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Workshop 1

At the completion of this activity, participants will be able to:

- Discuss the various basic science research pathways that affect disparities in Health Disparities; and
- Identify the implications of basic science research on current or future clinical practices.

ACHIEVING HEALTH EQUITY through Access, Advocacy, Treatment, and Policy Development

Johnnie L. Early, II, PhD, RPh

OPENING REMARKS

Elucidating the Aggressive Phenotype of Triple-Negative Breast Cancer

ALEXZANDER A.A. ASEA, PHD

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Elucidating the Aggressive Phenotype of Triple-Negative Breast Cancer

5th Health Disparities Conference

Achieving Health Equity through Access, Advocacy, Treatment, and Policy Development

Xavier University of Louisiana, New Orleans, LA
March 6-8, 2012

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Triple-Negative Breast Cancer (TN-BC)

Despite lower incidence and the steady improvement in screening, African-American (AA) women are more likely to die of breast cancer than Caucasian women (CA).

ARTICLE

Race and Ethnicity and Breast Cancer Outcomes in an Underinsured Population

Original Contribution

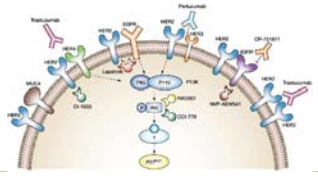
Risk Factors for Fatal Breast Cancer in African-American Women and White Women in a Large US Prospective Cohort

Triple-Negative Breast Cancer (TN-BC)

Recent studies on surface receptors and gene expression of breast tumors from African American (AA) and Hispanic (HP) women have come up with a term triple-negative breast cancer (TNBC).

The disease gets its name because of testing negative for:

Estrogen Receptor (ER)
Progesterone Receptor (PgR)
Human Epidermal Growth Factor Receptor 2 (HER2) gene



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Triple-Negative Breast Cancer (TNBC)

TN-BC ($HER2^-/ER^-/PgR^-$) - Creates a disease quite distinct from that seen in CA women ($HER2^+/ER^+/PgR^+$), and is a much more aggressive disease without tumor-specific treatment options and accounts for 15% of all types of breast cancer with higher percentages in premenopausal AA and HP women.

Although slightly responsive to chemotherapy, TNBC is more difficult to treat and generally insensitive to most available hormonal or targeted therapeutic agents.

Depending on its stage of diagnosis, TNBC can be extremely aggressive—recurring and metastasizing more often than other subtypes of breast cancer.

HSP are highly expressed in certain cancers

Elevated heat shock protein (HSP) levels have been found in various tumors, including:

- Breast cancer
- Prostate Cancer
- Pancreatic Cancer
- Gastric cancer
- Uterine cancer
- Ovarian cancer
- Head and Neck cancer
- Cancers arising from the nervous system and urinary system

What are heat shock proteins (HSP)?

Heat shock proteins (HSP) are molecular chaperones that are found in all cellular organisms, which function to protect cells from a wide variety of stressful stimuli including;

Environmental stimuli (U.V. radiation, heat shock, heavy metals and amino acids)

Pathological stimuli (viral, bacterial, parasitic infections or fever, inflammation, malignancy or autoimmunity),

Physiological stimuli (growth factors, cell differentiation, hormonal stimulation or tissue development)

Psychological stress and exercise

by activating the stress response

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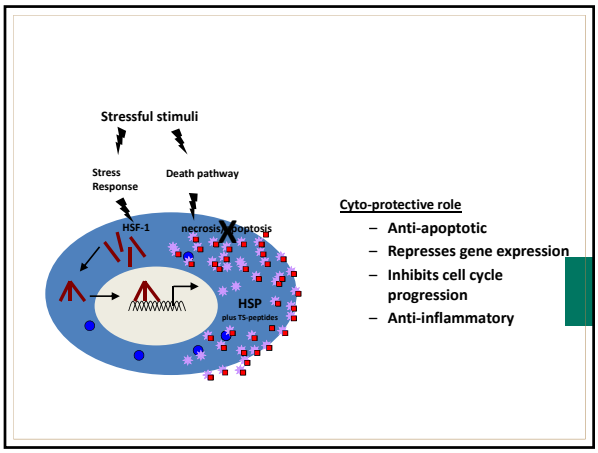


Cyto-protective role

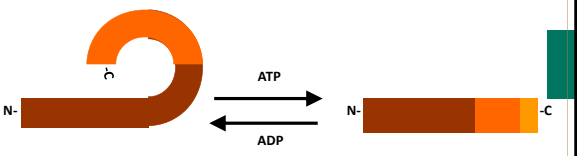
- Anti-apoptotic
- Represses gene expression
- Inhibits cell cycle progression
- Anti-inflammatory

How do HSP protect cells?

HSP are molecular chaperones

HSP protect cells by "holding" and "folding" proteins and peptides – a chaperone

This stops proteins within the cell from aggregating and allows proteins And peptides to function properly



Murine breast carcinoma 4T1 cells are a 6-thioguanine-resistant cell line selected from 410.4 tumor without mutagen treatment. When injected into the abdominal breast gland of female BALB/c mice (8–12 weeks old), 4T1 spontaneously produce highly metastatic tumors that can metastasize to the lung, liver, lymph nodes and brain while the primary tumor is growing in situ. The primary tumor does not have to be removed to induce metastatic growth. The tumor growth and metastatic spread of 4T1 cells in BALB/c mice very closely mimic human breast cancer.

