generated an exact match of control patients from the MGB database on age, sex, and Charlson comorbidity index. For both groups, we cross referenced COVID-19 infection data through June 19, 2020 from the Massachusetts Department of Public Health using date of birth, last name, and first four letters of the first name. We calculated odds ratios (OR) for COVID-19 diagnosis using a multivariate logistic regression adjusting for age, sex, race, CCI, zip code income, and local infection rate.

Results Twenty-one patients (1.3%) prescribed ICIs and 527 controls (2.0%) were identified as COVID positive in the Massachusetts department of health database. When controlling for local infection rate, age, sex, race, CCI, and zip code income, there were no significant differences in COVID infection between ICI recipients and matched controls (OR: 0.7, 95% CI: 0.45 – 1.09, p=0.1; table 1).

Conclusions In our experience, patients who were prescribed ICI were not more likely to contract COVID-19 than matched controls, which may assist in decision-making around continuation of therapy during the pandemic. More research needs to be conducted to determine potential behavioral and testing factors that may affect COVID-19 diagnosis.

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Immune cell biology

827 ELUCIDATING THE ROLES OF PIK3IP1/TRIP IMMUNE REGULATION ON DISTINCT T CELL SUBSETS IN THE CONTEXT OF CANCER

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Background The signaling pathways involving phosphoinositide-3-kinases (PI3Ks) are highly conserved and tightly regulated to influence the activation, proliferation, and survival of all cell types. PI3K signaling plays a major role in T cell responses to antigen due to its position directly downstream of T cell receptor (TCR)/CD28 ligation. Our lab has recently shown that the cell surface protein TrIP (Transmembrane Inhibitor of PI3K, gene name: Pik3ip1) is capable of downregulating PI3K signaling in CD4+ T cells and can act as a negative regulator of T cell immune responses.[1] This negative immune regulation was just recently reported to promote antitumor immunity, implicating TrIP as a potential immunotherapy target.[2] Interestingly, although all effector subsets re-express TrIP to varying degrees, public expression data shows that Treg cells maintain higher TrIP message than other T-effector subsets.[3]

Methods Using a conditional TrIP knockout mouse model developed in our lab, we have begun to interrogate how TrIP expression regulates the opposing activities of CD8+ T cells vs. Treg and how these affect the overall tumor immune landscape. With Treg-specific TrIP KO, we assessed the effects on syngeneic tumor growth in vivo, as well as analyzed primary and tumor-derived Treg phenotypes ex-vivo.

Results Thus far, we have found that TrIP knockout in the Treg compartment leads to no detectable differences in tumor burden. However, the lack of TrIP expression on Treg does have some effect on the effector phenotype of Treg cells isolated from the tumor.

Conclusions We describe preliminary data on the role of TrIP in Treg function and phenotype and have begun to explore its effects on the tumor microenvironment. To build on this work we are currently developing TrIP over-expressing lentiviral constructs to compliment the knockout approaches described here. We have also now obtained mice with tamoxifen-inducible TrIP KO in Treg, so we will determine whether the timing of TrIP deletion affects the impact of TrIP deficiency.

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828 IMPROVED GROWTH PROPERTIES AND IMMUNE SURVEILLANCE IN K-RAS G12V-TRANSFORMED CELLS THROUGH OVEREXPRESSION OF BIGLYCAN

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Background The extracellular matrix protein biglycan (BGN) plays an essential role in matrix assembly, cellular migration, adhesion, proliferation and apoptosis. Recently, BGN expression has been shown to be impaired upon HER-2/neu overexpression, which was associated with an up-regulation of MHC class I surface expression. However, there exists no information about the link between K-RAS-mediated immune escape and BGN expression.

Methods In vitro models of human K-RAS G12V transformed mouse fibroblasts and two human colorectal carcinoma (CRC) cell lines carrying a K-RAS G12V mutation (RKO and SW480) were used for the analysis of BGN expression by qPCR and Western blot. At the same time, the major histocompatibility complex (MHC) class I surface expression, as well as CD4+ and CD8+ cells, were determined by flow cytometry. The different K-RAS G12V cells and respective controls were stably transfected with BGN. Growth properties were analyzed by proliferation, migration and invasion assays. Luciferase reporter assays were used to determine the transcriptional regulation of MHC class I APM components. Tumorgenicity of BGN transfectants in comparison to control cells was evaluated by injection of respective transfectants s.c. into mice and tumor growth was monitored over time.

Results Both murine and human K-RAS G12V cells express low levels of BGN compared to control cells. Overexpression of BGN caused an inhibition of cell proliferation, a diminished anchorage-independent growth and a reduced migration rate. The altered in vitro growth properties of BGNhigh K-RAS G12V+ correlated with a delayed tumor growth and a reduced frequency of tumor formation in vivo. Restoration of BGN expression increased the expression of decorin as well as enhanced MHC class I expression in K-RAS G12V-transformed cells. This is due to a BGN-induced transcriptional upregulation of major components of the MHC class I antigen processing machinery (APM), such as the transporter associated with antigen processing TAP1, TAP2 and LMP2, in BGN transfectants of K-RAS G12V+ cells. The results were further