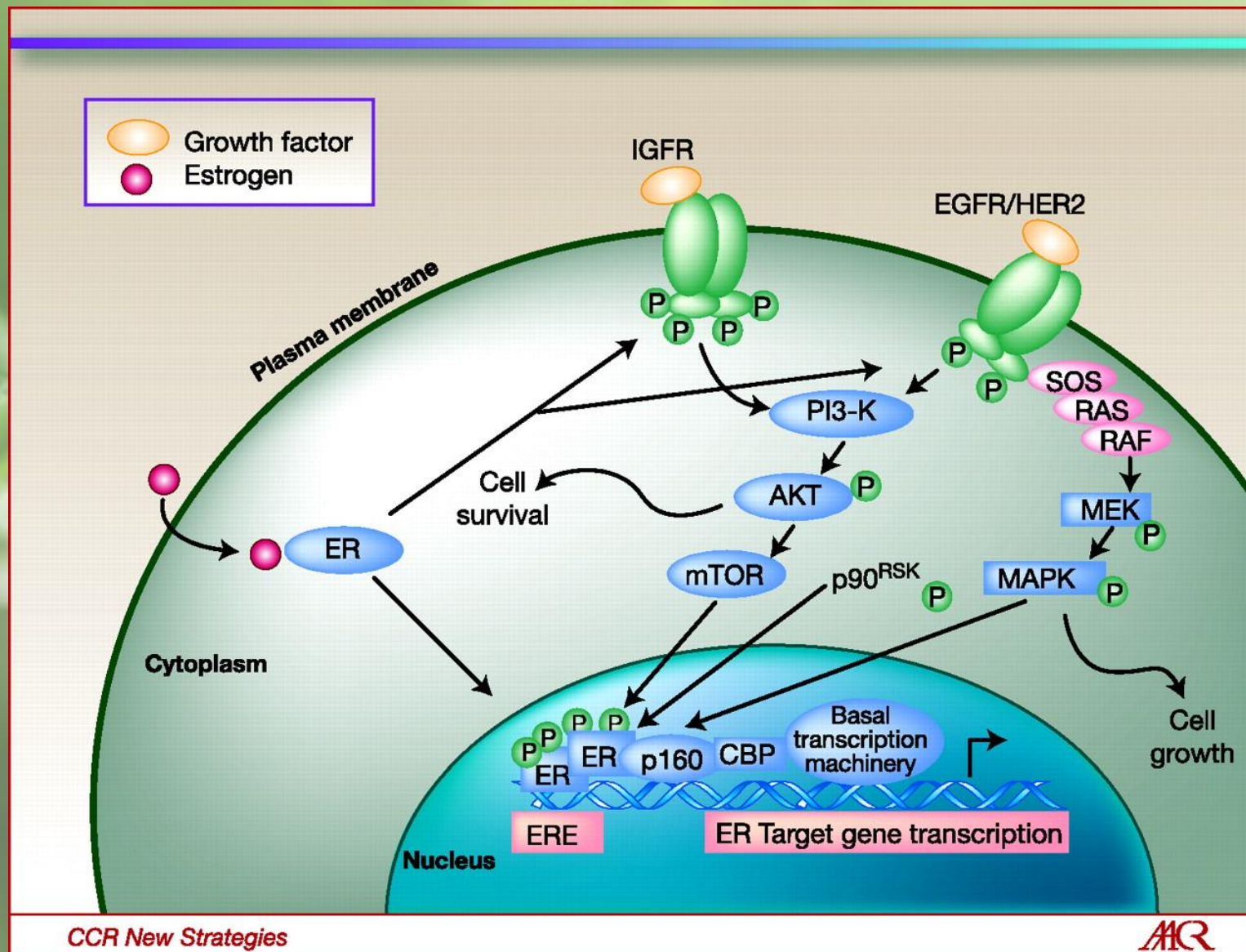


# **Identification of molecules associated with tamoxifen resistance**

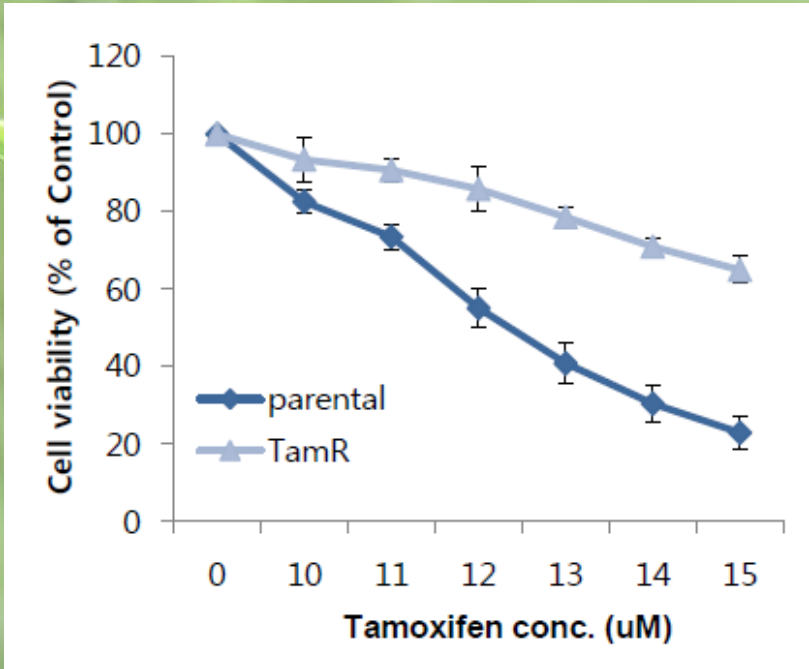
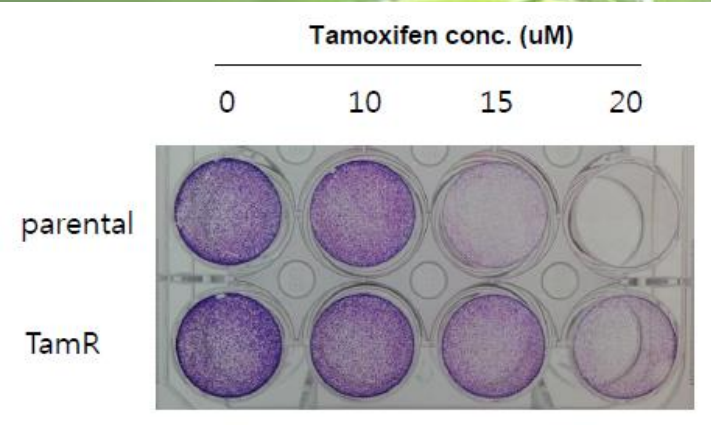
**Korea Institute of Radiological & Medical Sciences**

