

Resources for Ovarian Cancer Discovery and Validation Studies: The PREDICT Consortium

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Phase 2 (case-control) and phase 3 (prospective) studies: discrepancies in findings

- **Methodologic biases** [lack of “internal” validity]
- **Lack of specificity for [early stage] tumors**
Discrimination markers may be related to late-stage epi-phenomena of tumor development →
lack of tumor specificity
- **Lack of sensitivity for early-stage tumors**

Particularly relevant for ovarian cancer given late stage at diagnosis

Individual prospective studies → limited number of cases diagnosed within relatively close proximity to blood collection

- „OMICs“ type discovery → multiple testing: avoidance of chance findings
- Multi-marker panels → development of algorithms, avoidance of overfitting → re-sampling approaches: training-test, bootstrapping
- Comparison of detection discrimination between sub-sets of cancer cases

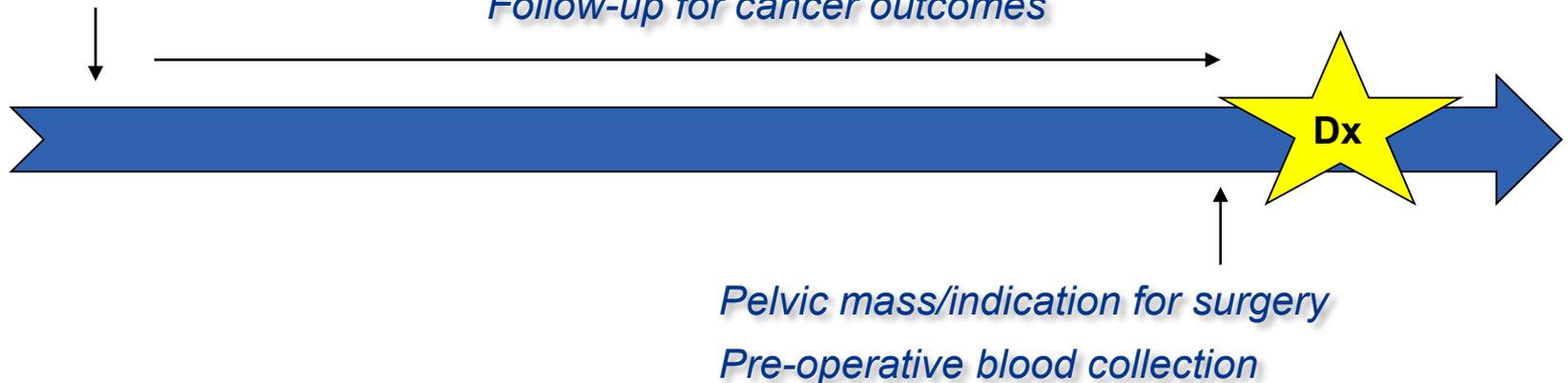
PREDICT: Prospective Early Detection Consortium for Ovarian Cancer

- DoD funded consortium
 - application of state-of-the-art “omics” technologies for biomarker discovery and validation using “PROBE” criteria
 - large-scale prospective cohort studies and biobanks with blood samples collected up to 18 months prior to diagnosis/diagnostic surgery

