Cancer-induced hypercalcemia (CIH) is common in cancer patients with metastatic disease and in up to 30% of cases without metastasis. During secondary malignancy to the bone and rs1801726 CaSR SNP is significantly associated with Neoplasms of the skin. Additionally, several cancer-related SNPs are racially correlated among Caucasian and African American patients, respectively. A 986S SNP is more common in Caucasian patients whereas, Q1011E is more common in African American patients. Although the CaSR is the major cell surface Ca²⁺ sensor in most cell types, its function in the Ca²⁺-rich bone microenvironment remains unclear. The PheWAS analysis revealed that the rs1801725 CaSR SNP is significantly associated with secondary malignancy to the bone and rs1801726 CaSR SNP is significantly associated with Neoplasms of the skin. Additionally, several cancer-related phenotypes are associated with an increased genetic risk for high calcium. The expression level and inactivating mutation status in exon 7 of the CaSR is cell type specific. Overall, this data supports study provides novel insights into how mutations of the CaSR at rs1801725 are predictive of the likelihood for metastasis to bone.

Materials and Methods
Genotyping of various BC cells was conducted using specific primers for EXON 7 of the CaSR. Using the biorepository at Vanderbilt University, we estimated the effects of both CaSR variants on clinical cancer diagnosis, secondary malignancy diagnosis, and laboratory measurements through logistic regression models and a mediation analysis in a European descent (n = 53,682) and African descent (n = 15,283) genotyped sample.

Conclusions
- The PhewAS analysis revealed that the rs1801725 CaSR SNP is significantly associated with secondary malignancy to the bone and rs1801726 CaSR SNP is significantly associated with Neoplasms of the skin.
- The expression level and inactivating mutation status in exon 7 of the CaSR is cell type specific.
- Several cancer-related phenotypes are associated with an increased genetic risk for high calcium.
- Overall, this data supports study provides novel insights into how mutations of the CaSR at rs1801725 are predictive of the likelihood for metastasis to bone.

Acknowledgements
This work is supported by NIH 1SC1 CA211030; 2U54CA 163069-07 from NCI; NIH/NIGMS S22CA170244 (AMS); NIH/NIMHD 8U54MD007593

Contact information
The Sakwe Laboratory:
PhD Candidate: Heather Beasley *email: heatherkbeasley@gmail.com
PI: Amos Sakwe,PhD *email: asakwe@email.mmc.edu