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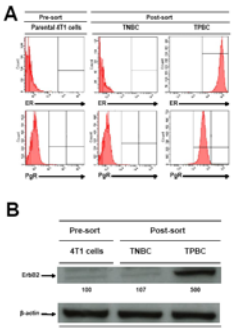
Transfection of rat HER2, ER and PgR genes into 4T1 cells produces a population of TNBC and TPBC.



Selection of triple-negative breast cancer-cancer ste C-TICs).

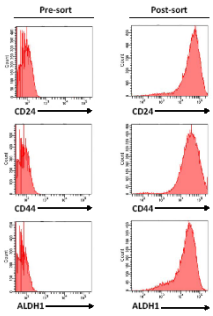


Table 1. TNBC-TICs exhibit a greater clonogenic growth potential as compared to TNBC, TPBC-TICs, TPBC or parental 4T1 cells.

Table 1. TNBC-TICs exhibit a greater clonogenic growth potential as compared to TNBC, TPBC-TICs, TPBC or parental 4T1 cells.

Cell type[a]	Number of cells transplanted	Fraction of mice with tumors[b]
TPBC-derived:		
$CD24^+ALDH1^+CD44^{low}$	500	5/5
$CD24^+ALDH1^+CD44^{low}$	100	5/5
$CD24^+ALDH1^+CD44^{low}$	50	4/5
$CD24^+ALDH1^+CD44^{low}$	25	2/5
$CD24^+ALDH1^+CD44^{low}$	10	3/5
TPBC-derived:		
$CD24^+ALDH1^+CD44^{int}$	500	1/5
$CD24^+ALDH1^+CD44^{int}$	100	0/5
$CD24^+ALDH1^+CD44^{int}$	50	0/5
$CD24^+ALDH1^+CD44^{int}$	25	0/5
$CD24^+ALDH1^+CD44^{int}$	10	0/5
TNBC-derived:		
$CD24^+ALDH1^+CD44^{low}$	500	5/5
$CD24^+ALDH1^+CD44^{low}$	100	5/5
$CD24^+ALDH1^+CD44^{low}$	50	5/5
$CD24^+ALDH1^+CD44^{low}$	25	5/5
$CD24^+ALDH1^+CD44^{low}$	10	4/5
TNBC-derived:		
$CD24^+ALDH1^+CD44^{int}$	500	1/5
$CD24^+ALDH1^+CD44^{int}$	100	0/5
$CD24^+ALDH1^+CD44^{int}$	50	0/5
$CD24^+ALDH1^+CD44^{int}$	25	0/5
$CD24^+ALDH1^+CD44^{int}$	10	0/5

[a]Tumor cells derived from TPBC or TNBC cells were stably transfected with eGFP using the lentivirus transduction technique as described in detail in the Methods section.
[b]Twenty-one days post tumor cell transplantation into the mammary pad of naive female BALB/c mice, animals were scanned and eGFP signal from the tumors were measured using the Maestro™ in vivo imaging system (CRI), and spectral unmixing was performed to segregate skin and hair auto fluorescence and to measure the true eGFP signal, as described in detail in the Methods section. Data is the fraction of mice with tumors (n=5).

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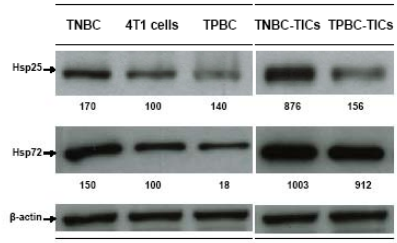
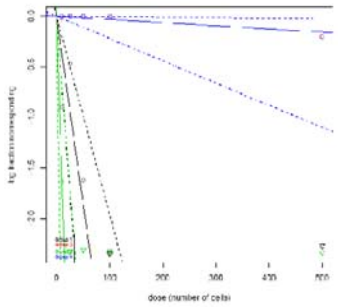
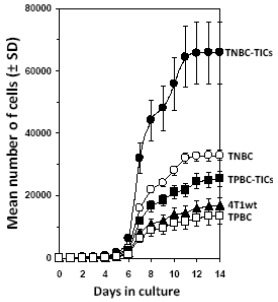
TNBC-TICs express higher levels of Hsp25 and Hsp72/HspA1A than TNBC, TPBC-TICs, TPBC or parental 4T1 cells.



CD24^{+}/ALDH1^{+}/CD44^{high} identifies a population of TICs in both TNBC and TPBC cell fractions.



TNBC-TICs proliferate significantly faster than TNBC, TPBC-TICs, TPBC or parental 4T1 cells.



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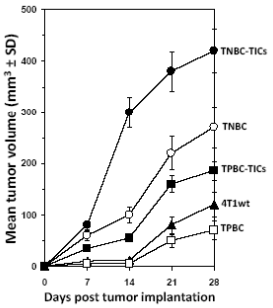
Tumors from TNBC-TICs grow significantly larger than TNBC, TPBC-TICs, TPBC or parental 4T1 cells.



TNBC-TICs produce significantly more metastatic foci than TNBC, TPBC-TICs, TPBC or parental 4T1 cells.

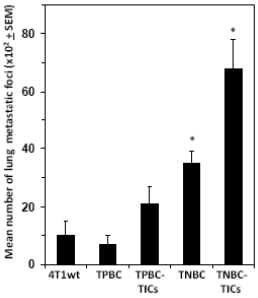


Table 2. Confidence interval (95%) for repopulating mammary cell frequency.

Table 2. Confidence interval (95%) for repopulating mammary cell frequency.

Cell type	Confidence intervals for 1/(TIC+ frequency)[a]		
	Lower	Estimate	Upper
TPBC-derived:			
$CD24^+/ALDH1^+/CD44^{high}$	51.0	27.03	14.4
$CD24^+/ALDH1^+/CD44^{low}$	22124.7	8168.93	454.3
TNBC-derived:			
$CD24^+/ALDH1^+/CD44^{high}$	14.9	6.22	2.8
$CD24^+/ALDH1^+/CD44^{low}$	22124.7	8168.93	454.3

[a]Confidence interval (95%) for repopulating mammary cell frequency for the data in Table 1. Data were generated using ELDA, a software application for limiting dilution analysis (LDA) as previously described [34].

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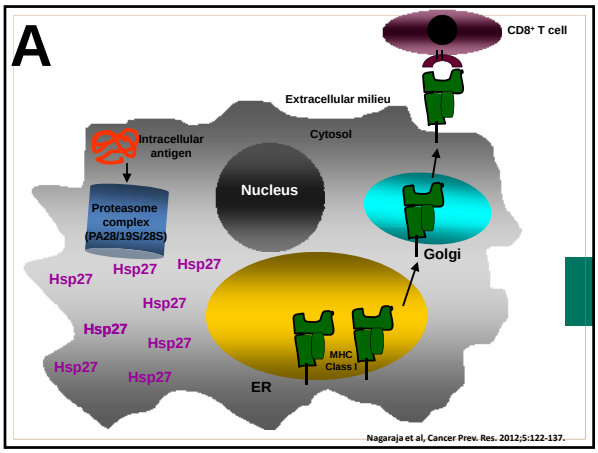

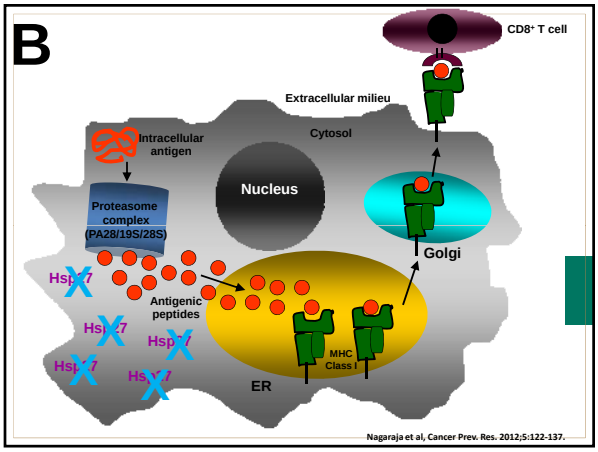

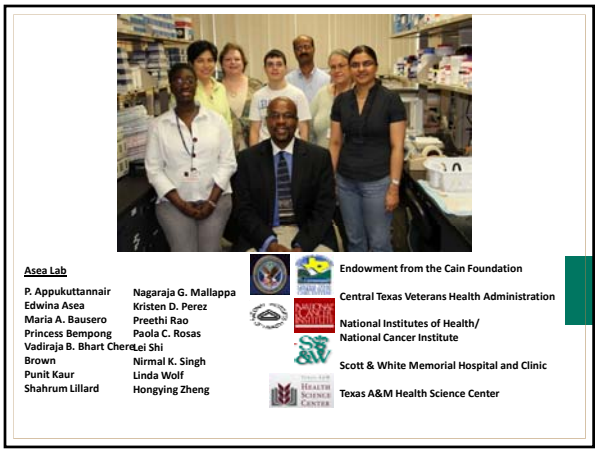

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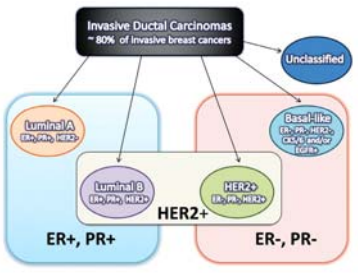
Glyceollins as Novel Targeted Therapeutic for the Treatment of Triple-Negative Breast Cancer

SYREETA L. TILGHMAN, PHD

Glyceollins as Novel Targeted Therapeutic for the Treatment of Triple-Negative Breast Cancer

Syreeta L. Tilghman, PhD
Xavier University of Louisiana
College of Pharmacy

Breast Cancer Subtypes



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Clinical Features of Triple Negative Breast Cancer (TNBC)

- 'Triple negative': Lacks ER, PR and HER2
- TNBC accounts for 10–17% of all breast carcinomas in US
- More common among African-Americans
- Earlier age of onset- premenopausal women
- Aggressive clinical history with poor clinical outcome
- Higher relapse rate than other subtypes
- No specific targeted therapy

TNBC is a Disease of Health Disparity

- Population differences in tumor ER status and disease grade
- Race/ethnic disparity in prevalence of basal-like/triple-negative breast tumors

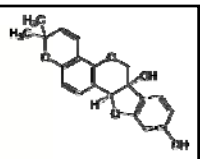
Table 2. Prevalence of Breast Cancer Subtypes According to Race and Menopausal Status

		No. (%)			
		African American*		Non–African American†	
Tumor Status	All Cases	Premenopausal (n = 97)	Postmenopausal (n = 99)	Premenopausal (n = 154)	Postmenopausal (n = 136)
Basal-like	100	28 (29)	14 (14)	26 (17)	22 (16)
HER2+/ER–	33	9 (9)	7 (7)	9 (6)	8 (6)
Luminal A	256	36 (36)	58 (59)	83 (54)	79 (58)
Luminal B	77	18 (18)	16 (16)	30 (19)	23 (16)
Unclassified	31	6 (6)	4 (4)	16 (10)	5 (4)

*P<.001, χ^2 test by basal-like vs other tumor types in premenopausal vs postmenopausal African American women.
†P = .04, χ^2 test by basal-like vs other tumor types in premenopausal vs postmenopausal non–African American women.