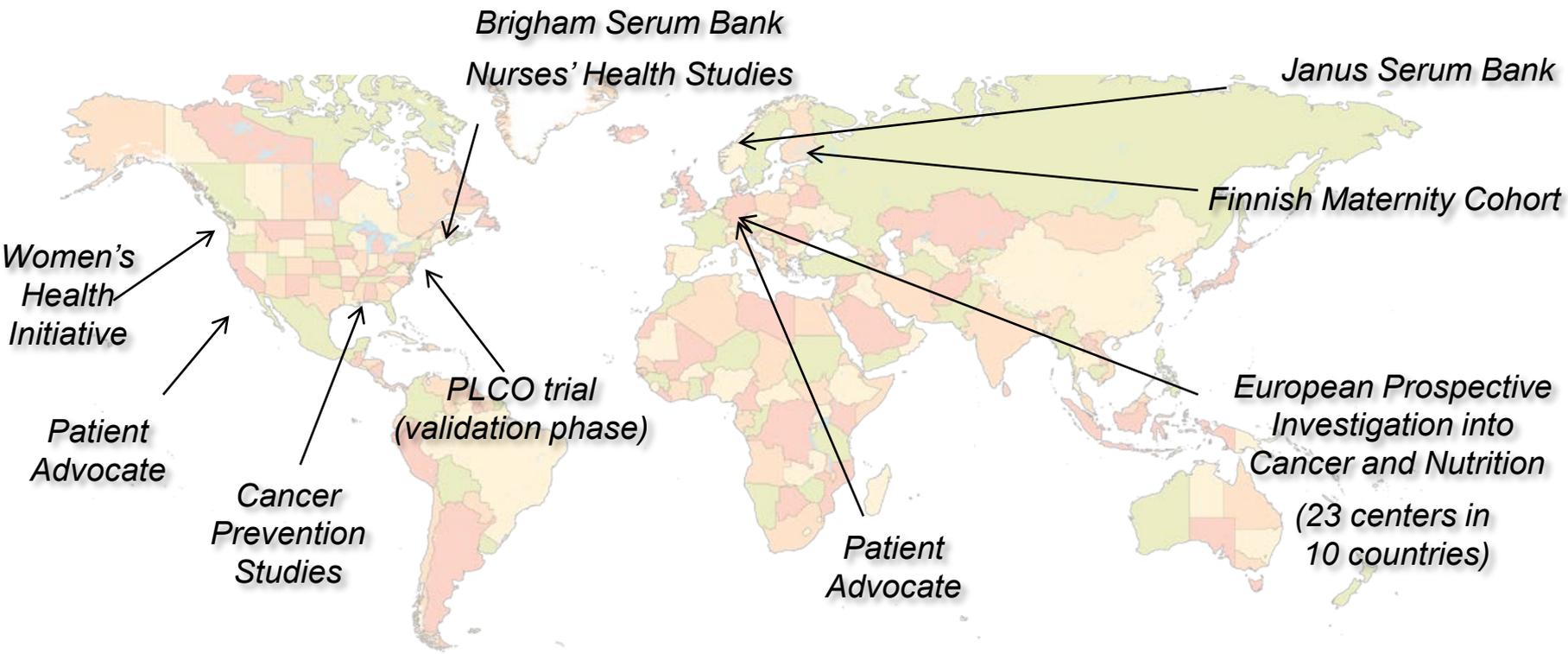
Cohort recruitment:

Blood collection

Follow-up for cancer outcomes



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- “Proof of concept” Aims
 - Cross-cohort standardization of already-measured CA125
 - validate candidate tumor associated autoantibodies (AABs) identified in the BWH repository and EPIC, alone and in combination with CA125
 - leverage existing data microRNA (miRNA) signatures for *in silico* cross-validation and to identify an miRNA panel for full cross-validation
- Extended aims for upcoming expansion grant:
 - omics discovery and validation of other marker types
 - tumor associated protein antigens
 - n-glycan markers
 - others ...

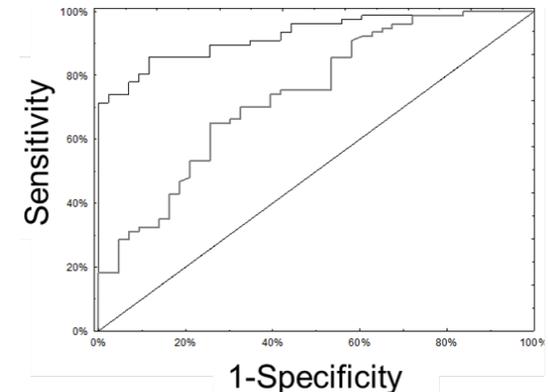


Figure 3. Performance of a serum miRNA signature (top line) outperformed CA125 (bottom line), with a significantly lower false positive rate (Elias 2017).

