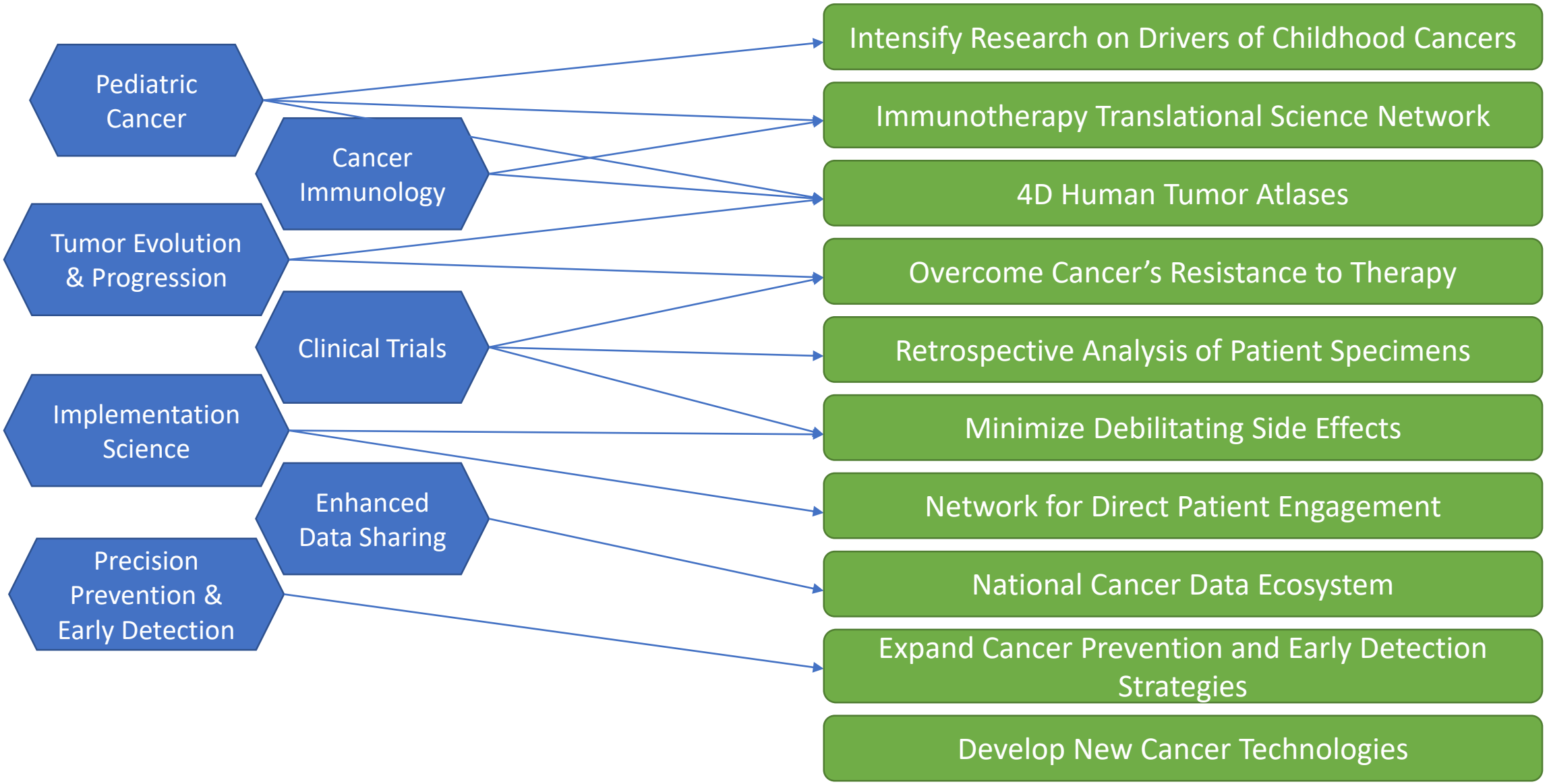
NCI Cancer Moonshot Initiative: Activities to Promote Human Immune-Representing Oncology Models (APHIROM)

Tony Dickherber (CSSI) & Jennifer Couch(DCB)