**Sang Hyeok Woo**

# Cross-talk between signal transduction pathways and ER signaling in endocrine-resistant breast cancer

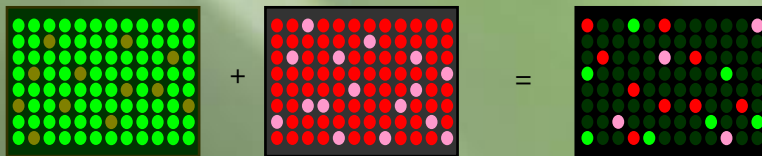
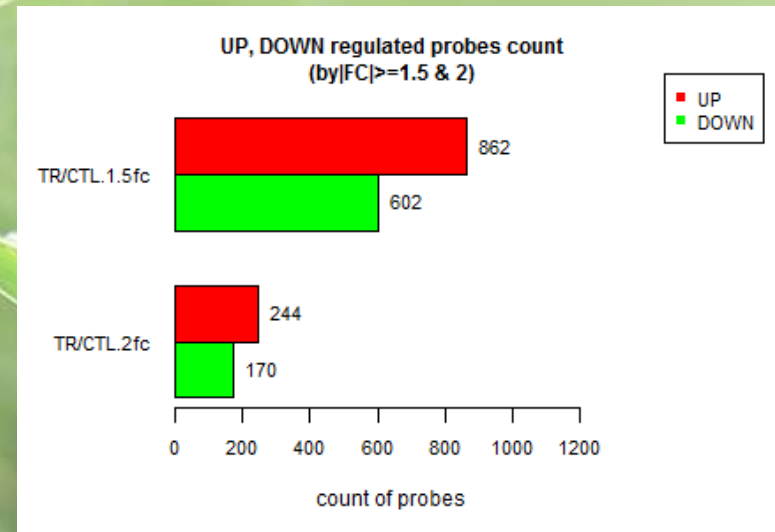
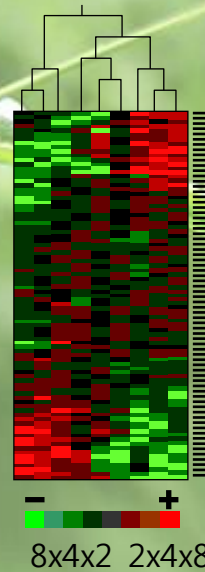
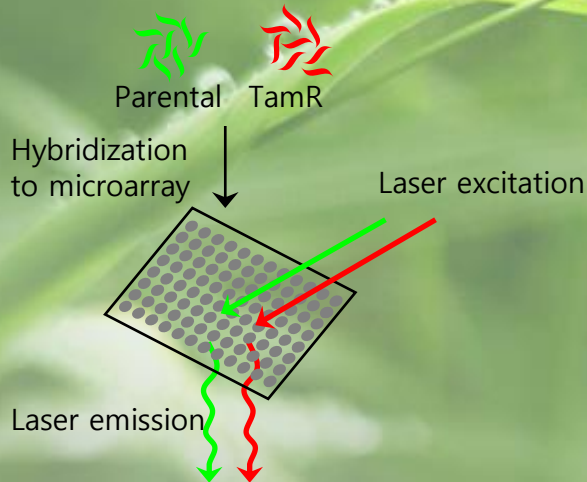


