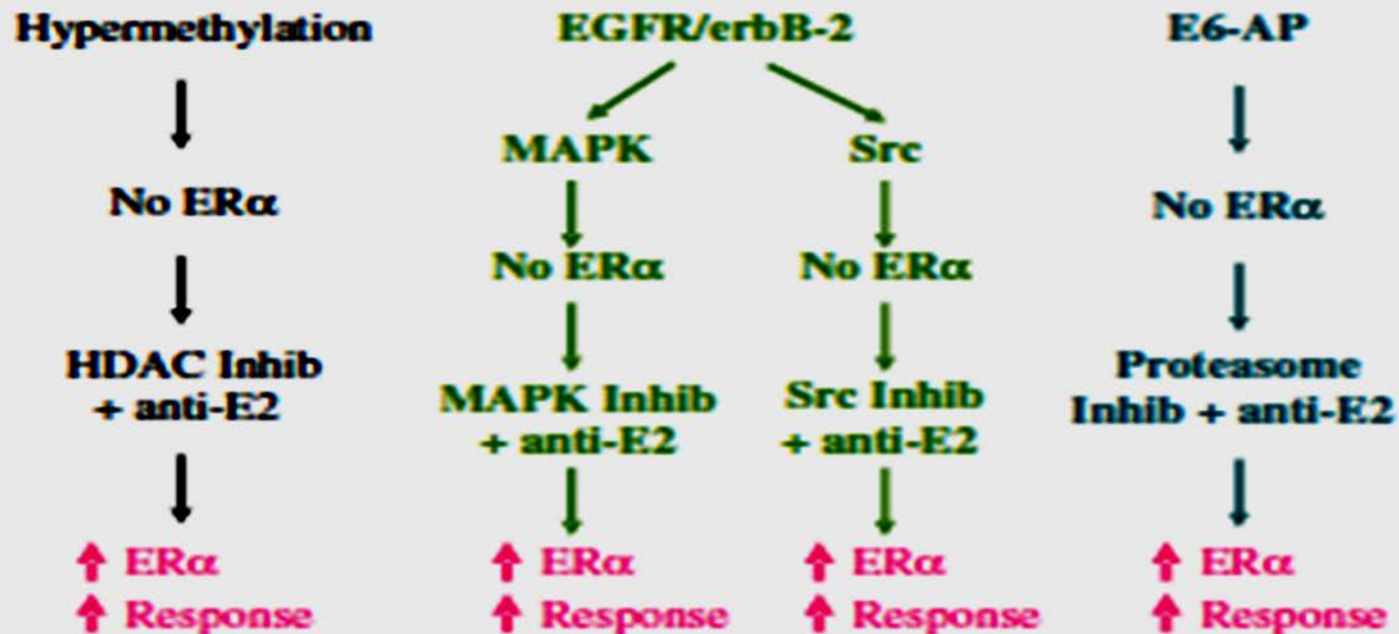


Biologic effect :up and down 700 gen in breast cancer progression follow 1300 others gen, involved in proliferation,invasive,metastasis, growth, differentiation, apoptosis,angiogenesis and epigenetic process.



# ER Re-expression and Re-sensitization to Endocrine Therapies in ER-negative Breast Cancers

Joeli A. Brinkman • Dorraya El-Ashry



**Figure 3** Subsets of ERα<sup>-</sup> breast cancer and possible therapeutics. Representative model of ERα<sup>-</sup> breast cancer subsets with potential mechanisms and therapies for each.

# Estrogen receptor- $\alpha$ polymorphism in a Taiwanese clinical breast cancer population: a case-control study

Wei-Chiang Hsiao<sup>1</sup>, Kung-Chia Young<sup>2</sup>, Shoei-Loong Lin<sup>3</sup> and Pin-Wen Lin<sup>1</sup>

- The same three SNPs reported in Western studies were found in the Taiwanese population studied, **but at different frequencies than in Western studies**. Small but statistically significant correlations were found between allele distribution, and individual and familial manifestation of breast cancer.