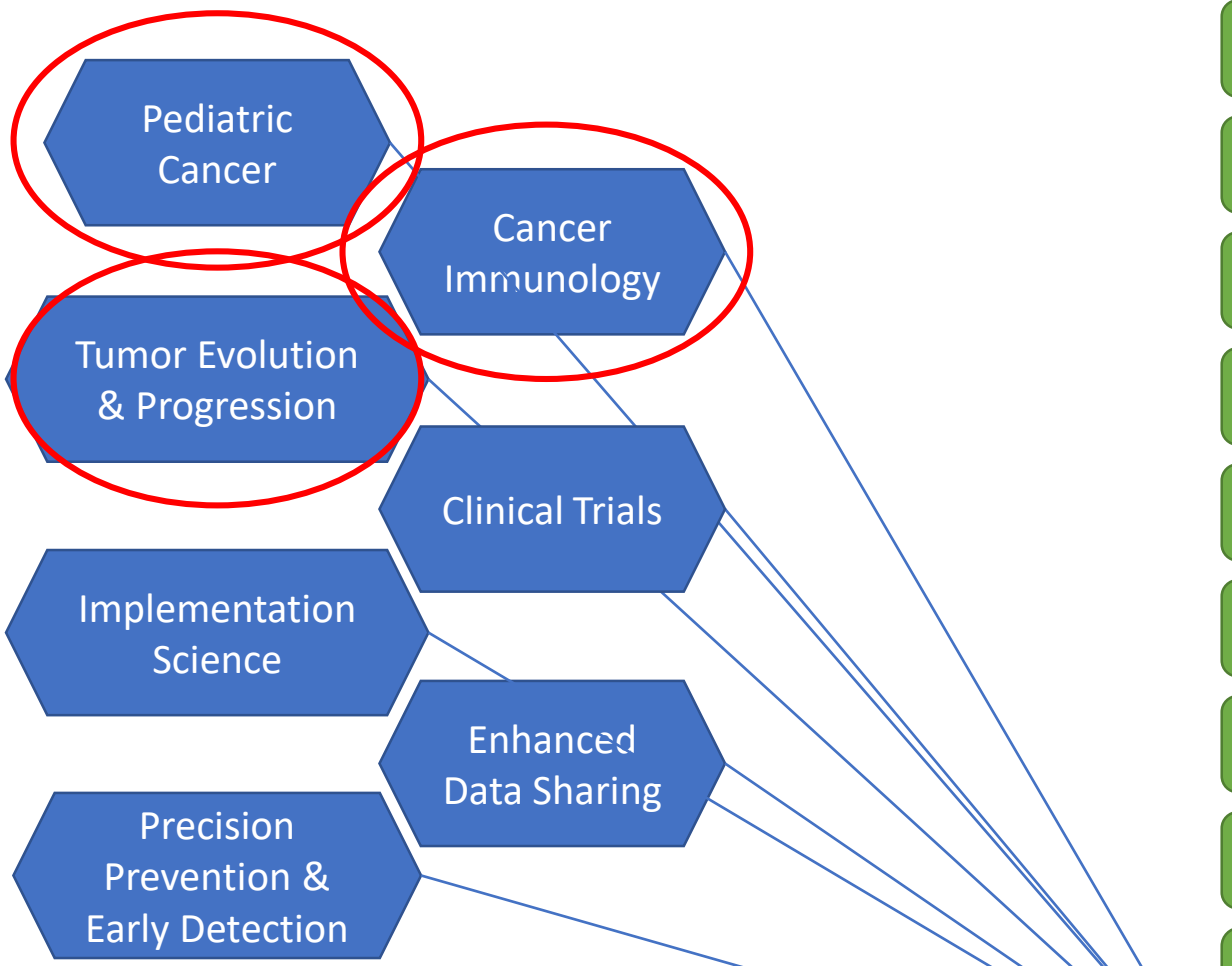
NIH NATIONAL CANCER INSTITUTE

March 25, 2019

Blue Ribbon Panel Recommendations



Blue Ribbon Panel Recommendations



- Intensify Research on Drivers of Childhood Cancers
- Immunotherapy Translational Science Network
- 4D Human Tumor Atlases
- Overcome Cancer's Resistance to Therapy
- Retrospective Analysis of Patient Specimens
- Minimize Debilitating Side Effects
- Network for Direct Patient Engagement
- National Cancer Data Ecosystem
- Expand Cancer Prevention and Early Detection Strategies
- Develop New Cancer Technologies

Blue Ribbon Panel Recommendations

Tumor Evolution & Working

Develop and characterize systems

- generate tumor-bearin "humanized" immune
- Priority: *mouse mode interrogating aspect as they relate to dru address these proces of an intact immune*