# Establishment of TamR cell line



# cDNA microarray to screen genes related to tamoxifen resistance

Make cDNA reverse transcript  
Label cDNAs with fluorescent dyes



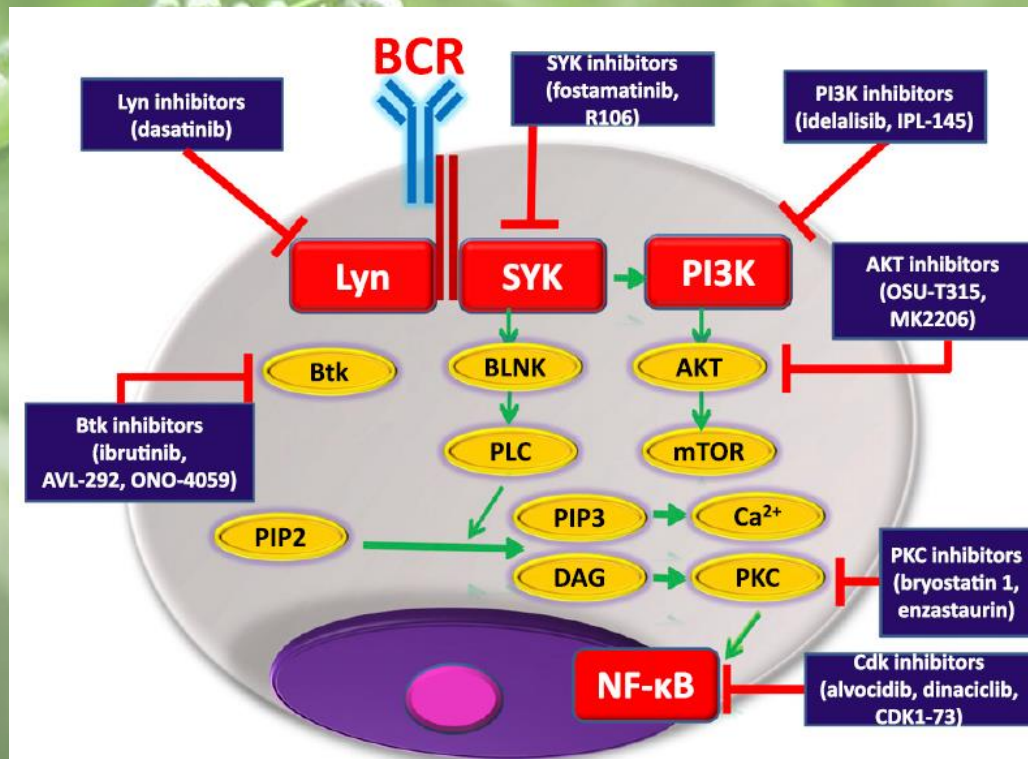
TargetID	RefSeq_NM	GeneSymbol	Gene_ID	TR/CTL.fc
ILMN_1781155	NM_002350.1	LYN	4067	12.551324
ILMN_1733042	NM_003657.1	BCAS1	8537	10.088061
ILMN_1699772	NM_021244.3	RRAGD	58528	6.32188
ILMN_1811272	NM_032554.2	GPR81	27198	4.470288
ILMN_1803811	NM_025195.2	TRIB1	10221	3.914347
ILMN_2228732	NM_004354.1	CCNG2	901	2.284721
ILMN_3229324	NM_005627.3	SGK1	6446	-2.926907
ILMN_1711894	NM_005375.2	MYB	4602	-4.119575



## Lyn (Lck/Yes novel tyrosine kinase)

A member of the SRC family of protein tyrosine kinases

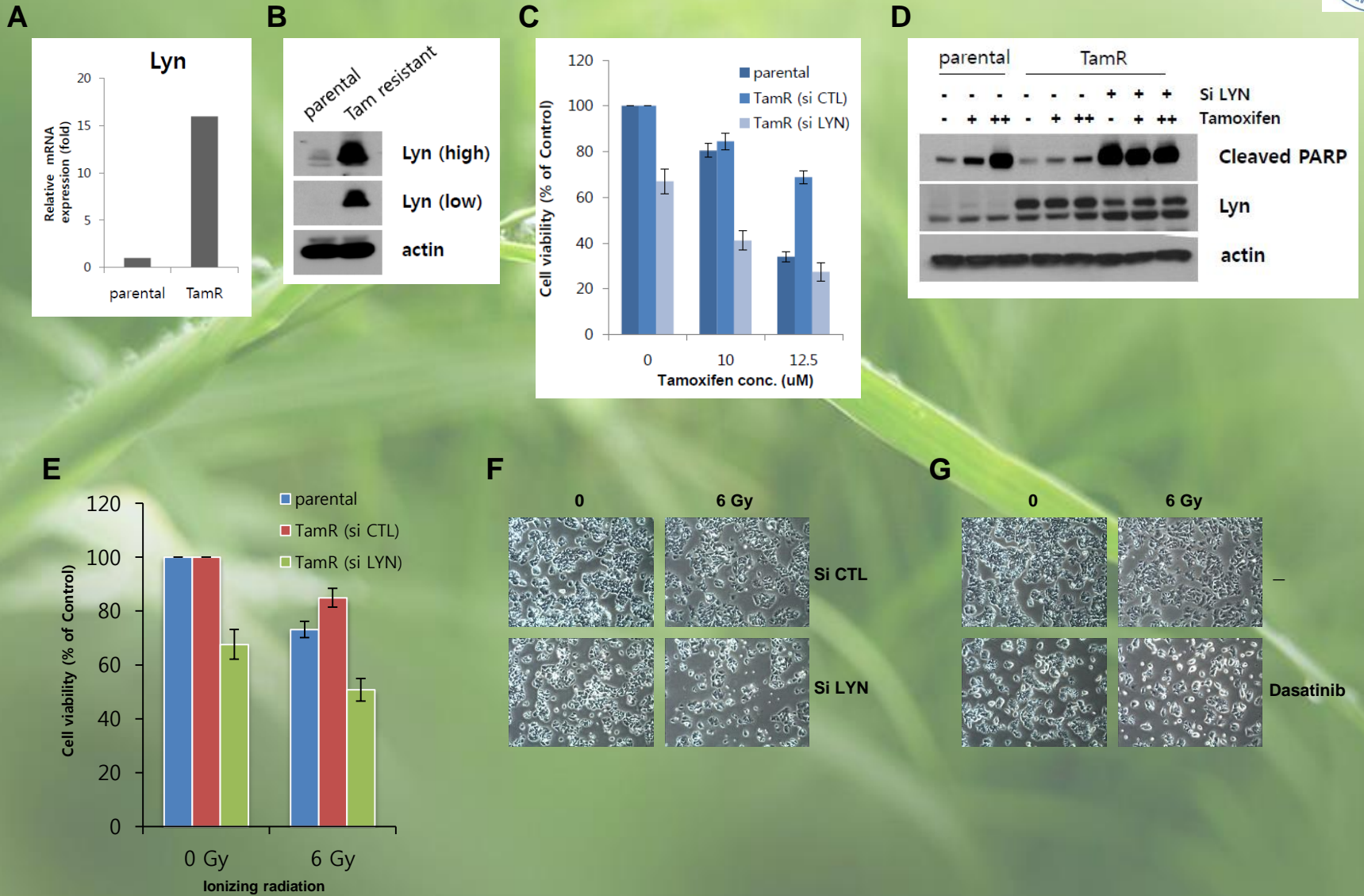
Key regulators of several cellular processes, including cancer cell growth, migration, invasion, and survival  
Overexpression of LYN is associated with an epithelial-to-mesenchymal transition and correlates with a shorter overall survival in breast cancer.



