

Differential Interactions of Vitamin D Binding Protein and Vitamin D Receptor in Different Ethnic Groups with Aggressive Thyroid Cancer

Kristiana Rood, BS¹, Celina Romi Yamauchi¹, BS, Ria T. Laxa¹, BS, Austin Gray, MD², Mia C. Perez, MD², Alfred A. Simental, MD³, Salma Khan, MD, PhD^{1,3}.

¹Center for Health Disparities and Molecular Medicine, ²Pathology & Human Anatomy,

³Otolaryngology, Loma Linda University School of Medicine, Loma Linda, CA

Thyroid cancer affects ethnic groups at different rates and severity. Despite this, thyroid cancer health disparities are still understudied area. Our laboratory has shown a differential expression of vitamin D binding protein (DBP) in Filipino Americans (FA) versus European Americans (EA) [1]. Higher DBP levels correlated to a better prognosis. Another study showed a DBP-dependent (VDR) promoter activation. In this study, we investigated whether VDR and DBP are expressed differentially in different ethnicities, including African Americans (AA), Hispanic Americans (HA), EA, and FA. We were also able to determine the differential DBP polymorphisms, VDR variant expressions, and DBP-VDR interactions in the different ethnicities. By PCR-Restriction Fragment Length Polymorphism (PCR-RFLP), we showed a higher frequency of DBP gene polymorphism in FA versus EA. Analyzing the Cancer Genome Atlas (TCGA) thyroid cancer datasets with the UALCAN assay, we found the differential expressions of DBP and VDR genes based on cancer stages, sample types, race, and histological subtypes. By immunohistochemistry, we detected strong nuclear VDR (nVDR) and very low membranous VDR (mVDR) expression that correlated with low DBP in FA thyroid cancer tissues. In contrast, there was a higher expression of both mVDR and DBP in HA versus the other ethnicities. Co-immunoprecipitation analysis revealed a stronger DBP interaction with mVDR in FA compared to other ethnicities. Our data suggest that low DBP correlates with low mVDR in FA, whereas high DBP correlates with high mVDR in the other ethnicities. In conclusion, the strong interaction of DBP with mVDR in FA may implicate the potential role of DBP-mVDR crosstalk in aggressive thyroid cancer. In the future, we will determine the pathways involved in BDP-mVDR crosstalk in thyroid cancer health disparities.

1. B. Mull, R. Davis, I. Munir, M.C. Perez, A.A. Simental, S. Khan, Differential expression of Vitamin D binding protein in thyroid cancer health disparities, *Oncotarget* 12(7) (2021) 596-607.

Contact: Salma Khan, MD, PhD, salmakhan@llu.edu