THE POTENTIAL OF SERUM AUTOANTIBODIES AGAINST TYPE III COLLAGEN IN CANCER

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Background Autoantibodies are classically associated with autoimmune diseases but have recently emerged as attractive cancer biomarkers as they can be easily assessed in serum. Certain autoantibodies have been shown to promote cancer while others contribute to the body's defense against it. Cancer progression is associated with excessive remodeling of the extracellular matrix (ECM) and collagen, but little is known about the role of autoantibodies against collagen in cancer. To investigate autoreactivity against collagen in cancer, we developed a novel biomarker assay to quantify autoantibodies against type III collagen products in serum from patients with various solid tumor types and compared levels with those found in healthy controls.

Methods The presence and levels of autoantibodies against denatured type III collagen were measured in pretreatment serum from 223 patients with bladder cancer (n=20), breast cancer (n=20), colorectal cancer (n=20), head and neck cancer (n=20), kidney cancer (n=20), liver cancer (n=3), lung cancer (n=20), melanoma (n=20), ovarian cancer (n=20), pancreatic cancer (n=20), prostate cancer (n=20), and stomach cancer (n=20), and compared to age-matched healthy controls (n=33). Statistical differences were analyzed using the Kruskal-Wallis test adjusted for Dunn's multiple comparisons test.

Results Serum levels of autoantibodies against type III collagen were significantly lower in patients with bladder cancer (p=0.0007), breast cancer (p=0.0002), colorectal cancer (p<0.0001), head and neck cancer (p=0.0005), kidney cancer (p=0.005), liver cancer (p=0.030), lung cancer (p=0.0004), melanoma (p<0.0001), ovarian cancer (p<0.0001), pancreatic cancer (p<0.0001), prostate cancer (p<0.0001), and stomach cancer (p<0.0001) compared to healthy controls. This autoimmunity biomarker could discriminate between cancer and healthy controls with an AUROC value of 0.88 (p<0.0001).

Conclusions In this study, we observed that cancer patients with different solid tumor types have downregulated levels of circulating autoantibodies directed against type III collagen compared to healthy controls suggesting that autoantibodies against type III collagen and tumor fibrosis may be important for tumor control and eradication. This autoimmunity biomarker may have the potential for studying and monitoring the close relationship between autoimmunity and cancer such as the risk of developing cancer on rheumatoid arthritis immunosuppressant or the risk of developing immune-related adverse events on cancer immunotherapy.

Ethics Approval The serum samples in this study were obtained from the commercial vendor Proteogenex and Bio-IVT, and according to the vendors, sample collection was approved by an Institutional Review Board or Independent Ethical Committee and patients gave their informed consent (Protocol numbers PG-ONC 2003/1 and WIRB® Protocol #20161665). All investigations were carried out according to the Helsinki Declaration.

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.022>