BCR-signaling pathway showing kinase inhibitors.

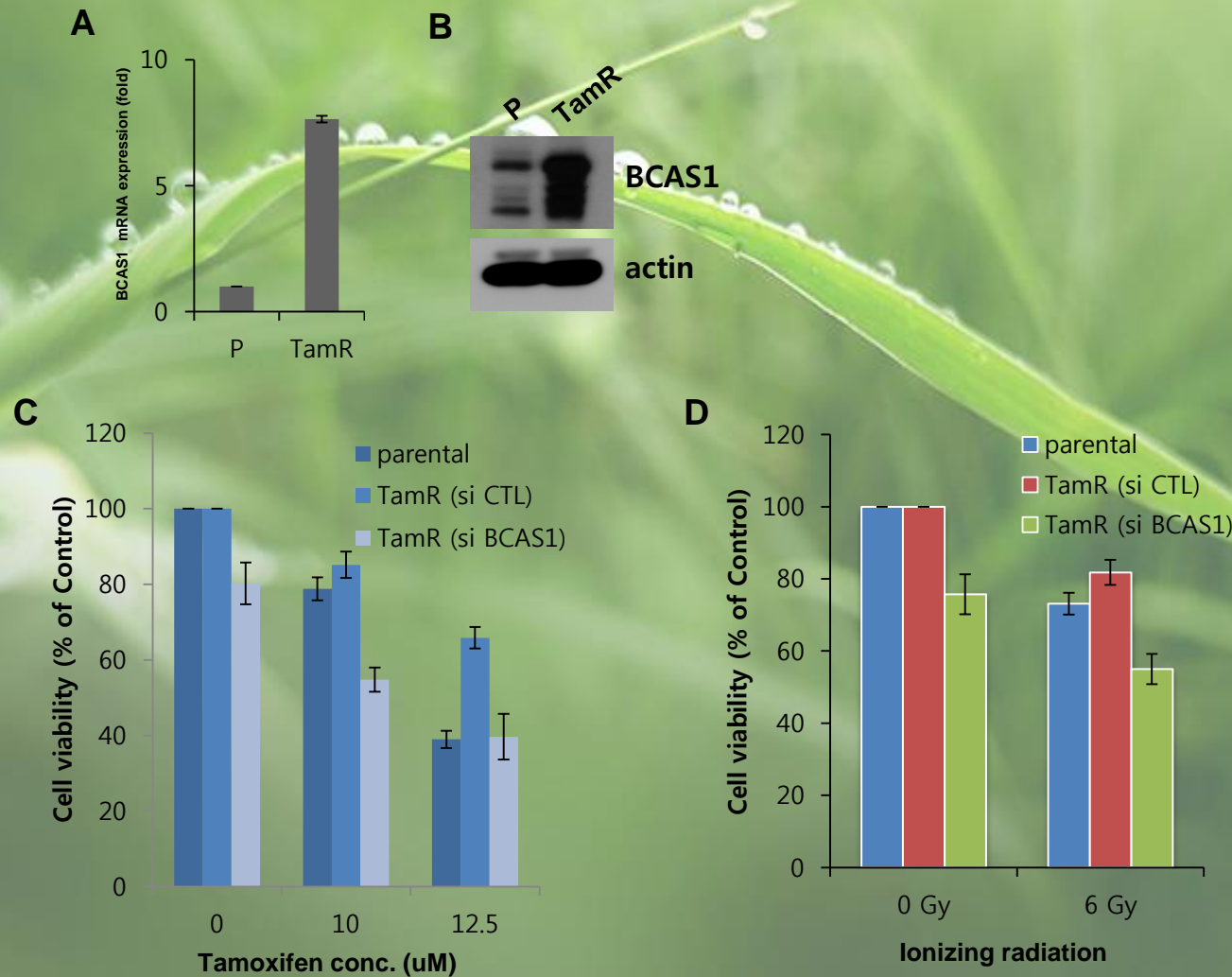
*Blood* (2015)

