Highlights of the EDRN Pancreas Collaborative Group

EDRN Steering Committee Meeting

July 1, 2020

CVC: MD Anderson; Maitra
CVC: Pitt and UNMC; Brand & Batra
BDL: VARI, Pitt and MSKCC; Haab, Brand & Allen
DMCC: Data Analysis by Ying Huang

Overview

- Team projects: leveraging the consortium structure
- Tangible outcomes: biomarkers with clinical utility
- Resource and opportunities for advancing the field
- SWOT results

Team Projects

- Purpose: blinded biomarker validation using a common sample set across multiple labs.
- Features of the consortium structure:
  - Controlled sample collection from multiple sites
  - Integrated involvement of statistical support from start to finish
  - High representation of resectable and pre-diagnostic cancer
  - Rapid execution of the studies

Team Projects

- Bakeoff 1
  - PDAC (n = 71) and healthy and benign (n = 68)
- Bakeoff 2
  - 340 Case/Control samples from UPMC and MD Anderson
  - Cases: PDAC, high grade IPMN/MCN, other pancreatic cancers (cholangiocarcinoma, neuroendocrine tumors, ampullary carcinoma)
  - Controls: healthy control with or w/o family history, pancreatitis, benign biliary obstruction, low grade MCN/IPMN and benign cysts
- Bakeoff 3
  - Pre-diagnostic UPMC cohort

Outcomes: improvement over CA19-9

Cross-validated performance of CA199 alone: Sens=0.61 at 90% Spec

	Spec		Sens	
	Naïve	Cross-Val	Naïve	Cross-Val
CA199+CA199.sTRA	**0.91**	0.89	**0.75**	0.73
CA199+CA199.sTRA+Angiostatin	**0.91**	0.89	**0.79**	0.76

Summary:

- **CA199.sTRA combined with CA199 helps improve sensitivity at high specificity**
- **Additional markers potentially improve performance further**

Pre-diagnostic UPMC Cohort

- Total of 272 samples sent
- All PDACs confirmed histologically
- Collected 6 months to 36 months from date of PDAC diagnosis
- Unique matching of controls
  - Control diagnoses matched in PLuSS
  - Control diagnoses matched to the diagnoses at the time of pre-diagnostic specimen collection
    - CP, AP, RAP, Extrahepatic biliary stricture or dilation, pseudocyst, IPMN
    - Genetic diagnoses also matched if possible
  - Paired pre-diagnostic and diagnostic specimens available in some case
  - Few cases have multiple pre-diagnostic time points.

Early Detection Research Network

Pancreatic Cyst Biomarker Alliance (PCBA)

- Blinded validation study involving multiple clinical sites and laboratories
- DMCC organized the blinding, distribution, and analysis
- Goal - improve upon current methods to:
  - Distinguish mucinous (cancer precursors) from non-mucinous
  - Distinguish between high and low malignant potential
- Biomarker results returned from 5 labs using >200 samples each

Reference Sets

- PDAC reference set
  - 242 blinded samples collected under the EDRN program
  - Distributed to multiple sites within and outside the EDRN
- Pancreatic cyst reference set
  - First of its kind
  - Multiple centers using the EDRN SOP
  - Enrollment goal of 450 (270 with resection)
  - Need just 15 with resection to complete the set
  - Blood & cyst fluid, imaging & operative findings

Current Opportunities

- Increased interactions with other consortia: CPDCP, PCDC, Imaging repository
- Pursuing a practical strategy for early detection: biomarker surveillance in high-risk groups combined with follow-up imaging
- Access the UK Biobank, WHI, PLCO, NOD cohorts
- Advancing our biomarkers with clinical utility