Pediatric Cancers Wor

- there is a marked paucity of mo the basic molecular mechanism

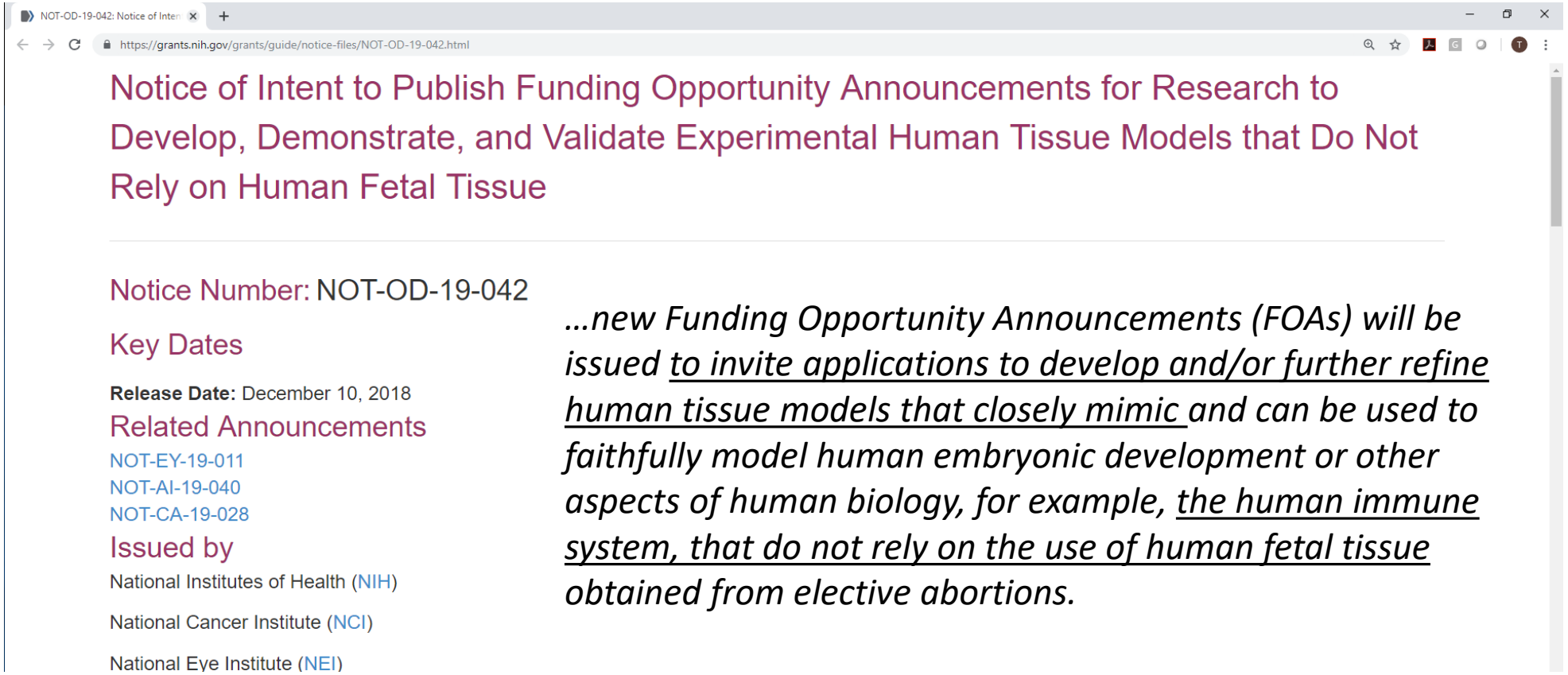
Recommendation:

- *Murine models that recapitu immunosuppressive tumor n characteristic of embryonal soli be developed and we need to c preclinical testing program that immune competent models a infrastructure to both test new st tumor efficacy, but also toxicity in the right systems*

Cancer Immunotherapy & Prevention Working Group

- A "Cancer Moonshot Clinical Trial Immunotherapy Network" … to test novel immunotherapies efficiently and with a deep understanding of how pathways work and influence each other, as well as additional fundamental obstacles to success
- Among myriad priorities, *the "Network will focus on…Developing animal models appropriate for these immune studies*

