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TITLE: Blood Types as Tumor-Associated Carbohydrate Antigens That Determine the Efficacy of Immune Checkpoint Inhibitor Therapy in Lung Cancer

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CONTRACTING ORGANIZATION: Children's Hospital, Boston, MA

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13. SUPPLEMENTARY NOTES

14. ABSTRACT Immune checkpoint inhibitors, such as nivolumab and pembrozilumab, is a novel class of cancer treatment that have dramatically improved the clinical outcome of advanced lung cancer. However, these checkpoint inhibitors show clinical activity in only a limited number of patients. It is not known, what determines response to this form of therapy. Despite significant research efforts, current predictors of response to checkpoint inhibitors, such as PD1/PD-L1 staining (the molecular target of these therapeutic agents) or tumor mutation burden (the estimated number of tumor antigens eliciting immune response) have rather limited ability to support clinical decisions.

We are proposing here a radical shift in our research focus from neoepitope peptide-based mechanisms to tumor associated carbohydrates (TACAs). Carbohydrates are a completely different, rather understudied class of tumor antigens. If this is indeed the case and in lung cancer tumor associated carbohydrate antigens also contribute to the efficacy to immune checkpoint inhibitor treatment, then our results will have a major impact both on the diagnostic and treatment strategy aspects of immune checkpoint inhibitor therapy. First, tumor associated carbohydrate antigens such as the aberrant expression of the Forssman antigen may produce a more accurate way to predict response to this treatment modality. Second, if the induction of cross-reacting antibodies to tumor associated carbohydrate antigens significantly contributes to immune checkpoint inhibitor therapy then we could design

15. SUBJECT TERMS
Tumor associated carbohydrate antigens, blood groups, immune checkpoint inhibitor therapy

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Introduction:

Immune checkpoint inhibitors, such as nivolumab and pembrozilumab, is a novel class of cancer treatment that have dramatically improved the clinical outcome of advanced lung cancer. However, these checkpoint inhibitors show clinical activity in only a limited number of patients. It is not known, what determines response to this form of therapy. Despite significant research efforts, current predictors of response to checkpoint inhibitors, such as PD1/PD-L1 staining (the molecular target of these therapeutic agents) or tumor mutation burden (the estimated number of tumor antigens eliciting immune response) have rather limited ability to support clinical decisions. We are proposing here a radical shift in our research focus from neoepitope peptide-based mechanisms to tumor associated carbohydrates (TACAs). Carbohydrates are a completely different, rather understudied class of tumor antigens. If this is indeed the case and in lung cancer tumor associated carbohydrate antigens also contribute to the efficacy to immune checkpoint inhibitor treatment, then our results will have a major impact both on the diagnostic and treatment strategy aspects of immune checkpoint inhibitor therapy.
First, tumor associated carbohydrate antigens such as the aberrant expression of the Forssman antigen may produce a more accurate way to predict response to this treatment modality. Second, if the induction of cross-reacting antibodies to tumor associated carbohydrate antigens significantly contributes to immune checkpoint inhibitor therapy then we could design strategies to enhance efficacy of treatment by e.g. boosting the plasma antibody levels against these antigens.

Keywords:

Tumor associated carbohydrate antigens, blood groups, immune checkpoint inhibitor therapy

Accomplishments:

We had to secure all appropriate IRB approvals for procuring tissue samples. This has taken longer than expected and we could not start research activities in earnest before the end of the first year of funding.

What opportunities for training and professional development has the project provided? Nothing to report.

How were the results disseminated to communities of interest? Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals? We will start performing the experiments as proposed in the application

What was the impact on the development of the principal discipline(s) of the project? N/A

What was the impact on other disciplines? Nothing to report.

What was the impact on technology transfer? Nothing to report.

What was the impact on society beyond science and technology? Nothing to report

CHANGES/PROBLEMS:

Changes in approach and reasons for change: There are no changes.

Actual or anticipated problems or delays and actions or plans to resolve them:
Obtaining IRB approvals took longer than expected. Now we have all necessary approvals for the work.

Changes that had a significant impact on expenditures: Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents: Nothing to report.

PRODUCTS:

Journal publications: Nothing to report

Books or other non-periodical, one-time publications: Nothing to report

Other publications, conference papers and presentations: Nothing to report

Website(s) or other Internet site(s): Nothing to report

Technologies or techniques: Nothing to report

Inventions, patent applications, and/or licenses: Nothing to report

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Name: Zoltan Szallasi, MD

Project Role: PI

Researcher Identifier (e.g. ORCID ID): 0000-0001-5395-7509

Nearest person month worked: 2 months

Contribution to Project: Dr. Szallasi obtained the necessary IRB approvals

Funding Support: