

Does the amount of Lipolysis-stimulated Lipoprotein receptors in breast cancer cells affect the survival probability?

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APR 14 2021





Introduction

Breast cancer is the second most common cancer in American women.

- About 1 in 8 American women will develop invasive breast cancer over the course of their life, and 2.6% of the patients will die from the disease.

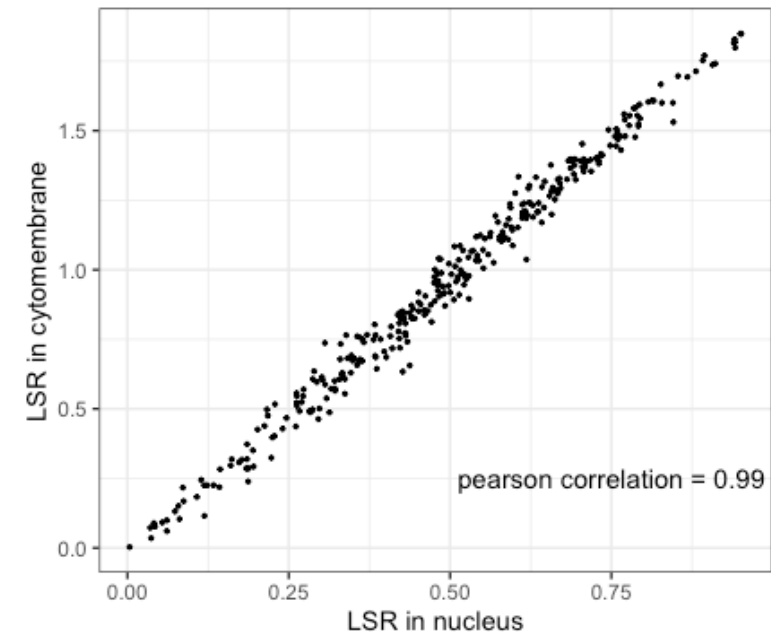
Lipolysis-stimulated lipoprotein receptor (LSR) is a protein that functions in lipoprotein endocytosis and tight junctions, and it was found to have multifaceted roles in directing breast cancer cell behavior.

- One of Dr. Fleming's vivo xenograft studies revealed that LSR expression enhances tumorigenesis.

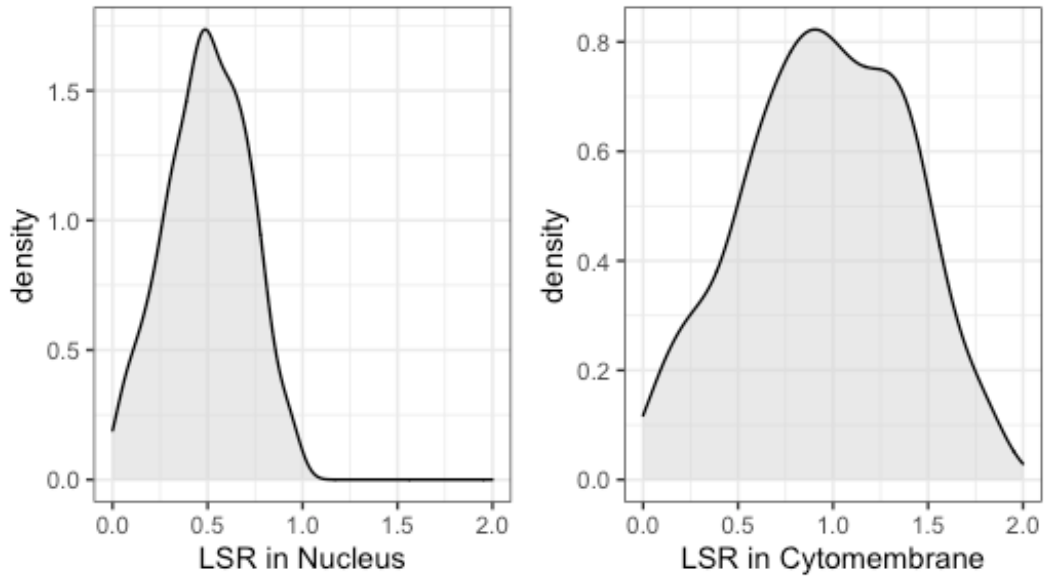
The main goal is to assess the effect of LSR amount in cancer cells, either in nucleus or in cytomembrane, along with other prognostic factors, on the overall survival time of female breast cancer patients.