(JAMA 2006, 295: 2492 – 2502)

Glyceollins



- Glyceollins are the primary group of phytoalexins produced in soybeans under stress
- Isolated from activated soy
- Novel antiestrogens that suppress human breast and ovarian carcinoma tumorigenesis
- Bind to ER, inhibit estrogen induced tumor progression and inhibit the expression of estrogen responsive genes

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Traditional mRNAs vs miRNAs

DNA

Transcription

(first step of regulation)

mRNA

inhibition of translation

...no protein... no function

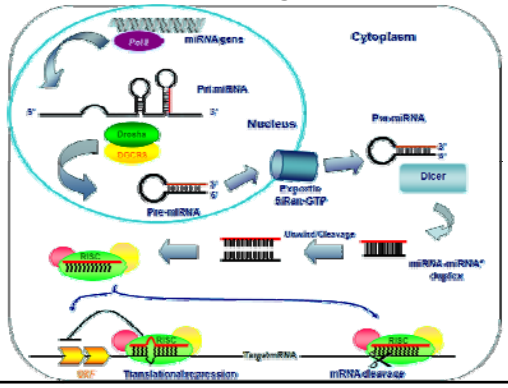
MicroRNAs are a new class of non-protein coding, endogenous, small RNAs

Regulates gene expression by inhibition of mRNA expression

Very small molecules ~22 nt

New step in the regulation of gene expression

miRNA Biogenesis



Roles in Cancer

- Recent studies show that some microRNAs regulate cell proliferation and apoptosis, processes that are important in cancer formation
- In addition, some miRNAs may function as oncogenes or tumor suppressors
- More than 50% of miRNA genes are located in cancer associated genomic regions or in fragile sites

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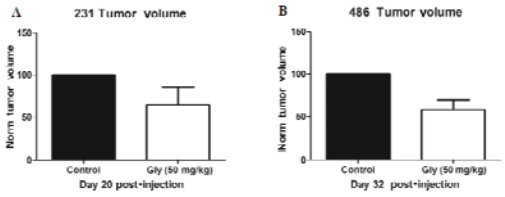
Hypothesis

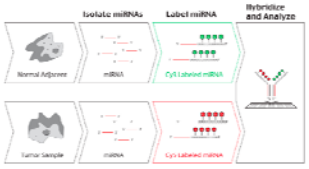
Glyceollins, novel phyto-antiestrogens, have antitumorigenic effects on triple negative breast cancer cells through alterations in miRNA and proteomic expression profiles

Glyceollins Decrease Tumorigenesis of Triple-Negative Breast Cancer Cells

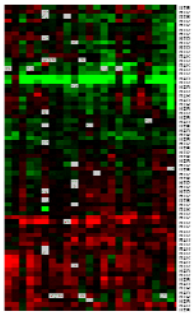


Altered Expression of miRNAs in Cancer

Colon Cancer vs. Normal Adjacent Tissue



Red indicates that miRNA is over-expressed relative to pooled sample



(Asuragen data)

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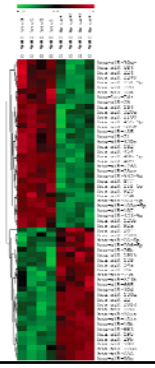
Glyceollins Alter the miRnome of Triple-Negative Breast Carcinoma Cells



miRNAs with Increased Expression Following Glyceollin Treatment

miRNA	Mean fold-change	p-value	miRNA	Mean fold-change	p-value
19a	2.91	<0.01	130a	1.69	<0.001
19b	1.35	<0.001	301a	1.22	<0.001
23	1.32	<0.001	138	1.34	<0.01
26b	1.79	<0.01	181c	7.03	<0.01
			181d	4.99	<0.01
28-3p	1.16	<0.01	199	1.51	<0.01
29b	2.92	<0.001	638	1.44	<0.001
29c	7.06	<0.01			
30d	1.19	<0.01	663	2.06	<0.01
34a	1.76	<0.01	940	1.58	<0.001
98a	1.31	<0.001	1280	1.27	<0.01
107	1.13	<0.01	1915	1.29	<0.01

Tumor suppressors

Epithelial to Mesenchymal Transition

miRNAs with Decreased Expression Following Glyceollin Treatment

miRNA	Mean fold change	p value	miRNA	Mean fold change	p value
10a	-1.80	<0.01	361-3p	-1.27	<0.001
21	-1.31	<0.01	493-5p	-1.47	<0.01
23a*	1.80	<0.001	434	1.73	<0.01
25	1.74	<0.001	455-3p	1.56	<0.01
30a*	1.43	<0.01	486-3p	2.00	<0.01
92a	1.10	<0.01	542-5p	3.03	<0.001
125b	-1.14	<0.001	584	-1.37	<0.01
151-3p	1.27	<0.01	720	1.36	<0.01
151-5p	1.17	<0.01			
182	1.48	<0.01	877	2.01	<0.001
183	-1.33	<0.001	923	-1.40	<0.001
193a-3p	-1.68	<0.001	1180	-1.96	<0.01
197	-1.99	<0.001	1246	-1.53	<0.01
221	-1.91	<0.01	1768	-1.89	<0.001
320a	-1.14	<0.01	let-7d*	-1.52	<0.01
320c	-1.11	<0.01			

OncomiRs promoting tumorigenesis

OncomiRs promoting metastasis

Maintenance of mesenchymal phenotype

Cell migration and invasion

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Glyceollins Alter the Proteome of MDA-MB-231 in a Manner Indicative of Tumor Suppressive Effects

