The Mammo-Grammie Monarchs (MGMs)

Cancer Molecular Subtypes

Fred Hutchinson Cancer Center

Description of the columns in our data set

barcode	project_id	ERBB2_expr	MKI67_expr	ESR1_expr	PGR_expr	patient	prior_treatment	days_to_diagnosis	age_at_diagnosis	year_of_diagnosis	days_to_birth	year_of_birth	days_to_death	race	ethnicity	age_at_index	progression_or_recurrence	BRCA_subtype
TCGA-AR-A5	TCGA-BRCA	8.35943178	8.7174808	0.57436643	0.35524071	TCGA-AR-A5QQ	No	0	24841	2011	-24841	1943	322	white	not hispanic or latino	68	not reported	Basal
TCGA-A2-A3	TCGA-BRCA	6.82885853	11.7442977	3.99363012	0.07003811	TCGA-A2-A3XT	No	0	16649	2006	-16649	1961	NA	black or african american	not hispanic or latino	45	not reported	Basal
TCGA-A7-A2	TCGA-BRCA	25.4068972	47.5577273	1.80913736	0.39898005	TCGA-A7-A26I	No	0	23948	2011	-23948	1946	NA	white	not hispanic or latino	65	not reported	Basal
TCGA-AN-A0	TCGA-BRCA	24.0239825	14.8998823	1.13404952	0.63922089	TCGA-AN-A0FX	No	0	19309	2010	-19309	1958	NA	white	not hispanic or latino	52	not reported	Basal
TCGA-E2-A1	TCGA-BRCA	17.3913055	6.37568271	0.36127531	0.07798599	TCGA-E2-A150	No	0	17580	2009	-17580	1961	NA	white	not hispanic or latino	48	not reported	Basal
TCGA-EW-A1	TCGA-BRCA	16.0145681	10.0905483	0.28951707	0.00493862	TCGA-EW-A1PB	No	0	25770	2009	-25770	1939	NA	black or african american	not hispanic or latino	70	not reported	Basal
TCGA-A7-A0	TCGA-BRCA	36.8773661	16.1777579	3.13212381	0.4267139	TCGA-A7-A0CE	No	0	20863	2009	-20863	1952	NA	white	not hispanic or latino	57	not reported	Basal
TCGA-A2-A0	TCGA-BRCA	11.8042933	19.6517318	0.05802095	0.00939343	TCGA-A2-A0D0	No	0	22115	2008	-22115	1948	NA	black or african american	not hispanic or latino	60	not reported	Basal
TCGA-EW-A3	TCGA-BRCA	18.6807353	10.3778063	0.2302837	0.04420298	TCGA-EW-A3U0	No	0	22520	2011	-22520	1950	NA	black or african american	not hispanic or latino	61	not reported	Basal
TCGA-D8-A2	TCGA-BRCA	20.0183694	25.0754109	0.18525301	0.10772623	TCGA-D8-A27F	No	0	14731	2010	-14731	1970	NA	white	not hispanic or latino	40	not reported	Basal
TCGA-D8-A1	TCGA-BRCA	21.8518152	24.819425	5.00484983	0.0078876	TCGA-D8-A1JM	No	0	21602	2010	-21602	1951	NA	white	not hispanic or latino	59	not reported	Basal

Subclassification of cancers

- Cancers that look similar can often have very different behaviors
  - How fast they grow, how likely they are to come back, how aggressive they are, or which treatment has the best response
- These cancers can be “subtyped” or grouped into categories
- A molecular subtype is a group of cancers that have similar characteristics based on genetic changes or biomarkers
  - Like mutations or differences in gene expression
- The main 4 subtypes are Luminal A, Luminal B, Basal and Her2+

Research Question:

What are the different marker genes and how are they associated with breast cancer subtypes?

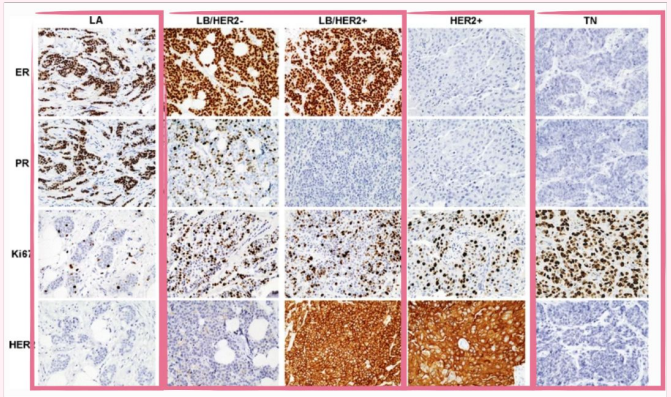
Breast cancer is the most common cancer type in the United States

