Student Checklist (1A)

This form is required for ALL projects.

1. a. Student/Team Leader: Alex Breslav Grade: 11

   Email: breslav.alex@yahoo.com Phone: (516) 743-5377

   b. Team Member: _____ c. Team Member: _____

2. Title of Project:

   Evaluating the efficacy of developed antibodies in detecting pancreatic ductal adenocarcinoma tumors

3. School: George W. Hewlett High School School Phone: (516) 792-4001

   School Address: 60 Everit Avenue, Hewlett NY 11557

4. Adult Sponsor: Dr. Terrence Bissoondial Phone/Email: tbissoondial@hewlett-woodmere.net

5. Does this project need SRC/IRB/IACUC or other pre-approval? ☐ Yes ☒ No Tentative start date: July 8, 2019

6. Is this a continuation/progression from a previous year? ☐ Yes ☒ No

   If Yes:

   a. Attach the previous year's ☐ Abstract **and** ☐ Research Plan/Project Summary

   b. Explain how this project is new and different from previous years on

   ☐ Continuation/Research Progression Form (7)

7. This year's laboratory experiment/data collection:

   07/08/19 (Actual Start Date: (mm/dd/yy)) 10/15/19 (End Date: (mm/dd/yy))

8. Where will you conduct your experimentation? (check all that apply)

   ■ Research Institution ☐ School ☐ Field ☐ Home ☐ Other: _____

9. List name and address of all non-home and non-school work site(s):

   Name: Memorial Sloan Kettering Cancer Center - Mortimer Zuckerman Research Center

   Address: 417 E 68th St, New York, NY 10065

   Phone/email: goosj@mskcc.org (646) 457-5104

10. **Complete a Research Plan/Project Summary following the Research Plan/Project Summary instructions and attach to this form.**

11. **An abstract is required for all projects after experimentation.**

Research Plan/Project Summary Instructions

A complete Research Plan/Project Summary is required for ALL projects and must accompany Student Checklist (1A).

1. All projects must have a Research Plan/Project Summary
   a. Written prior to experimentation following the instructions below to detail the rationale, research question(s), methodology, and risk assessment of the proposed research.
   b. If changes are made during the research, such changes can be added to the original research plan as an addendum, recognizing that some changes may require returning to the IRB or SRC for appropriate review and approvals. If no additional approvals are required, this addendum serves as a project summary to explain research that was conducted.
   c. If no changes are made from the original research plan, no project summary is required.

2. Some studies, such as an engineering design or mathematics projects, will be less detailed in the initial project plan and will change through the course of research. If such changes occur, a project summary that explains what was done is required and can be appended to the original research plan.

3. The Research Plan/Project Summary should include the following:
   a. **RATIONALE:** Include a brief synopsis of the background that supports your research problem and explain why this research is important and if applicable, explain any societal impact of your research.
   b. **RESEARCH QUESTION(S), HYPOTHESIS(ES), ENGINEERING GOAL(S), EXPECTED OUTCOMES:** How is this based on the rationale described above?
   c. Describe the following in detail:
      - **Procedures:** Detail all procedures and experimental design including methods for data collection. Describe only your project. Do not include work done by mentor or others.
      - **Risk and Safety:** Identify any potential risks and safety precautions needed.
      - **Data Analysis:** Describe the procedures you will use to analyze the data/results.
   d. **BIBLIOGRAPHY:** List major references (e.g. science journal articles, books, internet sites) from your literature review. If you plan to use vertebrate animals, one of these references must be an animal care reference.

Items 1–4 below are subject-specific guidelines for additional items to be included in your research plan/project summary as applicable.

1. **Human participants research:**
   a. **Participants:** Describe age range, gender, racial/ethnic composition of participants. Identify vulnerable populations (minors, pregnant women, prisoners, mentally disabled or economically disadvantaged).
   b. **Recruitment:** Where will you find your participants? How will they be invited to participate?
   c. **Methods:** What will participants be asked to do? Will you use any surveys, questionnaires or tests? If yes and not your own, how did you obtain? Did it require permissions? If so, explain. What is the frequency and length of time involved for each subject?
   d. **Risk Assessment:** What are the risks or potential discomforts (physical, psychological, time involved, social, legal, etc.) to participants? How will you minimize risks? List any benefits to society or participants.
   e. **Protection of Privacy:** Will identifiable information (e.g., names, telephone numbers, birth dates, email addresses) be collected? Will data be confidential/anonymous? If anonymous, describe how the data will be collected. If not anonymous, what procedures are in place for safeguarding confidentiality? Where will data be stored? Who will have access to the data? What will you do with the data after the study?
   f. **Informed Consent Process:** Describe how you will inform participants about the purpose of the study, what they will be asked to do, that their participation is voluntary and they have the right to stop at any time.

2. **Vertebrate animal research:**
   a. Discuss potential ALTERNATIVES to vertebrate animal use and present justification for use of vertebrates.
   b. Explain potential impact or contribution of this research.
   c. Detail all procedures to be used, including methods used to minimize potential discomfort, distress, pain and injury to the animals and detailed chemical concentrations and drug dosages.
   d. Detail animal numbers, species, strain, sex, age, source, etc., include justification of the numbers planned.
   e. Describe housing and oversight of daily care
   f. Discuss disposition of the animals at the termination of the study.

3. **Potentially hazardous biological agents research:**
   a. Give source of the organism and describe BSL assessment process and BSL determination.
   b. Detail safety precautions and discuss methods of disposal.