Data

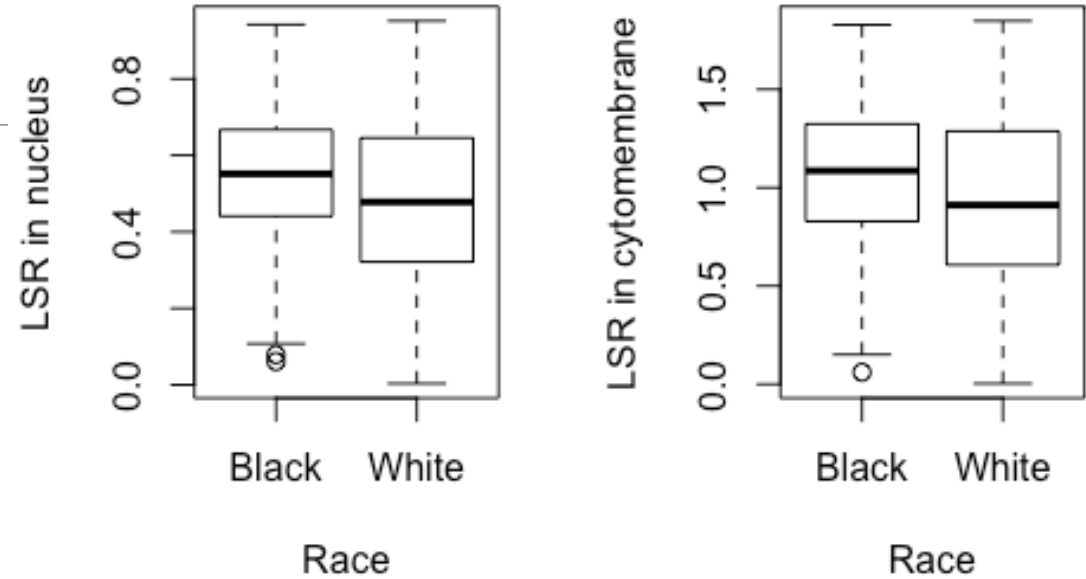
- The dataset consists of 323 patients with their clinical information and measured LSR data after cleaning.
- Each patient had 2 to 3 samples of the LSR data – we took the average for each patient
- Clinical variables:
 - Race, Age, ER, PR, HER2, Grade, Stage, Menopause
- LSR count variables
 - LSR in nucleus, LSR in cytomembrane, LSR in total
 - highly correlated
- Survival Time and Time to Relapse
 - 232 alive and 91 dead (median survival time = 63 months)
 - The longest censored survival time was 225 months.
 - The longest uncensored survival time was 210 months.