Spot	Gene symbol	Gene name	Mean intensity ratio	p value
203	EEF1D	Elongation factor 1-δ	36.30	<0.01
1004	ARHGDIA	Rho GDP-dissociation inhibitor 1	115.85	<0.001
2107	CLIC1	Chloride intracellular channel protein 1	179.94	<0.001
2103	TPD52L2	Isoform 2 of tumor protein D54	43.90	<0.01
2204	EIF2S1	Eukaryotic translation initiation factor 2 subunit 1	55.62	<0.01
3103	CLIC4	Chloride intracellular channel protein 4	41.37	<0.01
5004	NME1	Non-metastatic cells 1 (NM23-H1)	24.89	<0.01
5304	GIPC1	PDZ domain containing protein GIPC1	71.41	<0.01
5403	MAP2K2	Mitogen-activated protein kinase kinase 2	29.96	<0.01
5406	TARDBP	TAR DNA-binding protein 43	28.96	<0.01
7706	VIM	Vimentin	-11.84	<0.01
9903	DDX1	ATP-dependent RNA helicase DDX1	-34.75	<0.001
9904	KHSRP	Far upstream element-binding protein 2	-31.31	<0.01
7704	SPC13	SPC13 related protein	10.07	<0.01
5506	HNRPH1	Heterogeneous nuclear ribonucleoprotein H1	58.63	<0.001
7302	HNRPH3	Heterogeneous nuclear ribonucleoprotein H3	-66.36	<0.01
8404	HNRPD	Heterogeneous nuclear ribonucleoprotein D0	-15.78	<0.001
3605	FKBP4	FK506-binding protein	-17.83	<0.01

Metastasis suppressor gene and target of miR-486-5p and miR-542-5p

Epithelial to mesenchymal transition and target of miR-30d

Conclusions

- Glyceollins inhibit the tumor growth of triple negative breast cancer cell lines
- Glyceollins dysregulated the miRNA expression of which:
  - Hallmark of numerous carcinomas including breast cancer
  - Consistent with a less aggressive phenotype

Acknowledgements

- Lyndsay Rhodes-Vanhoy
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- NIH/NCRR RCMI 5G12RR026260-02
- Office of Naval Research 09-10N00012-10-1-0270

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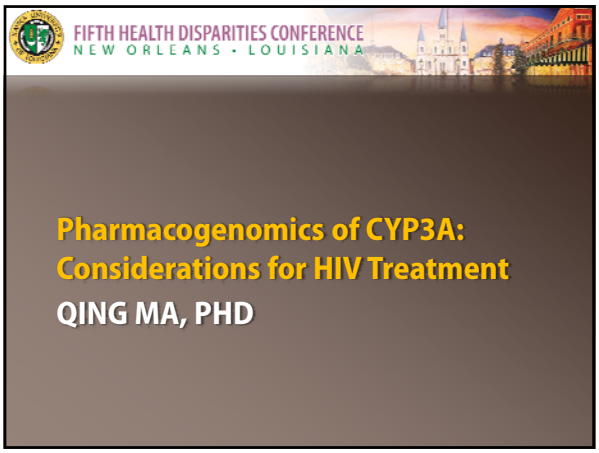

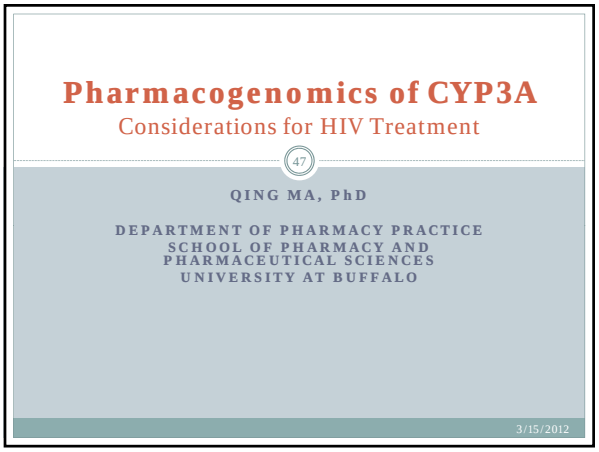

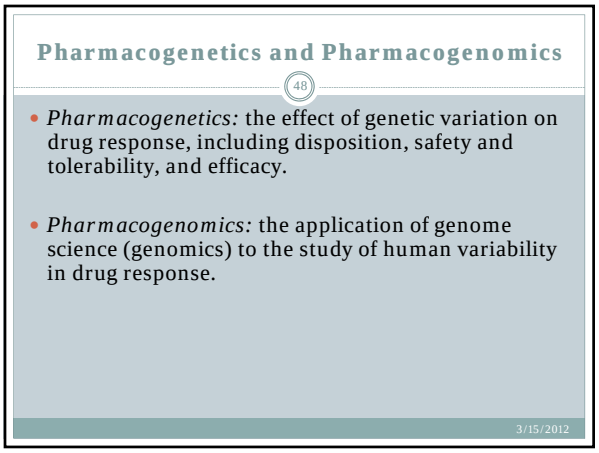

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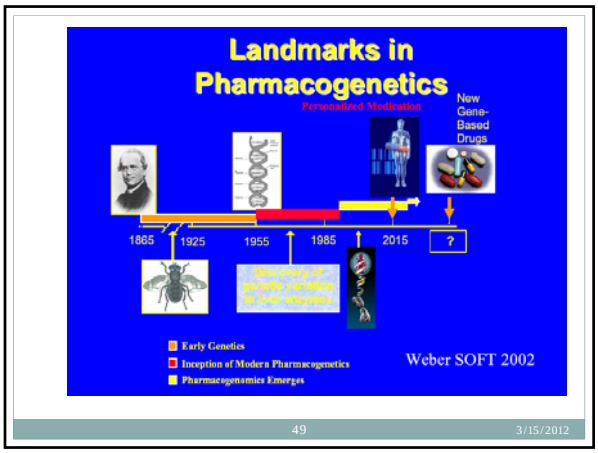

