Pancreatic Cancer Liquid Biopsies for Therapeutic Stratification & Monitoring

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The incidence of Pancreatic cancer is on the rise

Rahib, Matrisian Cancer Res 2014
Alternatives to tissue biopsies for pancreatic cancer

Cost of an IR Guided Biopsy = $5,000-8,000

Diaz and Bardelli, JCO 2014
Pancreatic cancer patients shed a lot of exosomes containing high molecular weight nucleic acid cargo.

Detection of mutant KRAS in exoDNA by NGS
Detection of mutant \textit{BRCA2} in exoDNA by NGS

ExoDNA

PBMC:

Ref: CTT GCC CCT TTC GTC TAT TTG TCA GAC
Liquid Biopsies can enable serial monitoring of genomic alterations during the course of therapy

Liquid biopsies can encompass the genotypic heterogeneity of pancreatic cancer
Other surrogate biospecimens for exoDNA

Pleural fluid & Urine

NGS on ExoRNA can find expressed mutations, fusion transcripts & neoantigens

Expressed fusions and missense mutations
*(tracking tumor neoantigens longitudinally)*
Longitudinal Monitoring of Treatment Response

68yo female, metastatic PDAC

Mutant KRAS in ExoDNA tightly correlates with clinical evolution.
“Surge” in ExoDNA Correlates with Progression in Advanced Pancreatic Cancer

>1% ExoDNA Mutant Allele Fraction

Bernard et al, manuscript in preparation
“Surge” in ExoDNA Correlates with Progression in Resected Pancreatic Cancer

Bernard et al, manuscript in preparation
“Surge” in ExoDNA Correlates with Progression in Locally Advanced Pancreatic Cancer

GV36 - 77yo male locally advanced

Stable disease based on imaging and CA19-9

Mutant KRAS surge in exoDNA

Overt liver metastasis

Bernard et al, manuscript in preparation
Early Detection of Pancreatic Cancer
(and a specter of overdiagnosis)

But as exciting and convenient (and, compared with biopsies, far less invasive or expensive) as the long-elusive technology might be, it does carry one big potential drawback: "I really think the field should be cognizant of the reality of over-diagnosis," said fellow panelist Dr. Anirban Maitra, scientific director of the Sheikh Ahmed Center for Pancreatic Cancer Research at the MD Anderson Cancer Center.

Grail is raising at least $1 billion to fund its early cancer screening test

This Simple Cancer Test Comes With a Big Caveat

- Guardant Health secured another $360 million in financing in a round led by Softbank.
- Guardant is engaged in an arms race to deliver on a promise for early-stage cancer detection via a blood test.
Identifying Cancer Specific Exosomes Through an Antibody Cocktail

Castillo, Bernard et al Ann Oncol 2017  CPRIT Grantee Poster Session A #167
Cancer Specific Exosomes Enhance Mutant KRAS Detection and Facilitate Molecular Barcoding (Specificity)

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Please visit posters 167 and 250 (Maitra Lab)