EDA on LSR

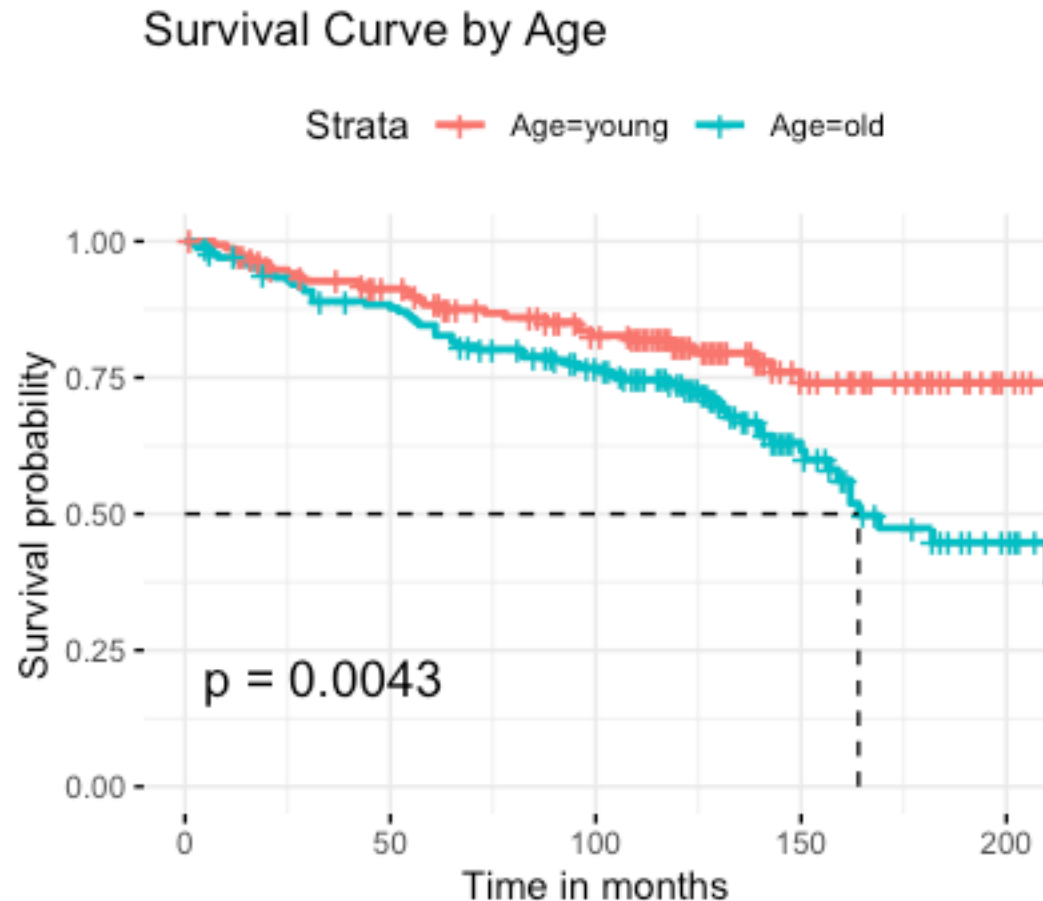


Density plots for LSR in nucleus and cytomembrane



- The plot suggests that the two groups are likely to be different
- Two sample t tests suggest that the mean LSR either in nucleus (p-value = 0.00537) or in cytomembrane (p-value = 0.0047) are different between black and white groups
- Black group has slightly higher mean LSR count than the white group

Kaplan-Meier Plots



- Median survival time for old group is 164 months.
- P-value of log rank test is 0.004
 - Strongly significant
 - Indicating that the age groups differ significantly in survival
- we found that **Age**, **PR**, **Grade**, and **Stage** variables have statistically significant group differences for the overall survival distribution.

Cox Proportional Hazards Model

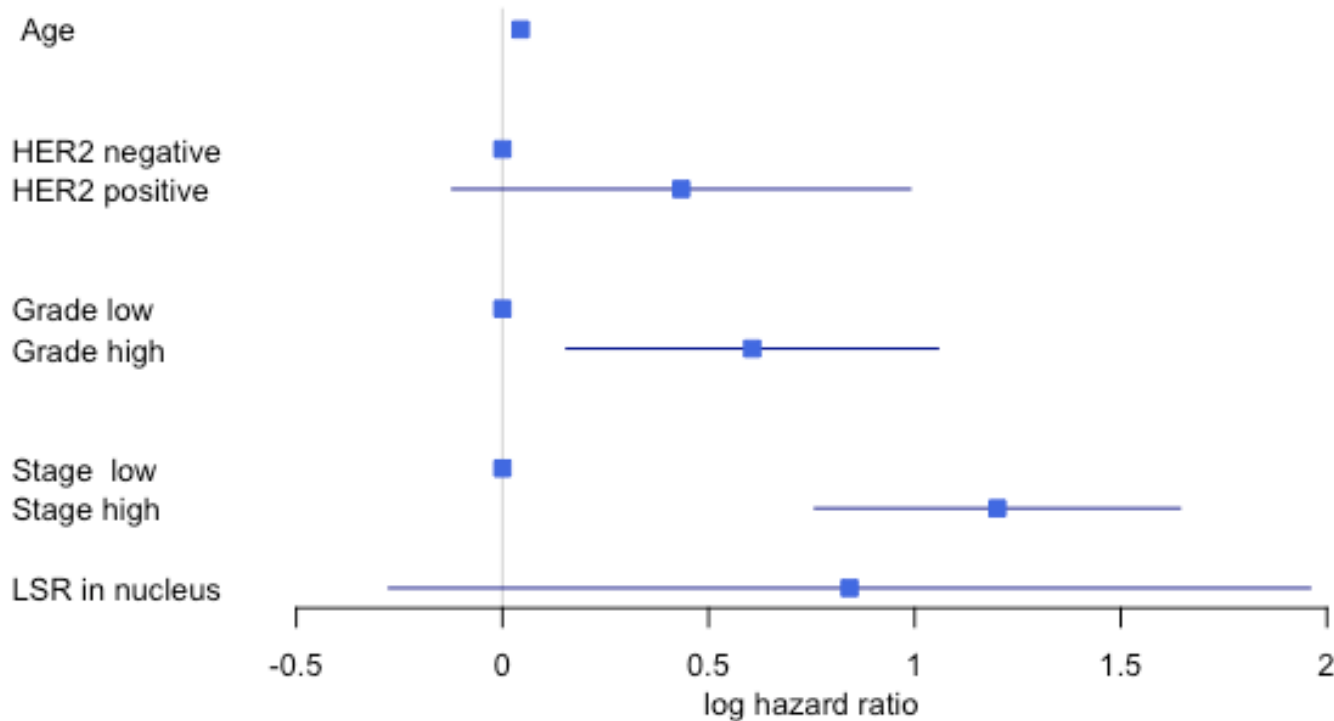
We first fit simple cox models using each one of the covariates:

LSR in nucleus, LSR in cytomembrane, and LSR in total

- The coefficient estimate is the estimate of log hazard ratio
- All three covariates have positive coefficient estimates and the proportional hazard assumption holds.
- The three p-values are very close
 - LSR in nucleus has the highest coefficient, but also the largest standard error