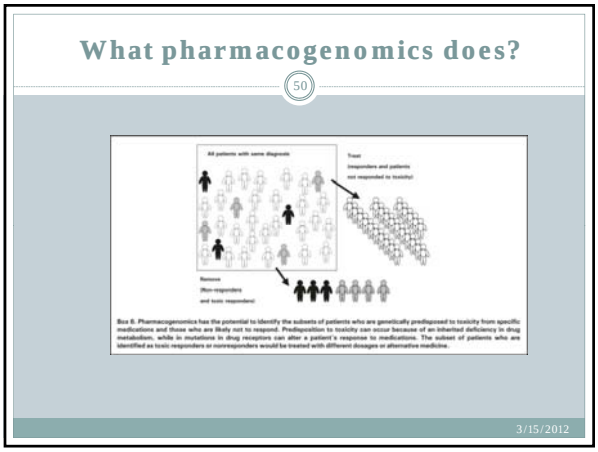

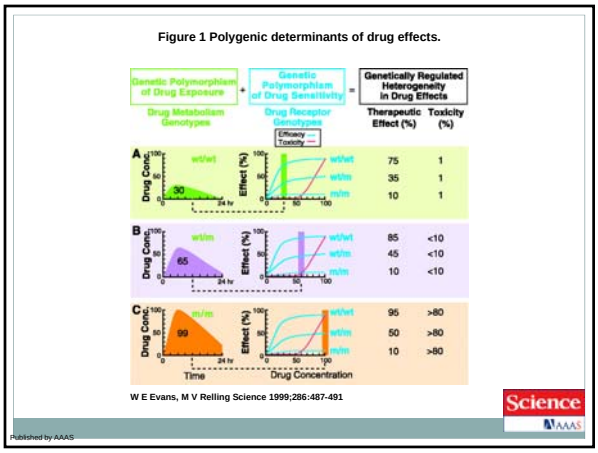

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Tracy Hampton, Researchers Draft Guidelines for Clinical Use of Pharmacogenomics, JAMA 2006

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HIV/AIDS

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EPIDEMIOLOGY, ETIOLOGY AND TREATMENT

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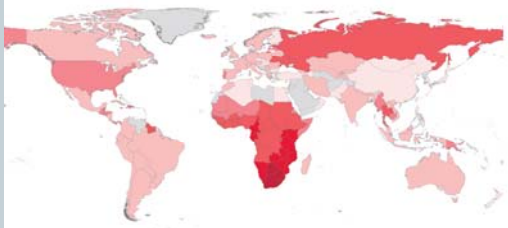
2010: A global view of HIV infection

33.3 million people [31.4–35.3 million] living with HIV, 2009



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HIV Lifecycle (figures adapted from HIV Web Study)

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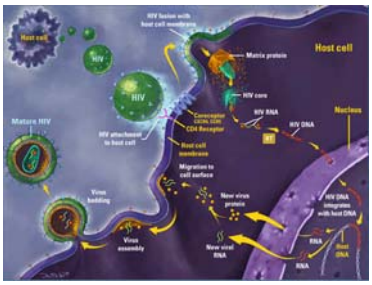

http://www.youtube.com/watch?v=9leO28ydyfU

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Potential Points of Intervention

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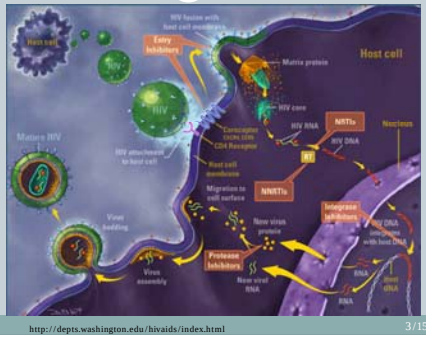

http://depts.washington.edu/hivaids/index.html

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Timeline of FDA-Approval for Antiretroviral Medications in the US

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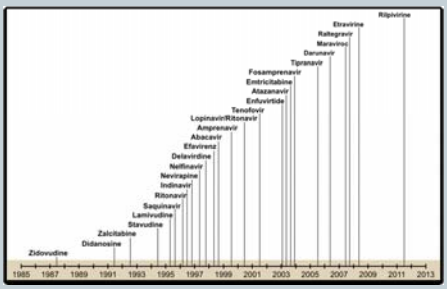

http://depts.washington.edu/hivaids/index.html

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Pharmacogenomics of CYP3A

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DRUG METABOLIZING ENZYMES, CYP3A FAMILY

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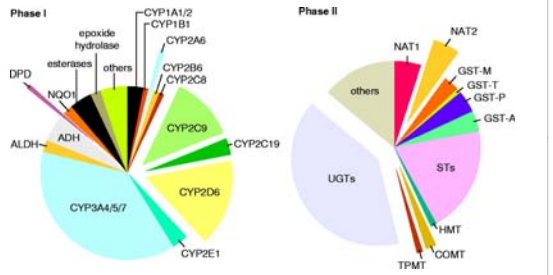
Figure 2 Most drug-metabolizing enzymes exhibit clinically relevant genetic polymorphisms.