Elias eLife 2017



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Invasive cases diagnosed <18 months post blood collection

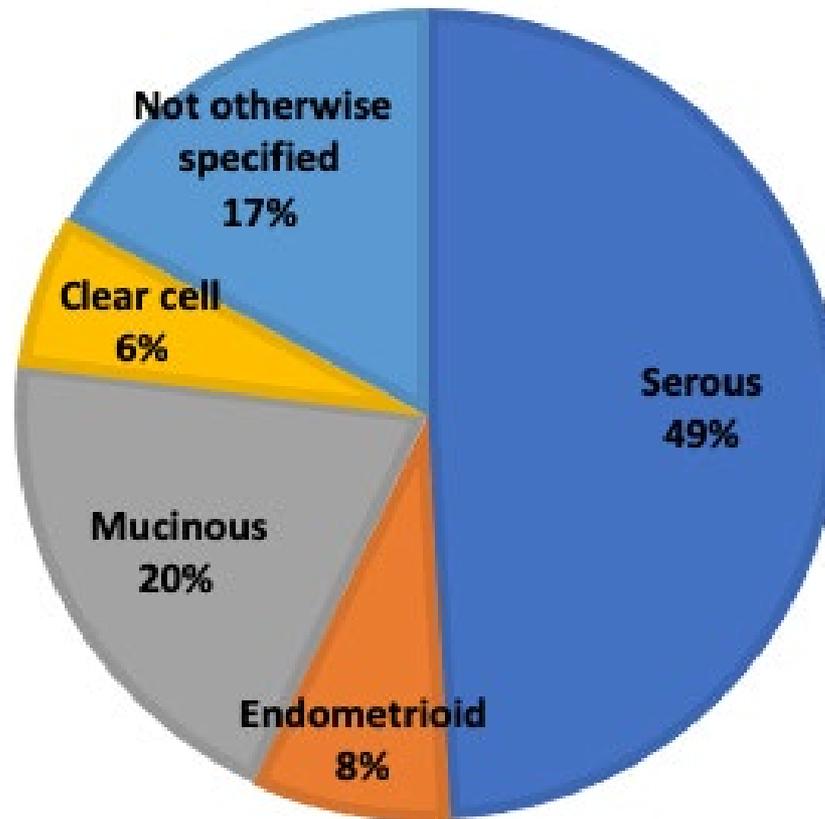
	EOC cases/ controls
EPIC	102/204
WHI	166/332
NHS/NHSII	40/80
CPS-II/CPS-3	55/110
Janus	49/98
FMC	44/88
PLCO (validation phase)	118/236
TOTAL	574/1148

