MYC Signaling

IN LUMINAL B BREAST CANCER

UC RIVERSIDE
School of Medicine
CENTER FOR HEALTH DISPARITIES RESEARCH

City of Hope
UC RIVERSIDE
U54 CARE Partnership

UCR/City of Hope Comprehensive Cancer Center Partnership (Full Project #1: MYC Signaling in Luminal B Breast Cancer)

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SUMMARY

The term “Breast cancer” does not refer to a single type of cancer. In fact, breast tissue cells can produce tumors with different features such as growth rates and resistance to anti-cancer treatments, and these different types of breast cancer can affect the overall risk of dying from any specific type of breast cancer. Luminal-B breast cancer is one type of breast cancer that is usually less aggressive than other breast cancers, but in some cases it can be more aggressive and resistant to available cancer treatments. What makes some Luminal-B breast cancers more aggressive and resistant to current therapies is unknown and is the topic of this research project.

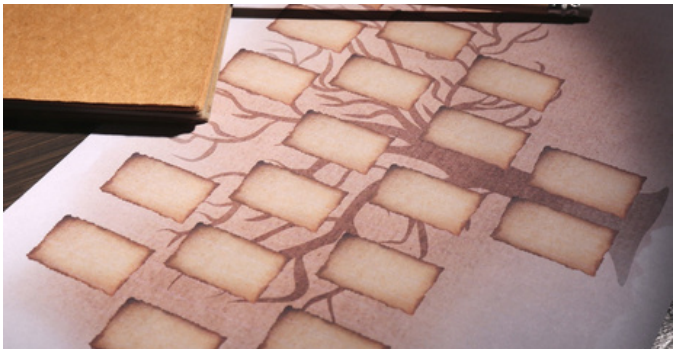
MYC GENE

In this study, research focuses on the MYC gene and its associated protein, whose expression is altered (amplified expression) in over 70% of all cancers and contributes to the development, maintenance and poor prognosis of most aggressive sub-types of breast cancer. Thus, we hypothesize that deregulated MYC expression and functions may be critical to the behavior of aggressive Luminal-B breast cancer.

Generally, cancer is caused by alteration in the expression or function of genes or proteins that are part of normal cell functions, and MYC is one protein known to play some very basic roles in cell behavior. MYC functions by regulating the expression of a wide variety of other genes, with effects on other genes and proteins in downstream cellular processes and pathways, such as cell growth and division. Alterations in MYC expression and function in cancer makes it an attractive potential target for cancer treatment, but unfortunately, since it is also involved in so many normal processes, it is a major challenge in trying to target MYC without having significant effects in normal cells.

RISK FACTORS

In addition to a person’s genes (ancestry and genetic risk factors) a variety of other factors can affect any patient’s likelihood of having a more aggressive form of Luminal-B breast cancer. In the case of Luminal-B breast cancer, Black/African American women have a higher frequency of aggressive disease but the factors behind this association are not known. Intriguingly, high MYC expression is more often observed in breast cancers, including Luminal-B breast cancers, of Black/African American women, suggesting that MYC is one important factor for the increased aggressiveness and poor outcomes of Luminal-B breast cancers in women with African ancestry.



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NEXT STEPS IN RESEARCH

To understand the ways in which MYC might be directly involved in these concerning associations, studies here have focused on the chemical modification of the MYC protein that may change its function in regulating other genes.

Chemical modifications of proteins and other biological structures are performed by other proteins called enzymes. In this case an enzyme called “histone acetyltransferase” can add a small chemical group to the MYC protein and to other proteins that control the way our genetic/DNA material is packaged in our chromosomes.

Interestingly, our preliminary results suggest that chemical modifications of MYC by these enzymes are important for MYC activation of specific genes that are key for the malignancy of breast cancer cells. Notably, other MYC-dependent biological processes important for normal cells are not affected by these chemical modifications of MYC.

With this key preliminary knowledge, this project aims to further understand in more detail the functions of MYC chemical modifications in aggressive Luminal-B breast cancer. This study is expected to lead to novel approaches for drug development against precise MYC pathways in aggressive Luminal-B breast cancers and other similar breast cancers that are resistant to current therapies and disproportionally impact women of African descent.

RESEARCH TEAM

Lead PI: Ernest Martinez, PhD (UCR)
Co-Lead: Veronica Jones, MD (CoH)
Co-Investigators: Maria A. Ninova, PhD (UCR)

PUBLICATION

1) MYC acetylated lysine residues drive oncogenic cell transformation and regulate select genetic programs for cell adhesion-independent growth and survival
2) Gene expression associated with endocrine therapy resistance in estrogen receptor-positive breast cancer

MORE INFORMATION

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