The Characterization of SGLT2 Expression in Human Lung Cancers

Objective: Previous studies suggest that SGLT2, a sodium-dependent glucose transporter, may play a role in the metabolism of lung adenocarcinomas. Our goal is to characterize SGLT2 expression with a large number of human tumor samples representing multiple lung cancer types.

Methods: Tissue microarray analysis (TMA), previously described (Yanagawa J, et. al, Clin Cancer Res, 2009), was constructed using University of California at Los Angeles Department of Pathology archival paraffin-embedded human lung cancer specimens from consecutively accrued cases that were obtained under Institutional Review Board (IRB02-07-011). SGLT2 expression of the TMA was validated by performing immunohistochemistry using a polyclonal antibody at 1:250. Specificity of the antibody was confirmed using a blocking peptide specific for SGLT2 with the SGLT2 antibody in separate slides. Two pathologists reviewed the SGLT2 stained slides and scored SGLT2 expression only on the tumor cells, based on the intensity of the immunohistochemistry staining (0 = absent, 1 = weak, 2 = moderate, 3 = strong). We took the average of SGLT2 staining for each patient and analyzed it with the corresponding clinical database (grade, sex, race, histology, and stage). Using STATA 13, we performed descriptive statistics, and ANOVA test to characterize SGLT2 expression in lung cancer.

Results: The TMA included 578 tumors with corresponding histology and SGLT2 expression. 544 (94%) tumors demonstrated some degree of SGLT2 expression (weak n=156 [27%], moderate n=262 [45%], strong n=126 [22%]). When stratified by histology, strong SGLT2 expression was present in 29% (97/340) adenocarcinomas, 7% (10/135) squamous cell carcinomas, 32% (8/25) adenosquamous carcinomas, 50% (3/6) carcinoids, 12% (7/59) large cell carcinoma cases, and 8% (1/13) small cell carcinomas. The degree of average SGLT2 expression varied significantly by sex, histology, and grade (Table 1). When comparing by tumor grade for lung adenocarcinomas only, the average SGLT2 expression in grade 1 is 2.26, in grade 2 is 2.24, and in grade 3 is 1.89 (p-value = 0.0001).

Conclusions: SGLT2 expression is widely present in multiple lung cancer types, with the strongest expression in lung adenocarcinomas, adenosquamous carcinomas, and carcinoids. For lung adenocarcinomas, SGLT2 expression is correlated with grade, with the highest expression in low grade tumors and lowest expression in high grade tumors.

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Additional Resources

- https://files.aievolution.com/prd/aat2101/abstracts/abs_4735/SGLT2studytable101622.docx