4. **Hazardous chemicals, activities & devices:**
   - Describe Risk Assessment process, supervision, safety precautions and methods of disposal.
   - Material Safety Data Sheets are not necessary to submit with paperwork.

Evaluating the specificity of novel monoclonal antibodies for pancreatic ductal adenocarcinoma

Alex Breslav

RESEARCH PLAN

A. RATIONALE

Cancer is currently one of the leading causes of death, with roughly 9.6 million deaths annually globally and about 18.1 million newly diagnosed cancer cases every year (4). One of the most lethal types, as well as one of the most common types (8), is pancreatic ductal adenocarcinoma (PDAC). PDAC is an exocrine cancer (35) that is derived from the ducts of the pancreas (11) and makes up roughly 90% of all pancreatic cancers (8), while also being the 12th most common cancer worldwide (16).

Unfortunately, PDAC only has a 9% 5-year survival rate (23), with pancreatic cancer as a whole making up 7% of all cancer deaths (20), making it the 4th deadliest cancer in the United States, (29) and by 2020, it is expected to be the 2nd deadliest (12). However, due to the current lack of reliable therapeutic options for PDAC in-clinic, tumor resection surgery is the best method to treat this cancer (24). Furthermore, since the pancreas is located near many major blood vessels (5), and PDAC is a hyper-aggressive cancer that typically asymptomatic until metastasizing has begun (9), opportunities for tumor resection surgery is rare. Only about 15-20% PDAC patients can undergo tumor resection surgery upon diagnosis (9). At the root of this low survival rate is indubitably the consistent failure to diagnose PDAC at earlier stages, as well as the frequent misdiagnosis of PDAC. Approximately 31.3% of people with PDAC are misdiagnosed with other types of cancers, often resulting in unnecessary surgeries/treatment before the mistake is realized (36). Obviously, the asymptomatic characteristics of PDAC also

play a role in these consistent late diagnosis of PDAC, but unavailability of reliable treatments and efficient techniques to diagnose PDAC also plays a role.

Previous studies attempting to delineate PDAC tumors through the use of antibody-antigen interactions have focused on the interaction between the monoclonal antibody (5B1) and the antigen Carbohydrate Antigen 19.9, or CA19.9 (38). However, CA19.9 is an antigen not exclusive to pancreatic cancers (30), or PDAC. CA19.9 it was first discovered to be expressed by colorectal carcinoma cells (30) and since shown to be expressed in other cancerous and non-cancerous conditions (33). Concerning antibody uptake, numerous studies have shown using PET scans that PDAC tumor can significantly take up the radiolabeled 5B1 (19). However, since CA19.9 is rarely present in asymptomatic populations (30), it is difficult to use this antigen-antibody interaction as suboptimal imaging agent for early diagnosis of PDAC. CA19.9 is also often shed into circulation rather than remaining on surface membranes of cells (15), resulting in relatively high radiation exposure to other parts of the body.

There have also been other relatively successful studies for imaging PDAC tumors that utilize the Carcinoembryonic Antigen (CEA) biomarker, however, similarly to CA19.9, it is typically not expressed by asymptomatic populations (6), and is also shed into circulation (1). In addition, CEA is also expressed by other cancers (17).

Since there is no reliable antigenic markers, it is important to identify new antigenic markers that are exclusive to PDAC and are not shed into circulation as the cancer progresses. This study investigates if two developed antibodies (AB1 and AB2) can successfully reach a PDAC tumor.

B.

RESEARCH QUESTIONs

Can monoclonal antibodies AB1 and AB2 detect PDAC in vitro and in vivo? How specific is the binding of antibodies AB1 and AB2 to PDAC?

Hypothesis

Since antibodies AB1 and AB2 were generated from organoids derived from PDAC, they will show a selective binding to PDAC *in vitro* or *in vivo*.

The ideal antibody would only bind to PDAC tissue and other malignant tissues, but not normal tissue.

C.

PROCEDURE

The handling of radioactively labelled antibodies, tissue and animal studies will performed by mentor. I will ONLY analyze the results from these experiments.

Risk and Safety:

All experiments will be performed by mentor. I will only analyzed the data generated. There will be no more than minimal risk associated.

Analysis of Data:

For data analysis, Microsoft Excel, the BIOSCAN AR 2000, imageJ, the 3D Slicer software (v4.8.1), and the Inveon Research Workspace software (Siemens Medical Solutions, Knoxville, USA) will be used.

The BIOSCAN AR 2000 will be used to construct graphs of radiochemical purity after performing the iTLCs, and then to more accurately determine the exact radiochemical purities.

After the PET scans are performed, individual image volumes will be constructed using the cropping function of the Inveon Research Workspace software. To determine the actual activity concentrations, in % ID/g, of the images, the counting rates will be converted using a system calibration factor, which will be derived from a mouse-sized water-equivalent phantom containing ^{89}Zr. To finish constructing the images, the 3D Slicer software will be used.

The weights of each tissue will be calculated, and the radioactivity bound to each tissue, will be measured in % ID/g, using the 2480 Wizard gamma counter (performed by mentor). Excel will be used to calculate the percentage of tracer uptake, expressed as % ID/g, as the activity bound to the tissue per tissue weight per the actual injected dose, decay-corrected to the time of counting. Relevant graphs and charts composed of the calculated data will then be constructed.

ImageJ will be used on the immunohistochemical stainings to quantify the percentage of stained tissue area versus the percentage of unstained tissue area. The higher the percentage of stained area in the stainings, the higher the presence of an antigen being targeted by the subject antibody in that specific tissue type.

D. **BIBLIOGRAPHY**

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