Abstract citation ID: bvac150.1647

Thyroid

OR09-3

Integrins as Potential Molecular Targets in Thyroid Cancer Imaging and Therapy

Joanna Klubo-Gwiezdzinska, Sonam Kumari, Thakur Shilpa, Vasyl Vasko, and Zhantong Wang

Background: Integrins are cell adhesion receptors consisting of 24 transmembrane heterodimers generated from a combination of 18α integrin and 8β integrin subunits. A subset of integrins consists of receptors recognizing Arg-Gly-Asp (RGD) peptide motifs. One of the RGD-recognizing receptors is integrin αvβ3 that has been recently shown to play a role in neovascularization and progression of several cancers. Radiolabeled RGD analogs have emerged as potential imaging and therapeutic options in cancers characterized by a high expression of integrin αvβ3. Therefore, the aim of this study was to establish the expression of integrin αvβ3 in thyroid cancer (TC). **Methods:** We analyzed the mRNA expression of integrin αvβ3 in 496 BRAF-like and RAS-like human TC tissue samples, including 65 paired samples of tumor vs normal tissue based on The Cancer Genome Atlas. We assessed the protein expression of integrin αvβ3 in 70 TC tissue samples and 10 normal thyroid tissues, as well as in 14 TC cell lines. BRAF-like or RAS-like tumor status was determined by BRS score based upon standard expression profiles ranging from -1 to 0 for BRAF-like cancer and 0 to 1 for RAS-like tumors. The association between BRS and αvβ3 expression was tested using the Spearman correlation coefficient (r). T-tests and paired T-tests were used to compare the continuous variables between the two groups as appropriate, and Kruskal-Wallis test was used for multiple group comparisons with an adjusted p-value of ≤ 0.05 as statistically significant. **Results:** αv integrin subunit mRNA expression was significantly higher in TC than normal thyroid (log fold change 0.3, p=0.001), while the expression of the β3 subunit was similar between paired normal and malignant samples (log fold change -0.2, p=0.30). BRAF-like tumors were characterized by a higher mRNA expression of αvβ3 integrins as documented by a moderate negative correlation between BRS and αv (r=-0.5, p<0.001) as well as β3 (r=-0.27, p<0.001). Consistently, the BRAF-like TC cell lines OCUT2 (BRS=-1), TPC1 (BRS=-0.4), K1 (BRS=-0.29), as well as Hurthle cell TC cell line XTC1 (BRS=-0.46), were characterized by the highest αvβ3 mRNA and/or protein expression. Immunostaining revealed αv expression in all malignant samples, with classic papillary TC characterized by the highest expression as compared with follicular TC (p<0.001), poorly-differentiated TC (p=0.006) and normal thyroid (p<0.001). β3 protein expression had lower intensity than αv integrin and was present in 31.8% of papillary TC, 15% of follicular TC and was not detected in poorly-differentiated TC nor normal thyroid. **Conclusions:** TC is characterized by a differential expression of αvβ3 integrin, which is particularly high in the most common type of TC - BRAF-like papillary TC. The αvβ3 integrin could potentially serve as a molecular target for imaging and therapy with radiolabeled RGD analogs in TC.

Presentation: Saturday, June 11, 2022 12:00 p.m. - 12:15 p.m.