W E Evans, M V Relling Science 1999;286:487-491

Science AAAS

Published by AAAS

Table 1

SNPs in *CYP3A4* 3′- and 5′-UTRs

Study	Allele	Gene	Ref.
Gonzalez *et al.* (1988)	*CYP3A4*1A*	Wild-type	[37]
Rebbeck *et al.* (1998)	*CYP3A4*1B*	-392A>G	[36]
Kuehl *et al.* (2001)	*CYP3A4*1C*	-444T>G	[36]
	*CYP3A4*1D*	-62C>A	
Hamzeiy *et al.* (2002)	*CYP3A4*1E*	-369T>A	[44]
	*CYP3A4*1F*	-747C>G	
Fukushima-Uesaka *et al.* (2004)	*CYP3A4*1G*	20230G>A	[46]
	*CYP3A4*1H*	20230G>A, 26206C>A	
	*CYP3A4*1I*	6077A>G	
	*CYP3A4*1K*	-655A>G	
	*CYP3A4*1L*	-630A>G	
	*CYP3A4*1M*	-156C>A	
	*CYP3A4*1N*	14200T>G	
	*CYP3A4*1P*	15727G>A	
	*CYP3A4*1Q*	15809T>C	
	*CYP3A4*1R*	16775A>G	
	*CYP3A4*1S*	17815_17816delAT	
	*CYP3A4*1T*	26013T>C	

CYP3A4 SNPs in the coding region

Nucleotide changes		Effect	Ref.
Allele	*cDNA*	*Gene*	
CYP3A4*2	664T>C	S222P	[43]
CYP3A4*3	1334T>C	M445T	[43]
CYP3A4*4	352A>G	I118V	[39]
CYP3A4*5	653C>G	P218R	[39]
CYP3A4*6	830_831insA	277 Frameshift	[39]
CYP3A4*7	167G>A	G56D	[52]
CYP3A4*8	389G>A	R130Q	[52]
CYP3A4*9	508G>A	V170I	[52]
CYP3A4*10	1026G>C	D174H	[52]
CYP3A4*11	1088C>T	T363M	[52,53]
CYP3A4*12	1117C>T	L373F	[52]
CYP3A4*13	1247C>T	P416L	[52]
CYP3A4*14	44T>C	L15P	[28]
CYP3A4*15	1429G>A	R163Q	[28,44]
CYP3A4*16	554C>G	T185S	[28,46,53]
CYP3A4*17	566T>C	F189S	[54]
CYP3A4*18	878T>C	L293P	[46,54]
CYP3A4*19	1399C>T	S467S	[54]
CYP3A4*20	1461_1462insA	488 Frameshift	[56]

IADH

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***CYP3A5* SNPs in noncoding and coding regions**

Allele	UTR	Nucleotide change *Gene*	*cDNA*	Effect (enzyme activity)	Ref.
*CYP3A5*1A*	–	Wild-type	–	–	[173]
*CYP3A5*1B*-86G>A	–	–	–	–	[36]
*CYP3A5*1C*-74C>T	–	–	–	–	[36]
*CYP3A5*1D*31611C>T	–	–	–	–	[61]
*CYP3A5*1E*17163G>T	–	–	–	–	[45]
*CYP3A5*3*	–	6986A>G	Splicing defect	Severely decreased	[45,61,71]
*CYP3A5*4*	–	14665A>G	Q200R	–	[69]
*CYP3A5*5*	–	12952T>C	Splicing defect	–	[69]
*CYP3A5*6*	–	14690G>A	Splicing defect	None or severely decreased	[36]
*CYP3A5*7*	–	27131_27132insT	346 Frameshift	Null	[61]
*CYP3A5*8*	–	3699C>T	R28C	Decreased	[59]
*CYP3A5*9*	–	19386G>A	A337T	Decreased	[59]
*CYP3A5*10*	–	31611T>C	F446S	Decreased	[59]
*CYP3A5*11*	–	3775A>G	Y53C	Decreased	[59]

***CYP3A43* SNPs in noncoding and coding regions**

Study	Allele	Nucleotide change	Effect	Ref.
Domanski *et al.* (2001)	*CYP3A43*1A*	None	Normal	[74]
Cauffiez *et al.* (2004)	*CYP3A43*1*	33510C>T		[76]
	*CYP3A43*2*	8340delA	25 Frameshift	
	*CYP3A43*3*	31867C>G	P340A	

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Antiretrovirals Metabolized by CYP3A

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- Most protease inhibitors are primarily metabolized by CYP3A.

HIV-protease inhibitors	K_m (μM)
Amprenavir	25.50
Atazanavir	–
Indinavir/lopinavir	1.30
Nelfinavir	40.00
Ritonavir	20.00
Saquinavir	00.35

- Efavirenz and nevirapine are CYP3A substrates and inducers.

- *CYP3A5**1 is associated with a **2-fold increase** in saquinavir clearance compared with *CYP3A5**3.
  - Mouly SJ et al. Clin Pharmacol Ther, 2005
- CYP3A5 expressors had **faster** atazanavir CL/F and **lower C(min)** than non-expressors.
  - Anderson PL et al. J Antimicrob Chemother, 2009

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Genomic Considerations For HIV Treatment

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- The CYP3A subfamily is the most abundant of the CYPs playing a dominant role the metabolism of protease inhibitors.
- Identification of CYP3A polymorphisms in ethnically diverse groups may provide substantial knowledge regarding differences in drug response.

Pharmacogenomics ⟹ safety, efficacy and cost-effectiveness of HIV treatment

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Example of Pharmacogenomics in HIV

CYP2B6 AND EFAVIRENZ

I can see dead people...

- **Psychiatric symptoms**, including insomnia, confusion, memory loss, and depression, are common, and more serious symptoms such as psychosis may occur in patients with compromised liver or kidney function.