New NIH Priority



Use of Human Fetal Tissue to Support Cancer Research

Trends in Immunology

Sept 2018 CellPress REVIEWS

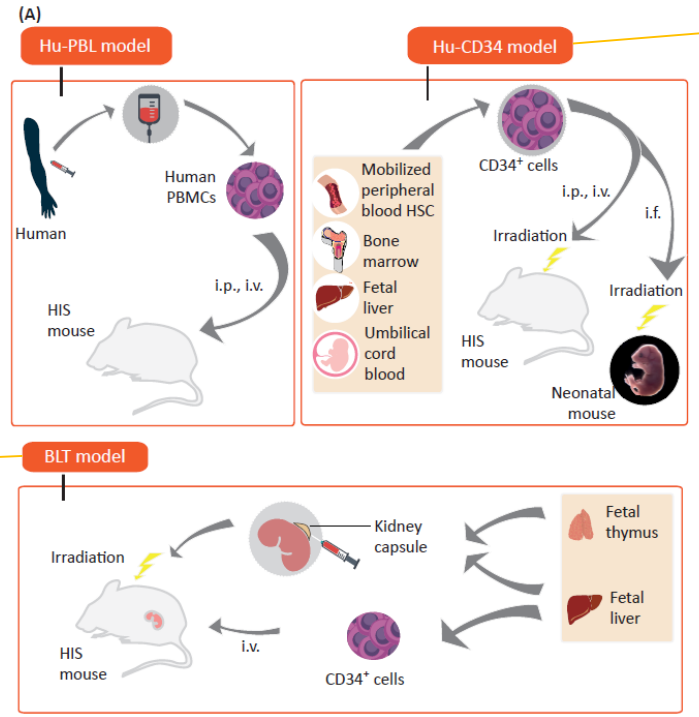
Review

Humanized Mice for the Study of Immuno-Oncology

Philippe De La Rochere,[1] Silvia Guil-Luna,[2] Didier Decaudin,[3] Georges Azar,[4] Sukhvinder S. Sidhu,[4] and Eliane Piaggio[1,*]

Key Figure

Schematic of Hu-PBL, Hu-CD34, and Bone Marrow–Liver–Thymus (BLT) Humanized Mouse Models, and their Use as AVATARs



- Higher incidence of GvHD
- Lack of cytokine and human growth factors
- $$$

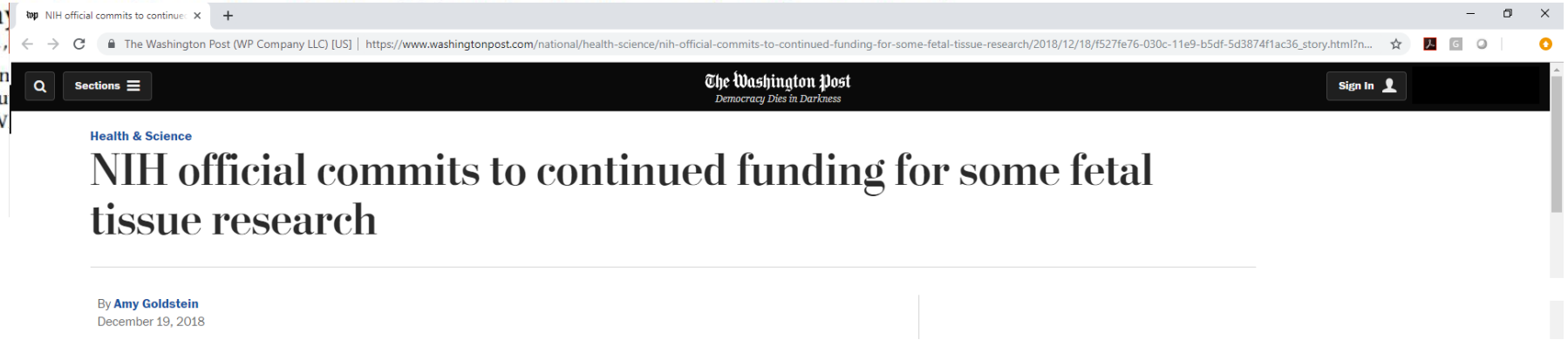
- B cells and monocytes fail to mature
- T and NK cells display some functional impairment
- TCR repertoire is restricted
- $$