Luminal A
- ~40% of breast cancers
- Tends: ER+/PR+/HER2-
- Slower growing - good prognosis & low recurrence

Luminal B
- ~20% of breast cancers
- Tends: ER+ & PR+/-, HER2+/-
- Faster growing - worse prognosis than luminal A

HER2 enriched
- ~20-30% of breast cancers
- Tends: ER-/PR-/HER2+
- Can be treated with targeted HER2 therapies

Basal-like
- ~15% of breast cancers
- Tends: ER-/PR-/HER2-
- Most aggressive and highest rate of recurrence



breastcancer.org; Gándara-Cortes, 2017; Kittaneh, 2013

ESR1 Gene

- The ESR1 gene encodes one of the two main types of estrogen receptor proteins.
- The receptors are vital in the development breast cancer, endometrial cancer, and osteoporosis.
- When mutations in the ESR1 gene occur, it can cause inordinate levels in some cancer cells such as those in breast cancer.
- There is a possibility that the cancer cells might spread and grow as a result, and it can even affect its response to anti-cancer medication.
- The ESR1 gene is associated with the Luminal A and Luminal B breast cancer subtypes.

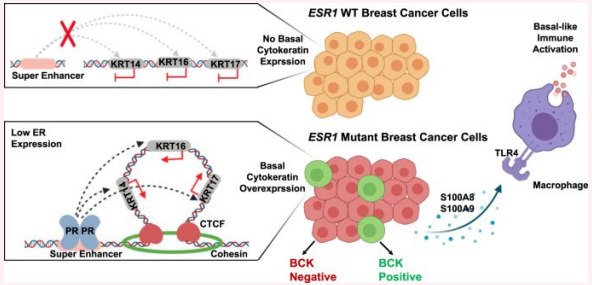
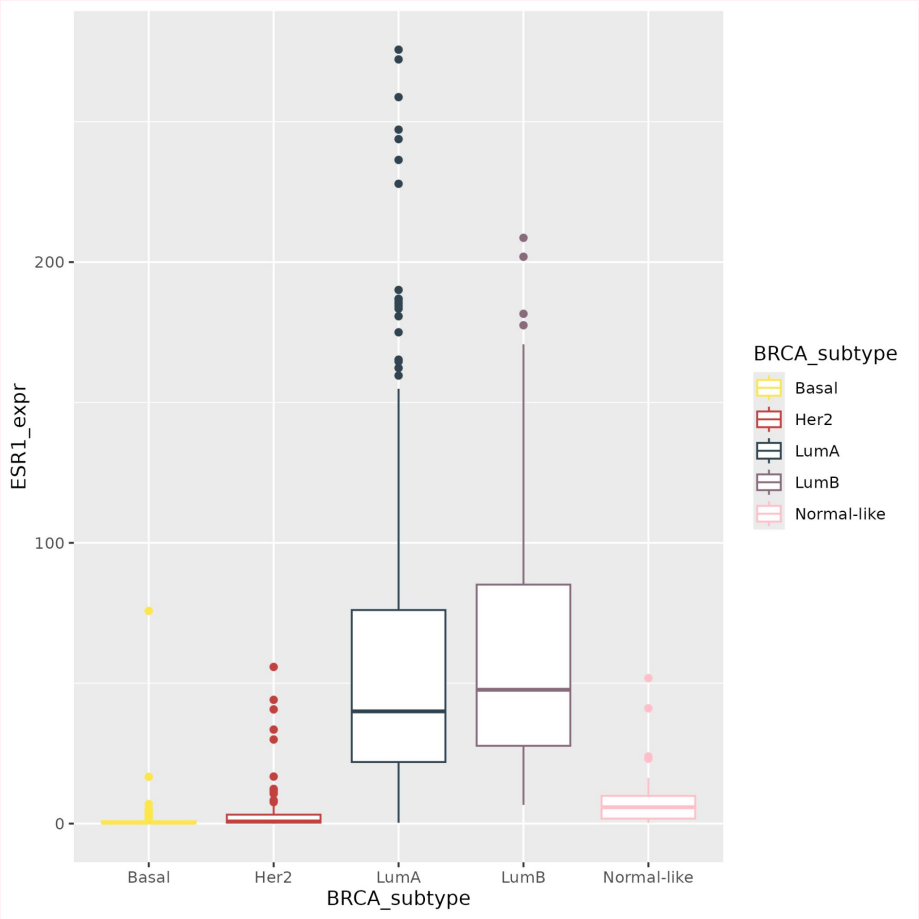