# Lyn is associated with tamoxifen resistance



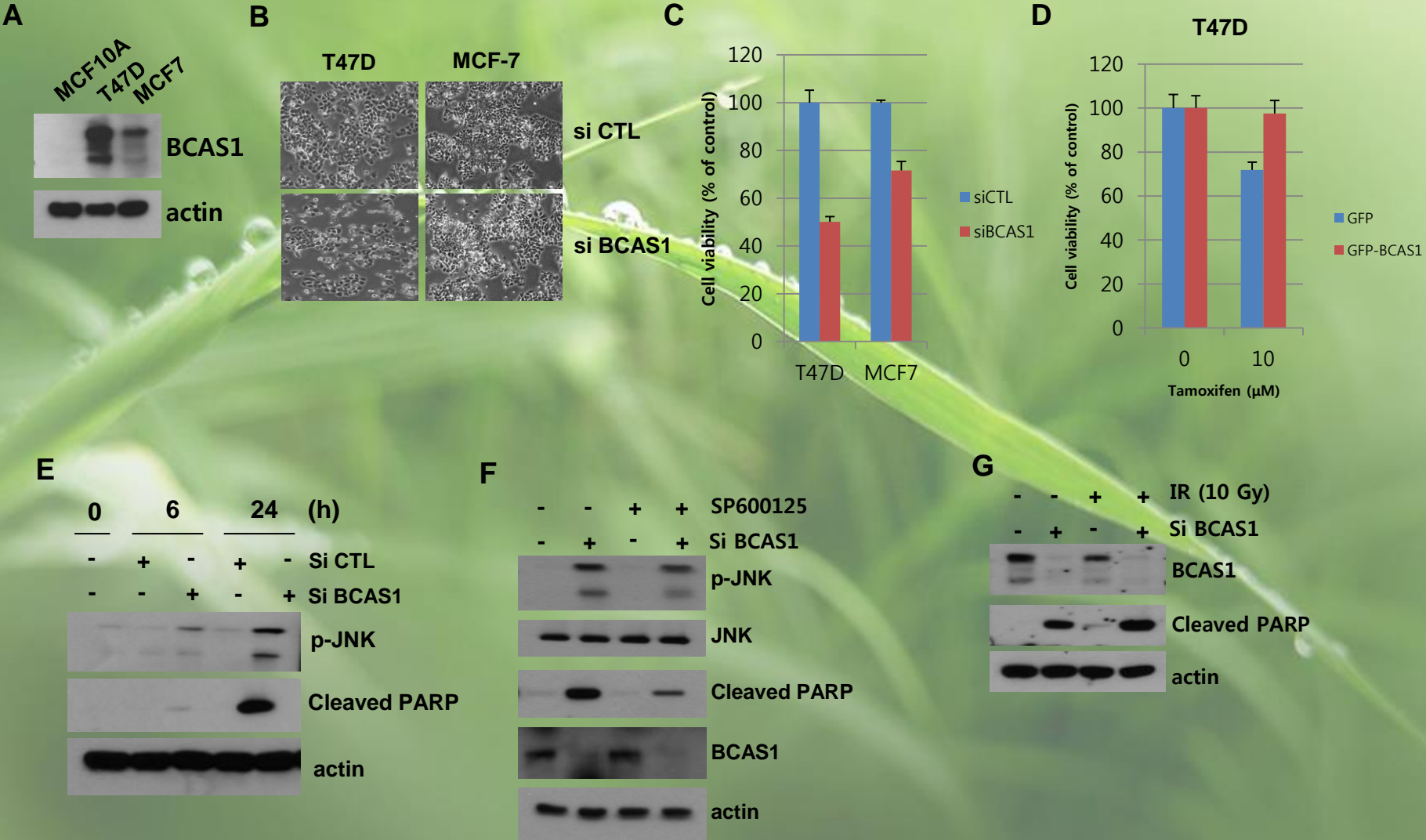
# BCAS1 (NABC1)

**Breast carcinoma-amplified sequence 1** is amplified in a variety of tumor types and associated with more aggressive tumor phenotypes.