2B6 or 3A4/5?

- The cytochrome **P450 2B6 (CYP2B6)** is the main catalyst of efavirenz primary and secondary metabolism: implication for HIV/AIDS therapy and utility of efavirenz as a substrate marker of CYP2B6 catalytic activity.
  - Ward BA, Gorski JC, Jones DR, Hall SD, Flockhart DA, Desta Z. J Pharmacol Exp Ther. 2003 Jul;306(1):287-300. Epub 2003 Apr 3.

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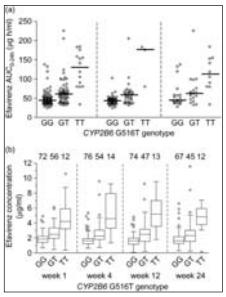
Associations between CYP2B6 G516T genotype and plasma efavirenz exposure



Haas DW, et al. AIDS, 2004

Wolters Kluwer Health | OvidSP

Pharmacogenomics is useful!

- **Successful use of reduced-dose efavirenz** in a patient with human immunodeficiency virus infection: case report and review of the literature.
  - Torno MS, Witt MD, Saitoh A, Fletcher CV. Pharmacotherapy. 2008;28(6):782-7.
- **Successful efavirenz dose reduction** in HIV type 1-infected individuals with cytochrome P450 2B6 *6 and *26.
  - Gatanaga H, Hayashida T, Tsuchiya K, Yoshino M, Kuwahara T, Tsukada H, Fujimoto K, Sato I, Ueda M, Horiba M, Hamaguchi M, Yamamoto M, Takata N, Kimura A, Koike T, Gejyo F, Matsushita S, Shirasaka T, Kimura S, Oka S. Clin Infect Dis. 2007;45(9):1230-7.

Further Readings

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PHARMACOGENOMICS AND HEALTH DISPARITIES

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ACCP White Paper

Research in Women and Special Populations

American College of Clinical Pharmacy
Kat I. Cheang, Pharm.D., Carol Ott, Pharm.D., Sandra Garner, Pharm.D., Hope Campbell, Pharm.D., Laura Hansen, Pharm.D., FCCP, Qing Ma, Ph.D., Elisheh Nazeri, Pharm.D., Karen Gunning, Pharm.D., and Daniel Wermeling, Pharm.D.

The American College of Clinical Pharmacy charged a Task Force on Research in Special Populations to review, update, and broaden its 1003 White Paper, Women as Research Subjects. Participants of the task force included pharmacy clinicians and investigators in the field. This resulting White Paper, Research in Women and Special Populations, discusses the current concepts regarding the conduct of research in women, as well as in special populations (children, the elderly, minorities, the cognitively impaired, and other vulnerable populations such as prisoners and refugees). For each specific population, the barriers to research participation, current guidelines and regulations, and available recommendations to address these barriers are discussed. The participation of research by these populations requires addressing special social and ethical challenges. Clinical pharmacy researchers should be cognizant of these guidelines and be an advocate for the inclusion and the rights of women and special populations in research participation.
(Pharmacotherapy 2008;28(9):93e–113e)

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Major Health Disparities

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Table 1. Major health disparities in ethnic/minority groups[36]

Ethnic/minority group	Health disparities
African Americans	1. Infant death rates more than double that of whites; 2. Death rates from heart disease and cancer more than 40% and 30% higher than those of whites, respectively; 3. Death rates from HIV/AIDS more than 7 times that for whites; 4. A rate of homicide 6 times that for whites.
Hispanics	1. Are almost twice as likely to die from diabetes as are non-Hispanic whites; 2. Account for 20% of the new cases of tuberculosis; 3. Exhibit higher rates of high blood pressure and obesity than non-Hispanic whites.
Other ethnic/minority groups	1. American Indians and Alaskan Natives have an infant death rate almost double that for whites. 2. The rate of diabetes for this population group is more than twice that for whites. 3. American Indians and Alaska Natives also have disproportionately high death rates from unintentional injuries and suicide. 4. New cases of hepatitis and tuberculosis are higher in Asians and Pacific Islanders than in whites.

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Pharmacogenomics is a challenge!

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Challenges in Research Involving Minorities

Genetic differences among ethnic/minority groups

It has been increasingly recognized that genetic difference among ethnic/minority groups is an important determinant in disease risk, progress, prognosis, and patient's responses to treatment. African Americans have high rates of heart disease, including coronary artery disease, stroke, high blood pressure, and heart failure. A report from the American Heart Association indicates approximately 40% of African Americans have some form of heart disease in comparison to 25% of Caucasians.[37] A recent study has shown that African American women with coronary artery disease are twice as likely to have a heart attack than white women.[38] It has also been reported

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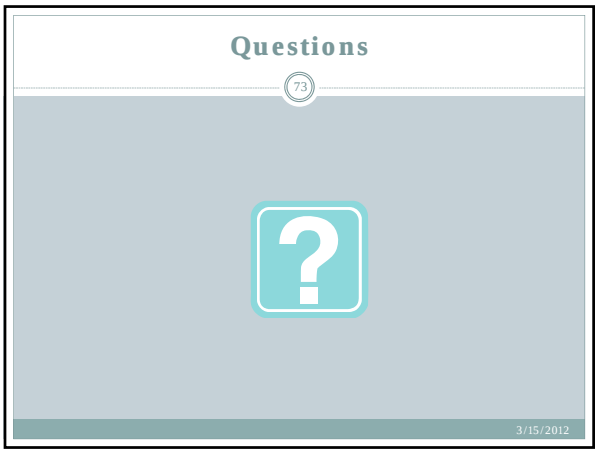

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