Exploring Potential Alternatives

Stem Cell Reports
Report
ISSCR
OPEN ACCESS

A Humanized Mouse Model Generated Using Surplus Neonatal Tissue

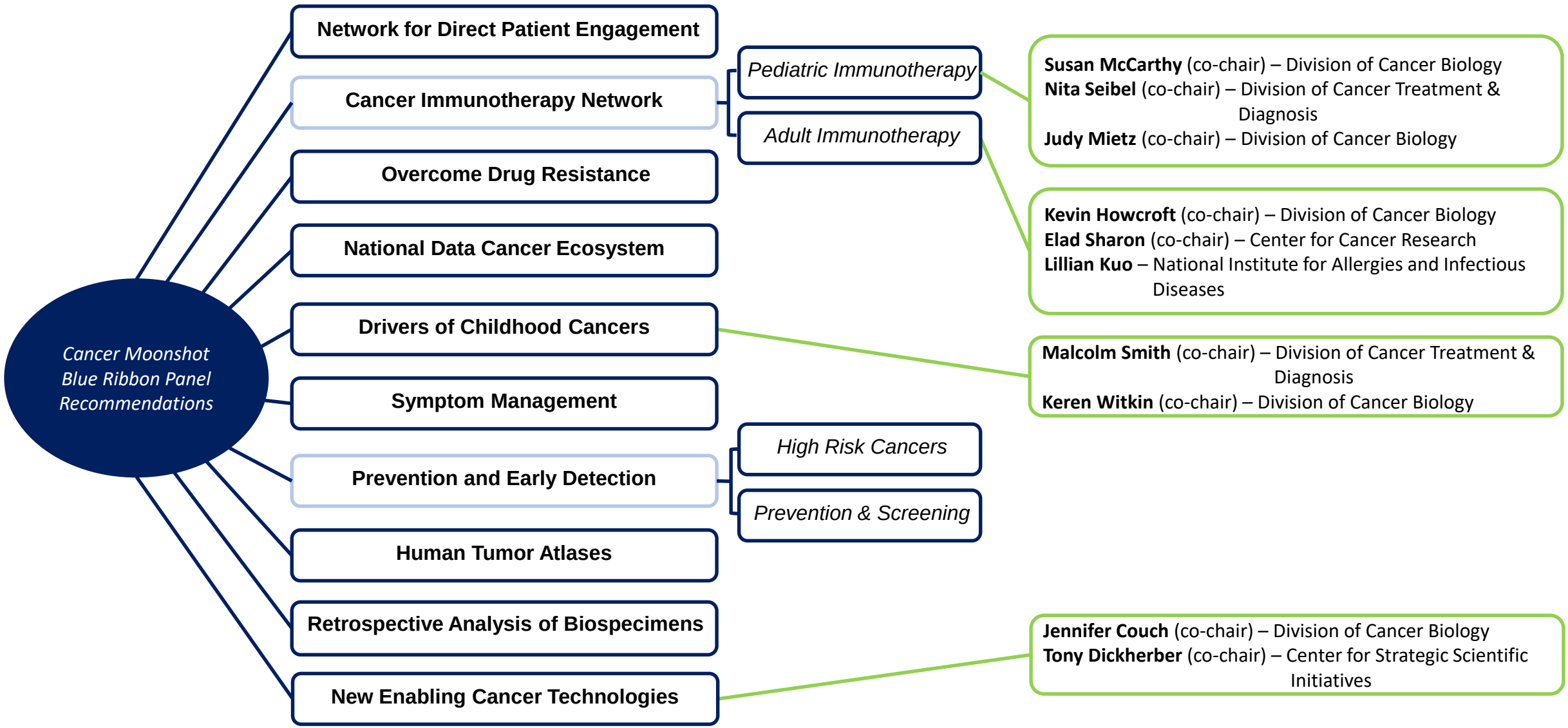
Matthew E. Brown,[1,2] Ying Zhou,[1] Brian E. McIntosh,[3] Ian G. Norman,[1] Hannah E. Lou,[1] Mitch Biermann,[4]
Jeremy A. Sullivan,[1] Timothy
and William J. Burlingham[1],
[1]Division of Transplantation/Departmen
[2]Regenerative Biology, Morgridge Institu
[3]Covance Laboratories Inc.. Madison. W


NIH official commits to continue
The Washington Post (WP Company LLC) [US] | https://www.washingtonpost.com/national/health-science/nih-official-commits-to-continued-funding-for-some-fetal-tissue-research/2018/12/18/f527fe76-030c-11e9-b5df-5d3874f1ac36_story.html?n...
Sections
The Washington Post
Democracy Dies in Darkness
Sign In
Health & Science
NIH official commits to continued funding for some fetal tissue research
By Amy Goldstein
December 19, 2018