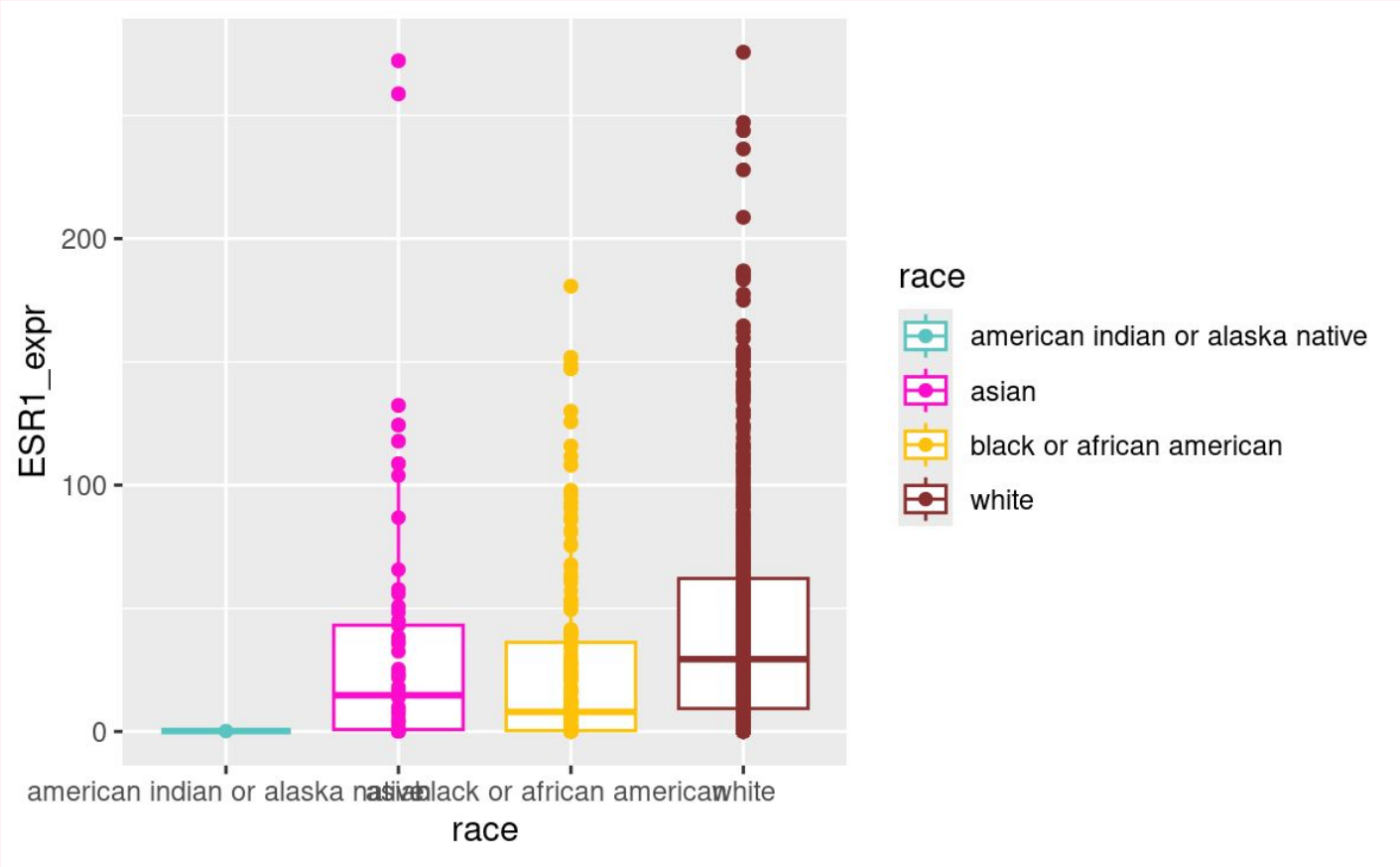
Image courtesy of *Nature*

https://www.cancer.gov/publications/dictionaries/cancer-terms/def/esr1-gene

This graph highlights the subtypes that correlate with the ESR1 Gene the most, The boxplot shows that Luminal A and Luminal B are strongly associated with ESR1.