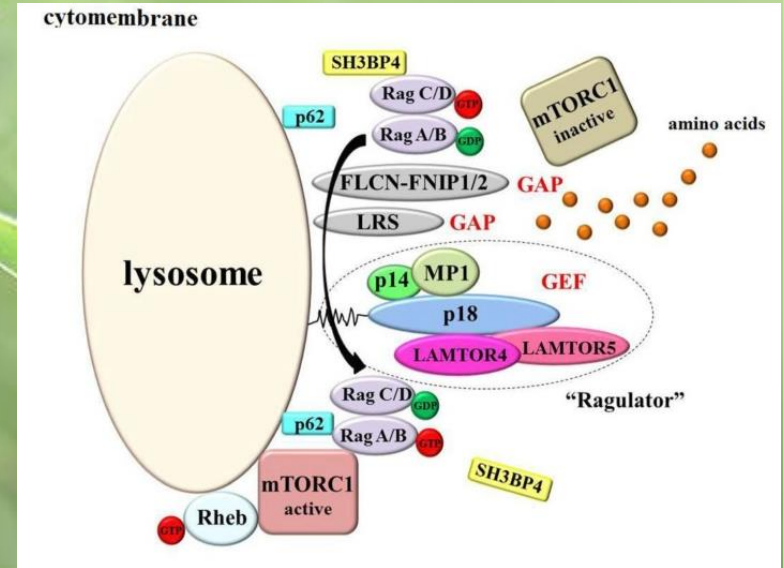
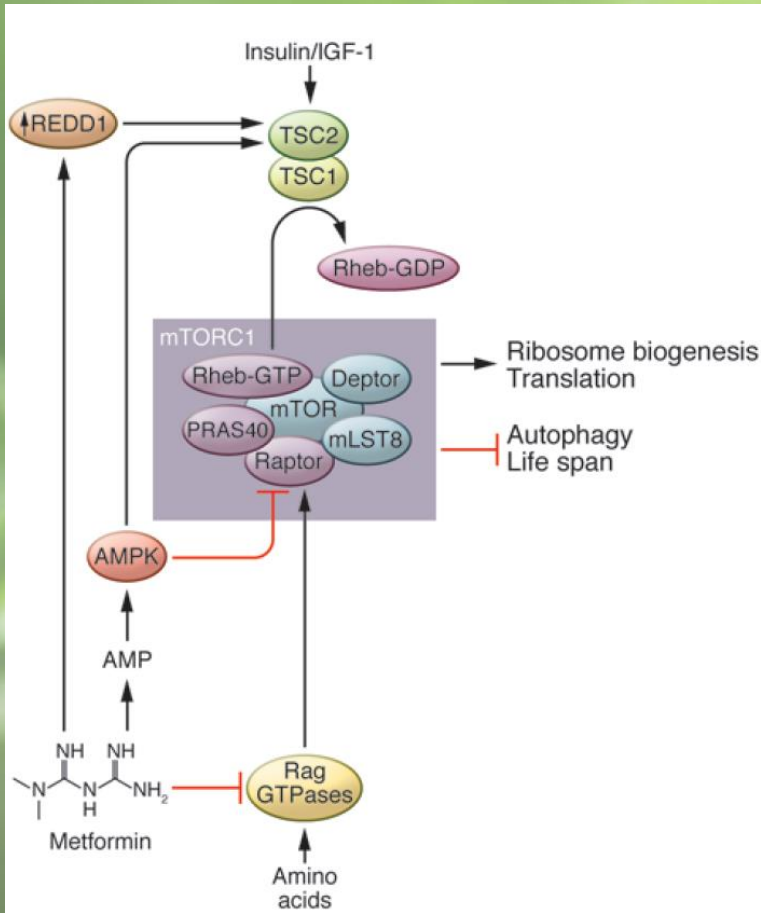