"…[HHS Asst Sec for Health] Giroir said that any alternative sources of tissue "must be as predictive, as reliable and as validated as existing models" that use fetal tissue…

The consensus of the meeting, also led by Daniel Rotrosen, director of NIAID's Division of Allergy, Immunology and Transplantation, was that no such models exist"

APHIROM Program Team



APHIROM Strategy

- FY19 – Administrative Supplements
  - Small awards for active model development projects to improve representation of human immune system

- FY20 – New Request for Applications [R33]
  - Larger awards to launch new efforts to address the broader goal of producing model systems that might replace those developed with human fetal tissue

https://grants.nih.gov/grants/guide/notice-files/NOT-CA-19-028.html

Notice of Special Interest: Administrative Supplements for Activities to Promote Human Immune-Representing Oncology Models

Notice Number: NOT-CA-19-028

Key Dates

Release Date: March 5, 2019

Related Announcements

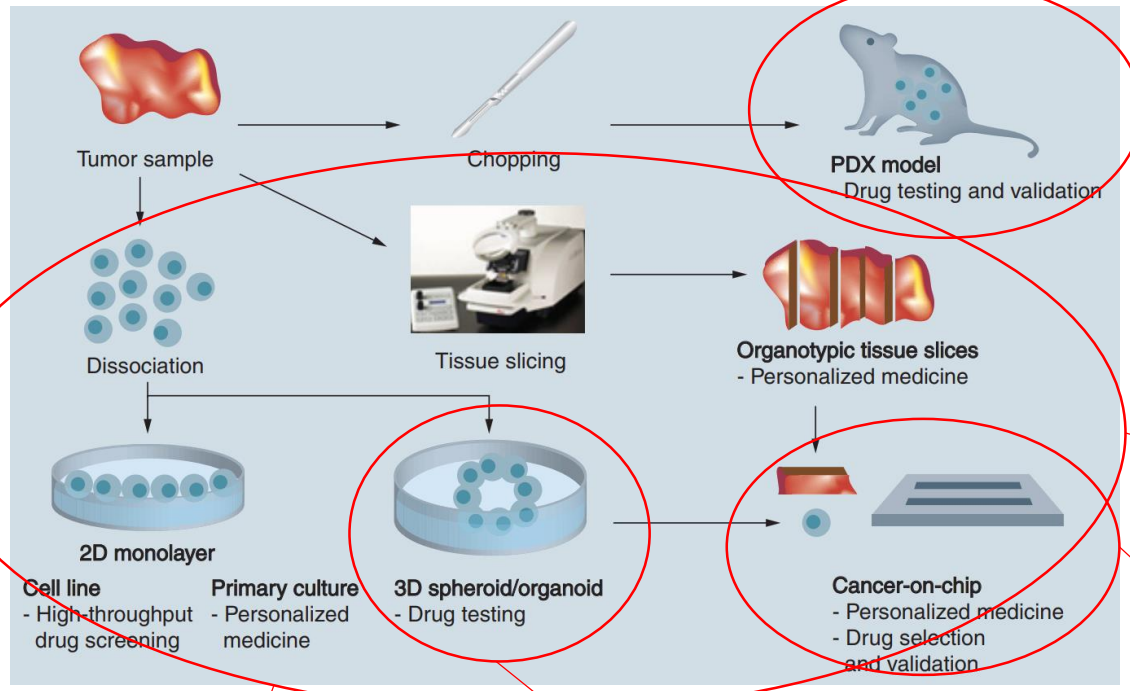
PA-18-591
NOT-OD-19-042

Issued by

National Cancer Institute (NCI)

- *"to improve representation of the human immune system in ongoing cancer modeling development projects that can be utilized in immuno-oncology research."*
- *"proposed research efforts must address recapitulating the tumor microenvironment with appropriate elements of the human immune system."*
- $125k direct cost capped administrative supplement
- Any ongoing NCI-supported project eligible
- **Applications due June 3, 2019**
- Anticipating 4-5 awards