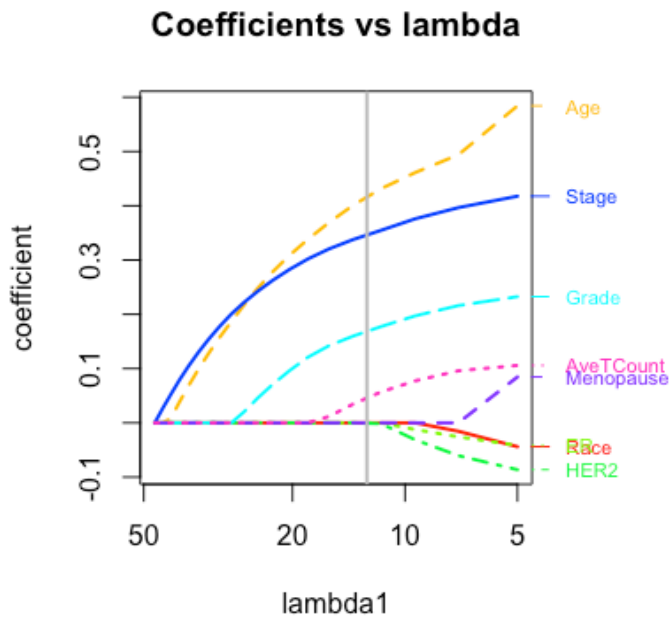
	Coefficient	SE	Hazard Ratio	Wald Test	P-value
Nucleus	0.97	0.51	2.64	1.915	0.055
Cytomembrane	0.51	0.25	1.67	2.019	0.043
Total	0.33	0.17	1.40	1.987	0.047

Variable Selection based on AIC

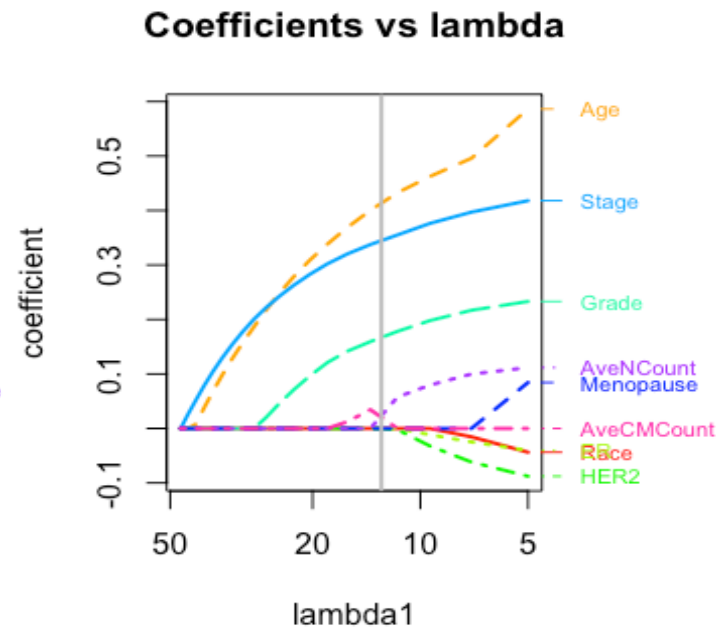


- 5 Variables were selected based on AIC
- Younger age, low grade and low stage group have a better survival rate
 - For example, the coefficient estimate of high-grade is 0.606.
HR = 1.83
- However, the coefficient of HER2 and LSR count in nucleus are not statistically significant.

Lasso Cox Model



Model1: only put LSR total
in



Model2: put all variables in

- Lasso method shrinks the regression coefficients and constraints the number of variables in the model
- Fit two models: the first model only use LSR total, and the second model use all three LSR variables
- The first model selects **Age**, **Stage**, **Grade** and **LSR total**
- The second model selects **Age**, **Stage**, **Grade**, **LSR in nucleus**, and **LSR in cytomembrane**

Results Summary

- Simple Cox Model
 - All three covariates have positive coefficient estimates
 - *The three p-values are very close, and the coefficients of LSR in cytomembrane and in total are statistically significant*
 - *Even though the effect of LSR in Nucleus on survival is not statistically significant, it has the largest coefficient with a relatively large standard error.*
- Multivariate Cox Model
 - The model chosen by AIC kept LSR in nucleus in the final model
 - After controlling the other variables, the effect of LSR on survival is not quite statistically significant, although it's close.
- Lasso Cox Model
 - LSR variables are kept in the model
 - Does not have the same interpretation of the coefficients as Cox model does

Discussion

- The mean LSR amount are different between black and white groups, but there is no difference in survival between the race groups.
- LSR amount seems to be associated with the risk of death, but some of the results are very close to the boundary between significant or not. They can be sharpened by using a larger sample size for study
- For further study, If the localization of LSR is of interest, LSR amount in the nucleus may be a good way to start.

Thank you!