# Diverse Associations between *ESR1* Polymorphism and Breast Cancer Development and Progression

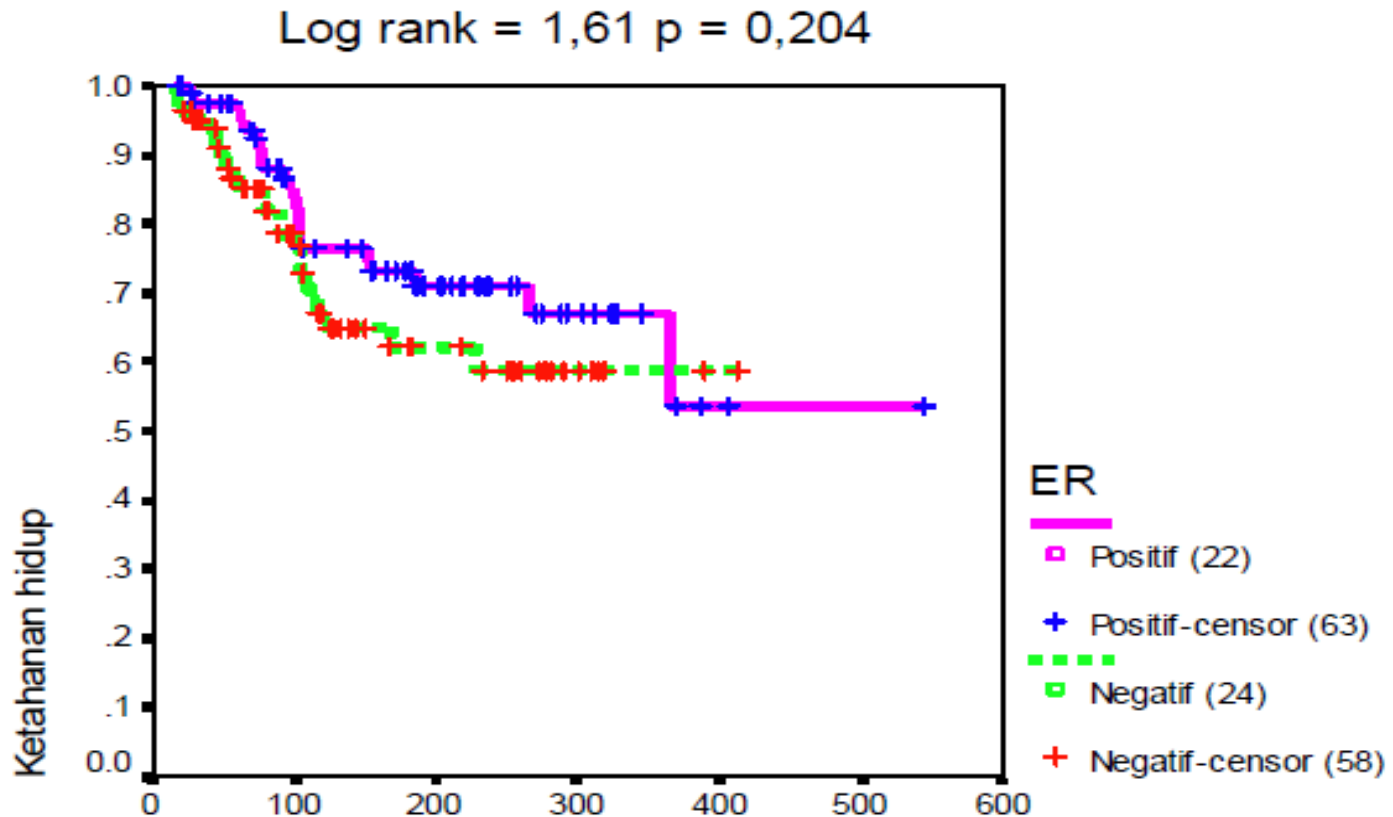
Shian-ling Ding, Jyh-Cherng Yu, Shou-Tung Chen, et al.

*Clin Cancer Res* 2010;16:3473-3484. Published OnlineFirst June 22, 2010.

- Conclusion The differences between the important *ESR1* SNPs identified in chinese women in this study and those identified in studies on western women with breast cancer suggest different roles of ER  $\alpha$  in this populations. *Clin Can Res* 16(13); 347-384.2010

# ER as prognostic factor

a. Pengaruh reseptor estrogen (ER) terhadap ketahanan hidup



Disertasi : Teguh Aryandono( Jogja,2006)

# Take home Message

- Ada perbedaan sifat biologi kanker payudara antara orang asia dan kaukasia
- Diperlukan penelitian multisenter agar didapatkan data akurat tentang latar belakang biologi molekular untuk penduduk indonesia
- Mungkin kita harus mengevaluasi dan mencari jenis pengobatan apa yang cocok spesifik untuk populasi kita

Terima kasih