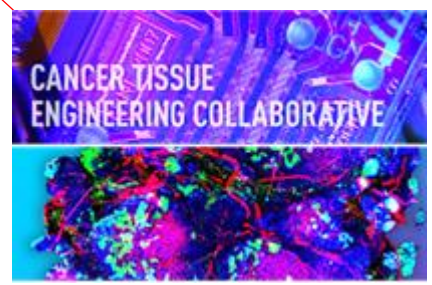
NCI Support for Cancer Model Development



T Meijer *et al*, Fut Sci OA March 2017

SBIR & STTR

IMAT
INNOVATIVE MOLECULAR ANALYSIS TECHNOLOGIES



ONCOLOGY MODELS FORUM

ex vivo models with human immune representation

CANCER TISSUE ENGINEERING COLLABORATIVE

"…ex vivo diagnostic systems that recapitulate patient-specific tumor biology with the potential to predict response to immune-based therapies in real-time."

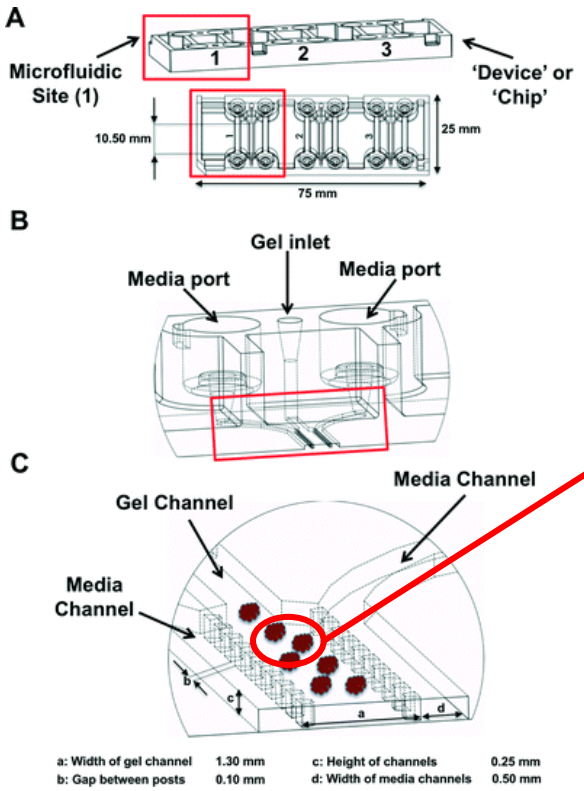
Aref *et al*, Lab Chip, Sept 2018

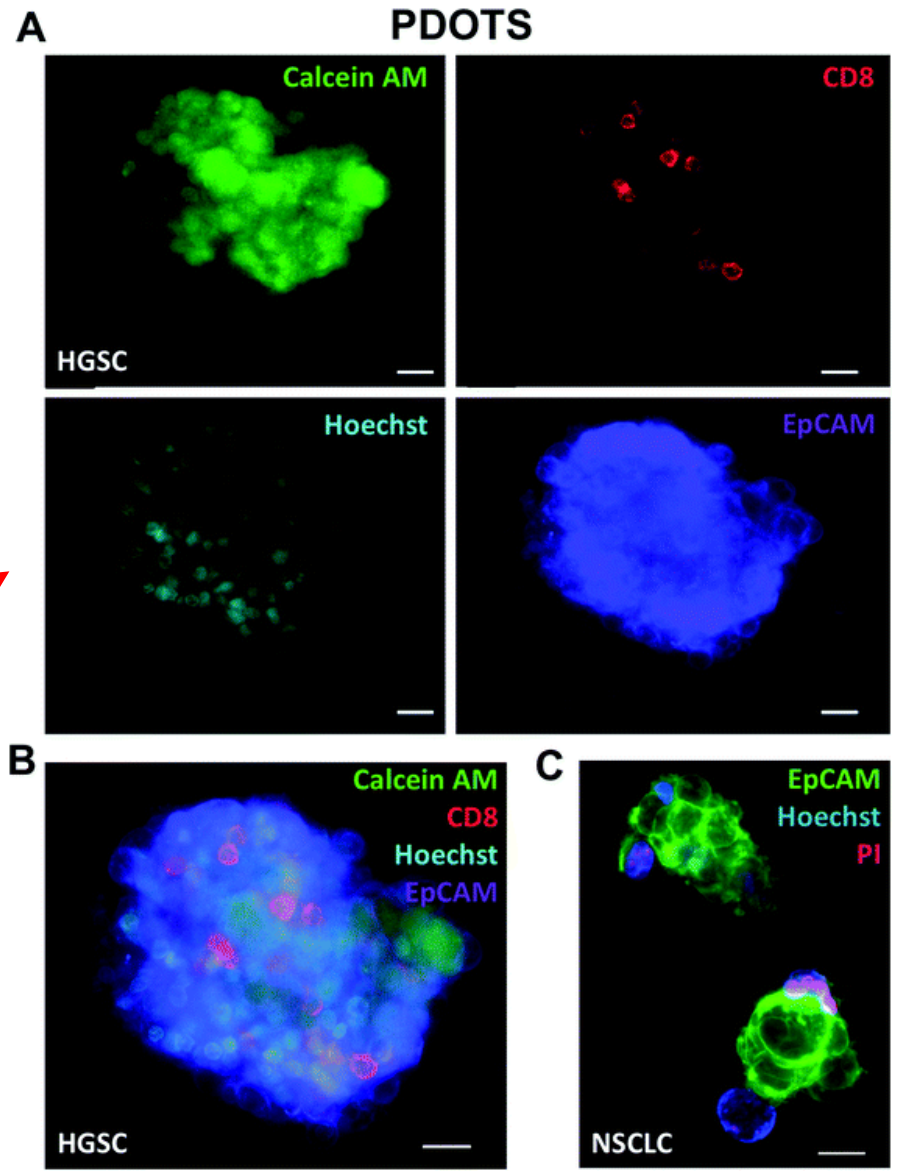
David Barbie, M.D.
Medical Oncology

DANA-FARBER CANCER INSTITUTE

Roger Kamm, Ph.D.
Biomedical Engineering

Massachusetts Institute of Technology





RFA Proposal

Purpose

- Support new model development research projects proposing to recapitulate innate and adaptive components of the human immune system without the use of human fetal tissue, in a manner that addresses the needs of immuno-oncology research. Models must demonstrate recapitulation of human immune function.

Scope

- Proposed research projects must focus on recapitulation of the human immune system in their proposed cancer model using human cells or tissues to regenerate and/or recapitulate the human immune system in *in vivo* or *in vitro* immuno-oncology models in a manner that matches or exceeds representation of the human immune system achieved with murine models developed using human fetal tissue.
  - **Non-responsive:** Models derived from genetically manipulated immune systems without introduction of human immune lineage cells will not be considered responsive.

RFA Details

Awards

- Single receipt date, anticipating support for 2-3 R33 projects