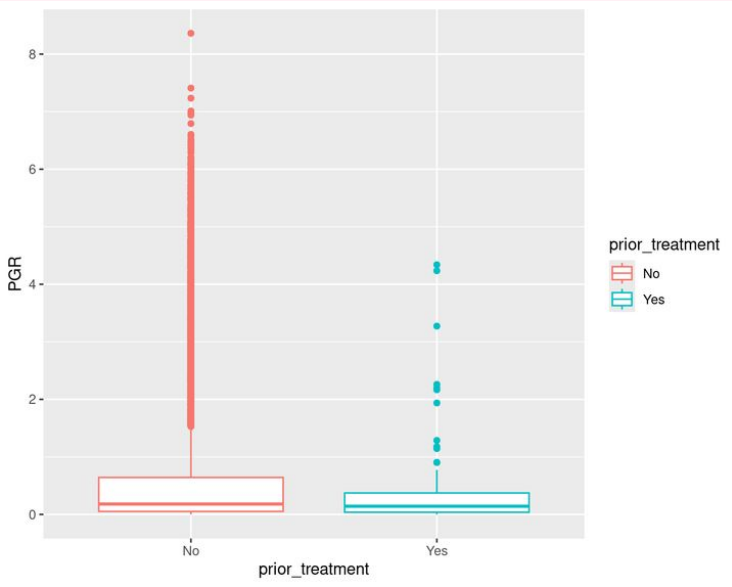
The box plot indicates how different races are affected by the ESR1 mutation. White and asian individuals are affected the most by the ESR1 gene, while american indians/alaska natives, and black/african americans aren't as impacted.



PGR Gene

- The encoded protein focuses on physiological effects of progesterone.
- Progesterone plays a central role in reproductive events associated with the establishment and maintenance of pregnancy.
- It uses 2 different promoters and translation start sites to produce several transcripts variants. protein coding and non protein

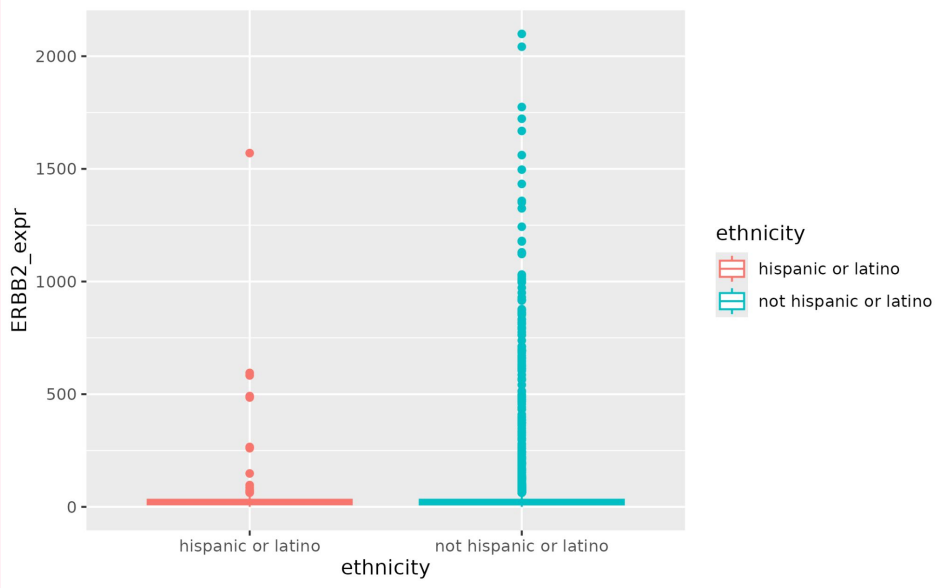
- The PGR gene is linked to the Luminals breast cancer subtypes.



https://www.ncbi.nlm.nih.gov/gene/5241

ERBB2 Gene

- The ERBB2 gene, also known as HER2 gene, is a shortened term for Erythroblastic Oncogene B, which is a receptor that controls cell growth and division.
- Many studies indicate that an amplified ERBB2 gene can disrupt normal cell-control mechanisms and can allow the rise of aggressive cancer cells.