**BCAS1 has a protective role in response to tamoxifen of breast cancer cells**

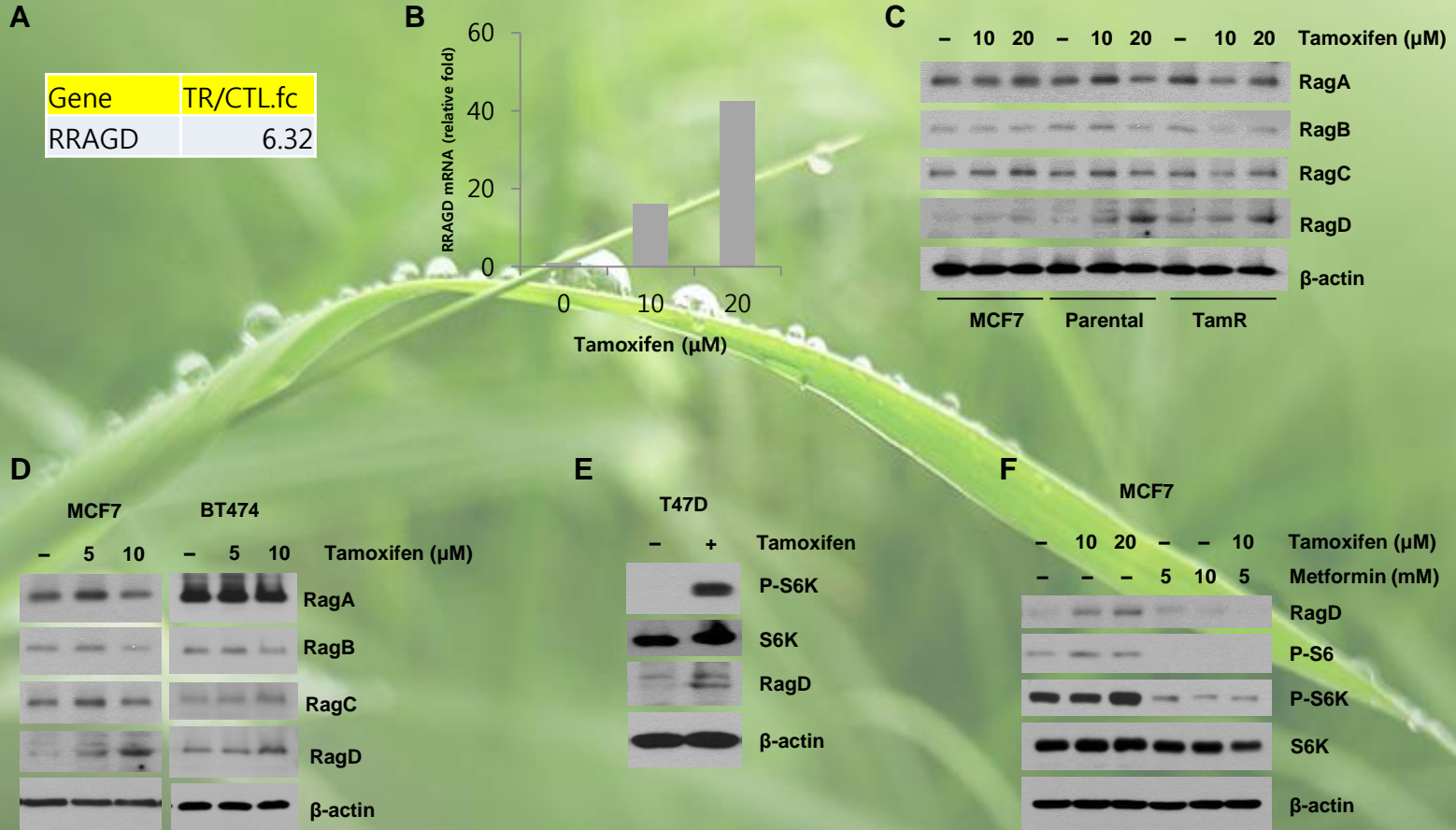




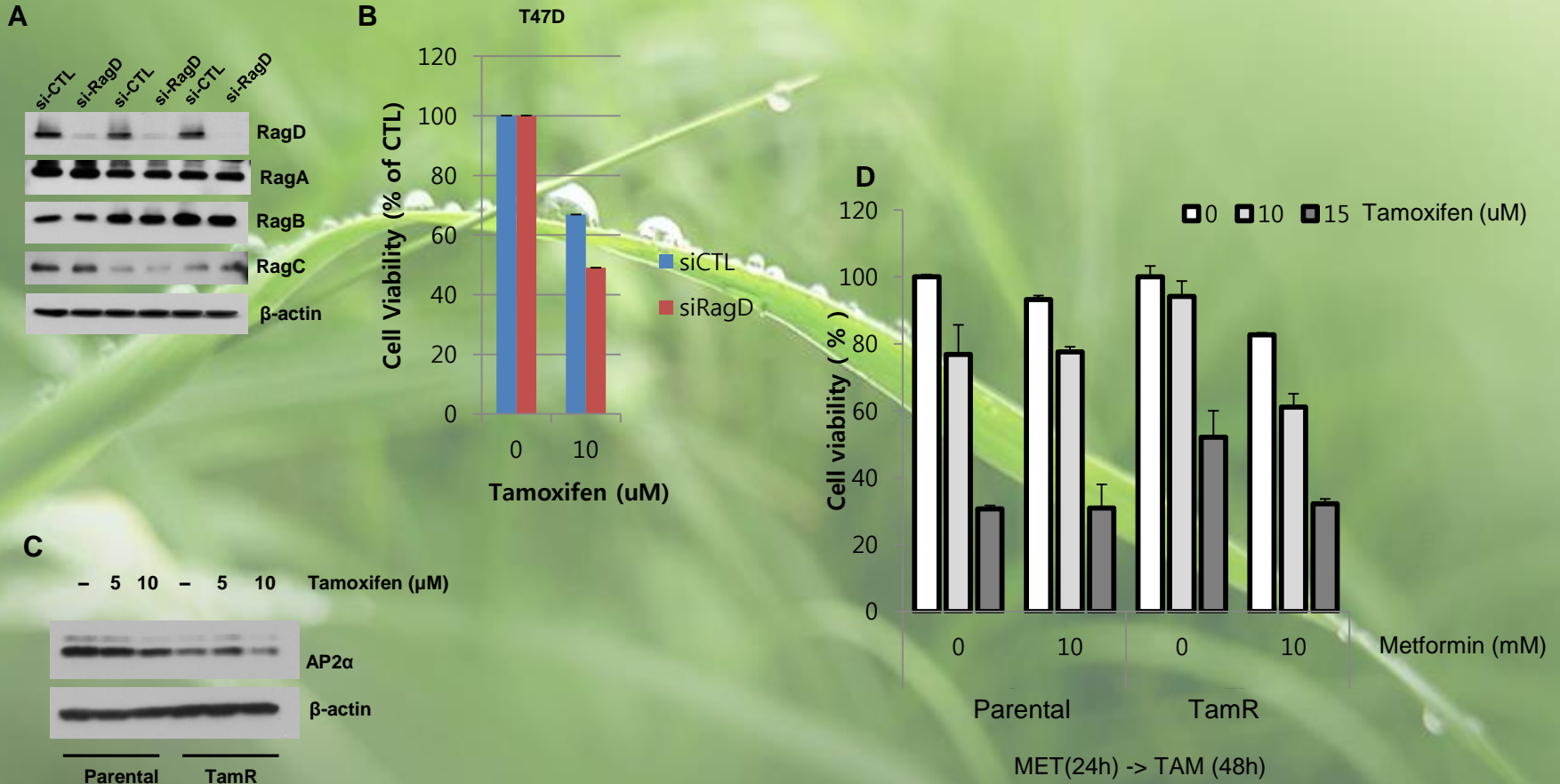


Int J Mol Sci (2014)