- Maximum budget of **$250,000 direct costs per year for up to 4 years** (adequate to support multi-PI teams)
- Accounts for up to $4,000,000 in total cost

Anticipated Schedule

- April 2019: Issue “Notice of Intent to Publish”
- June/July 2019: Publish RFA
- Nov/Dec 2019: Application Due Date
- June 2020: Award Date/Project Start Date

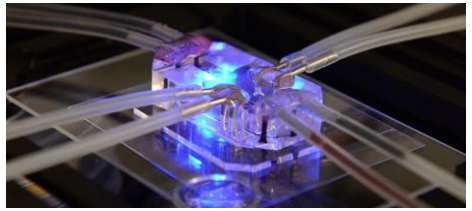
Outcome Measures

- Development Measures
  - Exhibit capabilities that support replacement of models developed using human fetal tissue
  - The number of projects that meet their proposed performance measures
  - Publications demonstrating progress towards proposed aims
  - Evidence of subsequent investment to pursue dissemination

- Dissemination Measures
  - The number of new collaborations explored by supported model developers and investigators associated with immuno-oncology research
  - The number of models that are adopted by immuno-oncology research groups (especially those replacing models developed using human fetal tissue)

Coordination across Cancer Moonshot

Courtesy Creative Biolabs



Courtesy NCATS-Tissue Chip

CIMAC-CIDC
Immuno-Oncology
Biomarkers Network

IOTN
Immuno-Oncology
Translational Network

PI-DDN
Pediatric Immunotherapy
Discovery & Development
Network

Immuno-Engineering to Improve Immunotherapy (i3) Centers

NCI CANCER MOONSHOT
A program of the National Cancer Institute of the National Institutes of Health

Fusion Oncoprotein in Childhood Cancer (FusOnC^2) Consortium

NCI Mouse Repository at FNLCR

Moonshot Pediatric Core at FNLCR

NCI Cancer Research Data Commons

NATIONAL CANCER INSTITUTE

www.cancer.gov

www.cancer.gov/espanol