Samples collected before diagnostic surgery

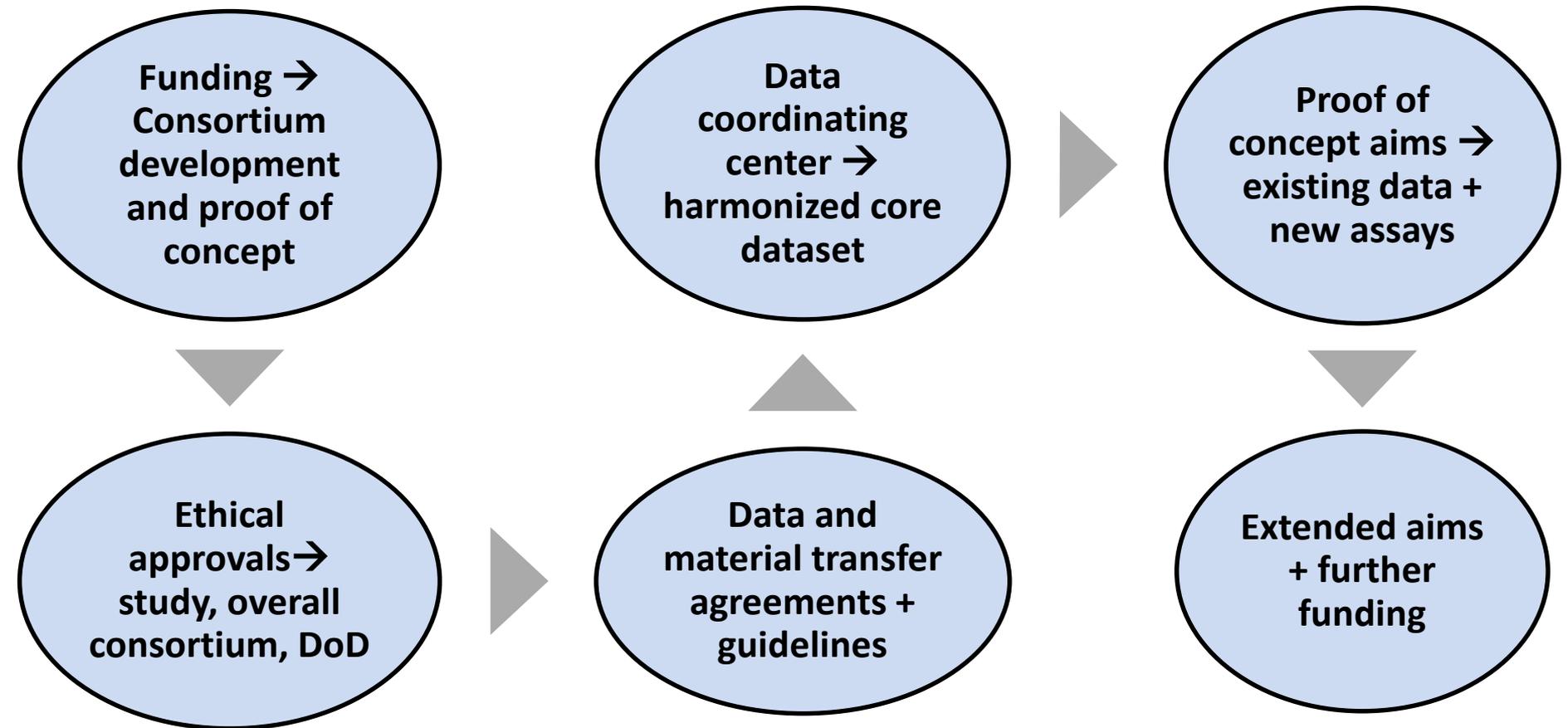
Brigham Pelvic Mass Study → 150 high grade serous cases + 150 controls
(ongoing recruitment >650 total cases)

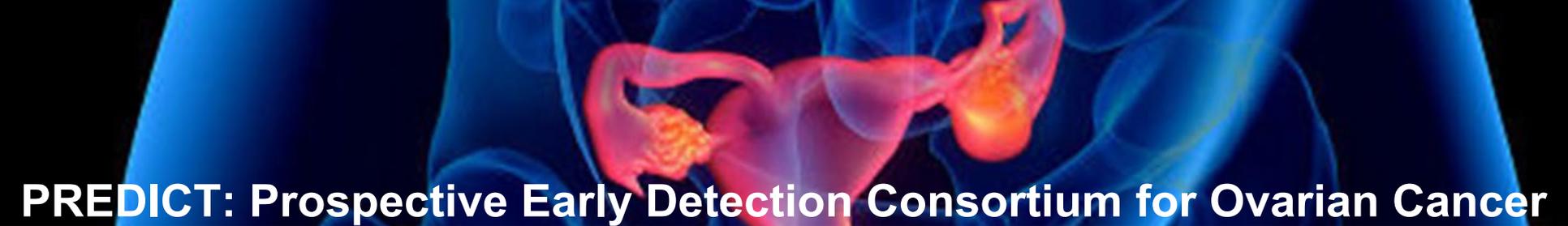
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Prospective studies: Early detection set by histology



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Working within PREDICT

- Open to collaboration!
 - in search of promising candidate markers for further evaluation
- Governance via steering committee of cohort representatives, laboratory collaborators, patient advocates
- Individual cohorts operate on an opt-in principle on a project-by-project basis for future projects
- New project proposals discussed and approved by steering committee

