Center for Personalized Cancer Therapy
Presentation to the Massachusetts Life Sciences Center
December 18, 2013
UMB – DF/HCC Partnership

Attendees

UMB
- Jill A. Macoska, PhD, Professor of Biology; Director, CPCT *(Presenter)*
- J. Keith Motley, Chancellor and Professor
- Andrew Grosovsky, CSM Dean and Professor

DF/HCC
- Edward J. Benz, MD, President and Chief Executive Officer, DFCI; Director, DF/HCC
- John Aster, MD, PhD, Professor, Department of Pathology, HMS; DF/HCC Specialized Histopathology Services.
- James DeCaprio, MD, Associate Professor, Department of Medicine, HMS; Faculty Director, DF/HCC Monoclonal Antibody Core.
- Bruce A. Chabner, MD, Professor, Department of Medicine, HMS; Director of Clinical Research, MGH Cancer Center, Massachusetts General Hospital.
- Donald W. Kufe, MD. Professor, Department of Medicine, HMS; Leader, Translational Pharmacology and Early Therapeutic Trials Program, DF/HCC.
CPCT Mission

- Create **research support platforms** to facilitate high-impact translational cancer research (academic and start-up biotech companies).

- Focus research efforts on the development, validation, and commercialization of cancer biomarkers with significant clinical utility: **tumor subtyping** and **early measures of tumor response to therapy**.

- **Train** and bring diverse student talent into DF/HCC.

- Provide UMB students with **skills** suitable for academic careers or employment in regional biomedical industry.
CPCT: Building Momentum

- Jill Macoska, PhD, hired as CPCT Director: Jan. 2013
- CPCT Wet Lab opened: Mar. 2013
- Collaborations formed with DF/HCC Advisors and Faculty: Apr. 2013-Present
- UMB Cancer Research Network formed: May 2013-Present
- Industry Collaborations Facilitated (ongoing):
  - Established: Sanofi: $1M gift including $$ for CPCT fellows, membership on CPCT Advisory board
  - Start-Ups: Boston Strategics (Fuji Film), Parabase Genomics
- Biomarker Facility Initiated: Oct. 2013
- Move to the Integrated Science Center: Aug. 2014
CPCT Will Address a Significant Clinical Need

Develop, test, and implement biomarkers that permit tumor subtyping to inform treatment decisions and provide early measures of tumor therapeutic response.

These studies are driven by scientists and clinicians vested in the creation and dissemination of tools (biomarkers) that enable successful cancer treatment.
Develop, Test, and Implement Tools that Permit Tumor Subtyping to Inform Treatment Decisions

Need biomarkers to identify tumors (the ‘30%’) that require aggressive treatment to prevent metastasis.
Develop, Test, and Implement Tools That Provide Early Measures Of Tumor Therapeutic Response

Brain tumor complete response after 3 months of chemotherapy

Thalamic tumor lack of response / continued progression after 6 months of chemotherapy
any of these molecular types or selected combinations may serve as diagnostic or prognostic cancer biomarkers

nucleic acid probes to detect RNA biomarkers

antibodies to detect protein biomarkers
CPCT Biomarker Facility: Development of Protein- and RNA-Based Tests for Tumor Subtyping and Treatment Response

Identify protein- and/or RNA-based biomarkers in clinical specimens

Validate biomarkers in pre-clinical studies

Validate biomarkers in clinical specimens
Antibody Development to Detect Protein-Based Markers: DF/HCC Antibody Facilities + CPCT Biomarker Facility

Develop antibodies that recognize tumor proteins (antigens)

Use immunohistochemistry to visualize antibody/antigen complexes
Antibody Development to Detect Protein-Based Markers: DF/HCC Antibody Facilities + CPCT Biomarker Facility

- Biomarker “targets” informed by DF/HCC Medical Oncology, Pathology, and other Programs.
- Antibodies generated at DF/HCC (James DeCaprio, MD).
- Antibodies screened and validated in CPCT Biomarker Facility (Jill Macoska, PhD).
- Promising antibodies undergo clinical testing at DF/HCC then multi-institutional testing (e.g. NIH/NCI Early Detection Research Network) (Jill Macoska, PhD).
- Antibodies with proven clinical utility are commercially marketed.
Recent advances in technology allow, for the first time, the development and use of reliable RNA-based biomarkers for disease diagnosis and prognosis.

RNA can be successfully recovered from:
- Bodily fluids (blood, urine, saliva)
- Tissues (fresh, frozen, preserved)
- Single cells

The sequences of an entire DNA-transcribed compendium (transcriptome) can be determined from these biological samples.
**CPCT Biomarker Facility:** Development of RNA-Based Tests for Tumor Subtyping and Treatment Response

- **Illumina HiSeq 2500**
  - Identify RNAs Highly Expressed in Tumor Subtypes and/or Associated with Therapeutic Response

- **Nanostring nCounter**
  - Validate Expression Levels of Informative RNAs

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CPCT Biomarker Facility: Development of RNA-Based Tests for Tumor Subtyping and Treatment Response

Nanostring nCounter
Biomarker Validation, Application, Commercialization

Based on the PAM50 gene signature initially discovered by Charles Perou, PhD (UNC).

Directly assay tissue extracts and whole-blood lysates, total RNA, cell lysates, and FFPE
CPCT: In Summary

• CPCT implementation plan is in place. CPCT lab is established. Collaborative arrangements with DF/HCC set.
• Committed to train and bring diverse student talent to the life science industry.
• Request $8M to complete Biomarker Facility and Vivarium to develop, validate, and implement biomarker assays for tumor subtyping and early response to therapy.
• Places CPCT in a unique position to support the academic and industry life science cluster in Massachusetts (esp. Boston area).