# mTOR activation by tamoxifen



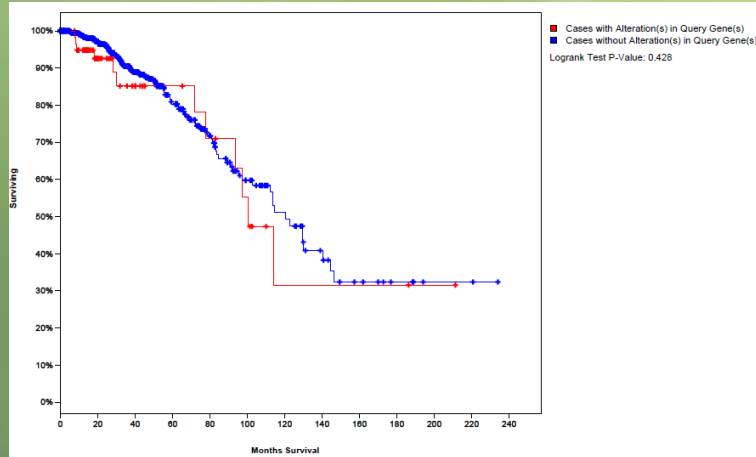
# RagD is associated with tamoxifen resistance



# RagD expression is associated with poor prognosis in breast cancer patients.

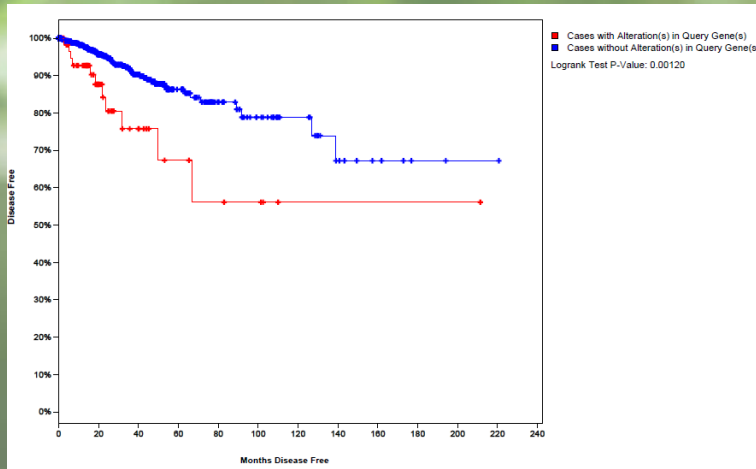


**A**



	#total cases	#cases deceased	median months survival
Cases with Alteration	72	12	100.62
Cases without Alteration	925	103	120.53

**B**



	#total cases	#cases deceased	median months survival
Cases with Alteration	67	11	N/A
Cases without Alteration	848	57	N/A



# GPR81 (G protein-coupled receptor 81)

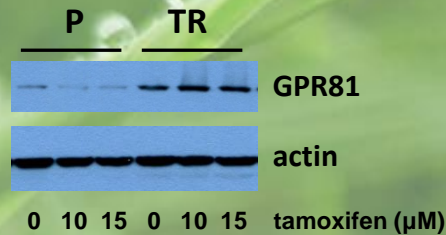
: GPCR for lactate, a key signal in metabolic regulation.

a regulator of lactate transport mechanisms needed for the survival of cancer cells in the tumor microenvironment.

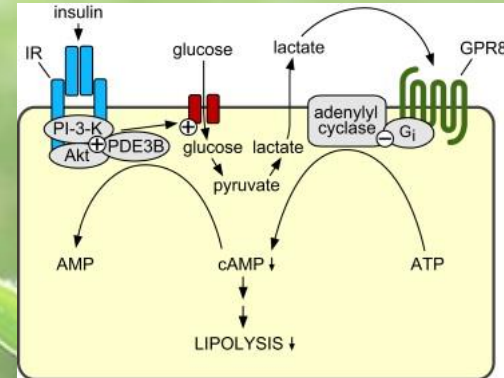
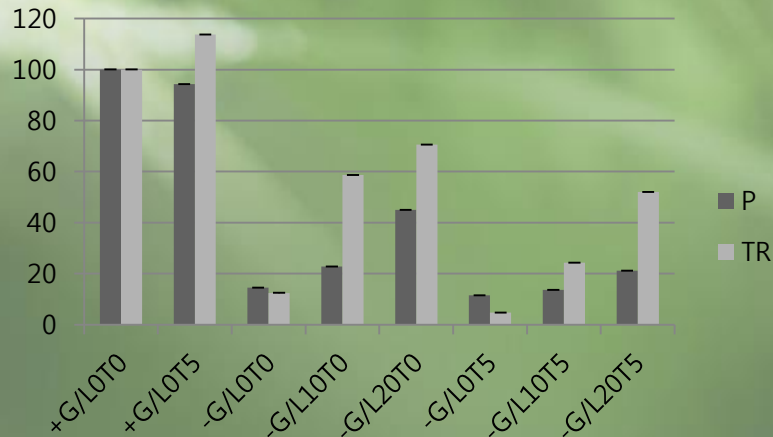
**A**

RefSeq_NM	GeneSymbol	TR/CTL.fc
NM_032554.2	GPR81	4.47

**B**



**C**



**P:** parental MCF7

**TR:** Tamoxifen-resistant MCF7

**+G:** with glucose (4.5 g/L) media

**-G:** without glucose media

**L:** lactate 0, 10, 20 mM

**T:** tamoxifen 5 μM

# Acknowledgments



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