Sources
https://www.ncbi.nlm.nih.gov/books/NBK6194/
https://www.ncbi.nlm.nih.gov/gene/2064

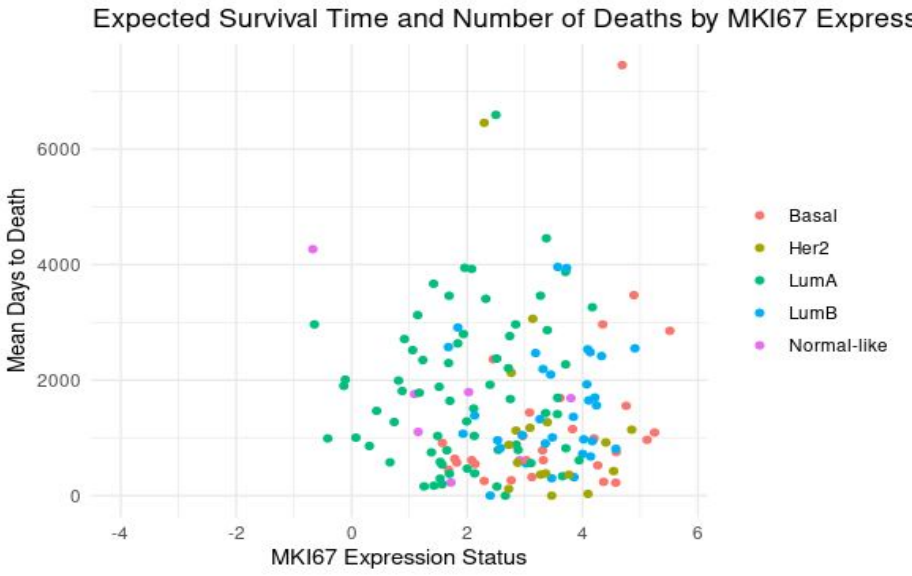
MKI67 Gene

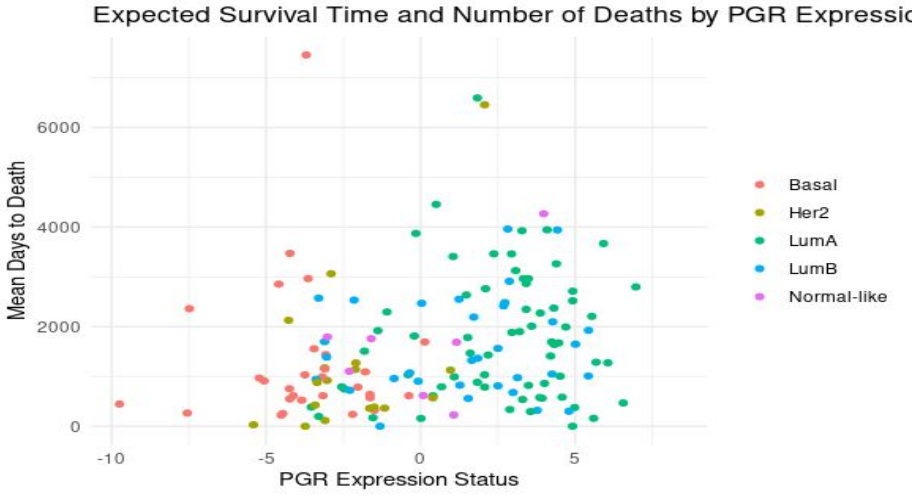
- What it does : Displays the number of cells that are dividing
- Significance: Indicates how aggressive a cancer is
- High levels:suggest the rapid growth of tumors/cancer
- Medical use: Helps doctors decide the right treatment
- Subtype: Associated with Her2+ and Basal breast cancer subtypes.
- Summary : It is a critical way to assess cancer growth

Sources

https://www.ncbi.nlm.nih.gov/pmc/?term=MKI-67

MKI67 Gene - GeneCards | KI67 Protein | KI67 Antibody





How can breast cancer be detected and how can we prevent having breast cancer?

- Breast Cancer can be detected via Breast ultrasound, Diagnostic mammogram, Breast magnetic resonance imaging (MRI), and a Biopsy.
- You can check your breasts to do a self check to feel for any lumps, or if you go for a mammogram screening and it comes back abnormal.
- When the mammogram screening comes back and it's abnormal, the Doctor will refer you to a breast specialist or a surgeon, who can then test one of these ways. If breast cancer is diagnosed, other tests will be run to find out if cancer cells have spread within the breast or to other parts of the body.
- Breast cancer can have a lower chance of happening if you do things like
- Get to and stay at a healthy weight,
- Be physically active, or
- Avoid or limit alcohol. There are also medicines to lower breast cancer risk, like Tamoxifen or Raloxifene.
- However, there are a few risk factors that can't be changed, such as being born a woman,
- getting older, and having a family or personal history of breast cancer.
- If someone inherited a mutation in the BRCA1 or BRCA2 gene, there can be a cause of hereditary breast cancer. In normal cells, these genes help make proteins that repair damaged DNA, however mutated versions of these genes can lead to cancerous cell growth.

Thank You