PREDICT Investigator Team

- **DKFZ (coordinating center)**
 - Rudolf Kaaks
 - Renée Fortner
- **ASU Biodesign**
 - Karen Anderson
- **Brigham and Women`s Hospital**
 - Katie Terry
 - Dan Cramer
 - Kevin Elias
- **Finnish Maternity Cohort/
University of Oulu**
 - Heljä-Marja Surcel
- **Fred Hutchinson Cancer
Research Center**
 - Holly Harris
- **H. Lee Moffitt Cancer Center**
 - Shelley Tworoger
 - Mary Townsend
- **American Cancer Society**
 - Alpa Patel
 - Lauren Teras
- **Janus Serum Bank/
Cancer Registry of Norway**
 - Hilde Langseth
 - Trine Rounge
- **National Cancer Institute**
 - Nico Wentzensen
- **Patient Advocates**
 - Jean Richardson
 - Andrea Krull

Funding

DoD OCRP W81XWH-19-1-0307



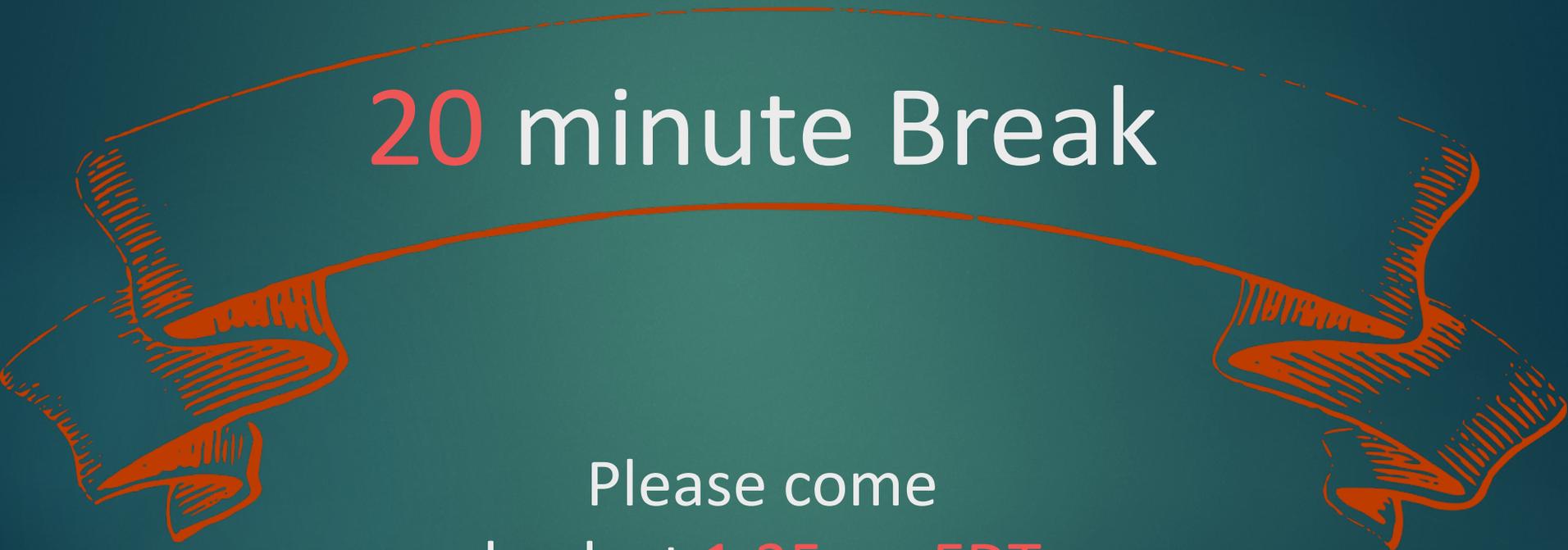
5 minute Q&A

SC Chair/Co-Chair

feed Zoom Q&A to presenter and Track Time

NCI and Production Team

flag Q&A, answer Chat and Slack



20 minute Break

Please come
back at 1:25pm EDT