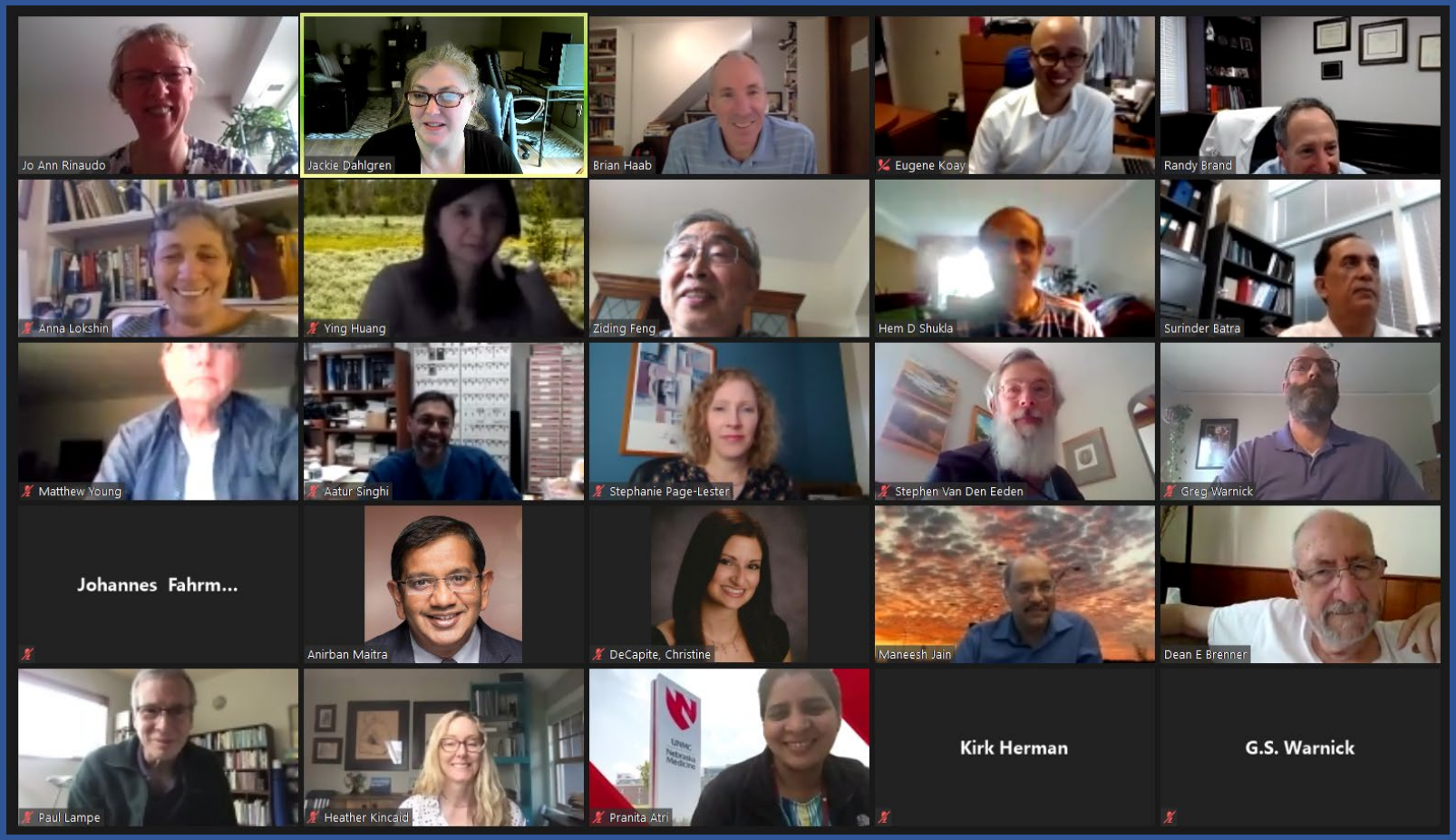
Highlights of the SWOT analysis

- Strengths: access to pooled resources & rare samples, reference sets, integrated statistical support
- Weaknesses: lack of precursor samples, difficulties obtaining pre-diagnostic samples, lack of strong interactions with other consortia
- Opportunities: increase samples from high risk groups, share samples with other consortia to increase diversity of analyses
- Threats: depletion of resources and funding, insurance issues

Summary

- First-of-kind studies in pancreatic cancer: Bakeoff studies, PCBA
- Unique reference sets
- Outcomes: improvement over CA19-9 in blinded studies
- Opportunities in interactions with other consortia to advance biomarkers with clinical utility

Collaborative Group Pic



SWOT analysis

Strengths	Weaknesses
Discuss the strengths of EDRN and suggestions to strengthen the Network	Identify weaknesses and discuss the solutions and strategies for mitigation
• Access to pooling resources for early stage PDAC resectable specimens collected following strict standardized SOPs through EDRN • Reference sets that are established through EDRN • Integrated access to statistical and informatics support at the planning stage, not just analysis stage • Access to validated pathology within the EDRN network • Industry	• Not a lot of samples available, hard to assemble early stage, biopsy and precursor samples – particularly for discover studies • Lack of matched serum and tissue samples with imaging not impacted by neoadjuvant therapy • More integration with CPDPC/PCDC • Lack of association of markers with subtypes and risk factors with subtypes • Diversity
Opportunities	**Threats**
Discuss opportunities and highlight prioritized opportunities	Discuss threats (competing interests/research) and mitigations
• Establish matched serum and tissue samples with imaging not impacted by neoadjuvant therapy • Late onset diabetes cases and markers specific to this high-risk group • Integrate with other networks • Apply and request samples from other networks that have imaging and circulating DNA analysis – access both ways • Integrating data together • Industry • Prioritize diversity	• Resources being depleted • Funding • Perception from non-pancreatic researchers that we are dealing with a disease that has less than 10% survival rate • Insurance issues