Application of Cytologic Techniques to Circulating Tumor Cell Specimens

Alarice Lowe, MD
Assistant Professor of Pathology
Director, Circulating Tumor Cell Lab
Brigham and Women’s Hospital
Harvard Medical School

Cytologic Techniques in Circulating Tumor Cells

Disclosure of Relevant Financial Relationships
No conflicts of interest to disclose.

Outline
• Background
• Circulating tumor cell (CTC) enumeration
• At BWH
• CTC characterization
• Application to non-blood specimens
• Summary/Future

Background
• Metastasis
  • Hallmark of malignancy
  • Primary cause of death in solid tumors
• Mechanism: invasion, survival in circulation, seeding, and establishment

Background
• “Liquid biopsy” – not clearly defined, tumor sampling via blood
• Encompasses
  • Circulating tumor derived nucleic acid
  • Tumor derived extracellular vesicles (exosomes, microvesicles, oncosomes)
  • Circulating tumor cells – intact cells, may be viable or dying
Background

- CTCs may arise from the primary tumor or metastases
- CTCs are rare, even in advanced disease
  - ~1 in 10^6 to 10^9 cells in blood
- First noted in 1869 by Ashworth
- Recent technologies allow reliable identification/isolation
  - Biophysical (size, deformability, density, charge, etc.) or antigenic differences from WBCs leveraged to enrich for and detect CTCs

Outline

- Background
  - CTC Enumeration
  - At BWH
  - CTC Characterization
  - Application to non-blood specimens
  - Summary/Future

CTC Enumeration

- Prognostic
  - At diagnosis and during treatment
  - For localized and metastatic disease
  - By numerous different technologies (only CellSearch is FDA cleared)
  - In many tumor types (carcinoma, also others)

The CellSearch™ System

- Automated sample preparation

CTCs

- CK+/DAPI+/CD45-

WBCs

- CK-/DAPI+/CD45+

Cristofanilli, NEJM, 2004

CellSearch™

Cristofanilli, NEJM, 2004
Cytologic Techniques in Circulating Tumor Cells

CTC Enumeration

• Not all patients have identifiable CTCs
  • Sampling (e.g., low stage disease and small sample volume)
  • CTC and identification technology mismatches

Outline

• Background
  • CTC Enumeration
  • At BWH
  • CTC Characterization
  • Application to non-blood specimens
  • Summary/Future

At BWH

• CellSearch system within Cytology since 2005
  • CLIA approved space
  • CTC Clinical Lab – enumeration
  • CTC Core Lab – enumeration and isolation

Current BWH Research

• Clinical protocols for enumeration with breast, GU, and H&N groups
• Clinical protocols for isolation with the breast and lung groups
• Reference for CTC technology development
• Developing CTC characterization protocols and other applications of the technology

Outline

• Background
  • CTC Enumeration
  • At BWH
    • CTC Characterization
  • Application to non-blood specimens
  • Summary/Future
Herringbone-chip (HB-chip)

Miyamoto, Cancer Discov, 2012.

Stott et al., PNAS, 2010.

CTC-iChip: CTC Culture

Yu, Science, 2014

CTC-iChip: Drug Susceptibility

Yu, Science, 2014

Concurrent tissue biopsy, CTC, and ctDNA analyses for T790M in EGFR mut patients on TKI


MagSense


Outline

- Background
- CTC Enumeration
- At BWH
- CTC Characterization
- Application to non-blood specimens
- Summary/Future
Outline

- Background
- CTC Enumeration
- At BWH
- CTC Characterization
- Application to non-blood specimens
- Summary/Future

Cytologic Techniques in Circulating Tumor Cells

Summary/Future

- Multiple CTC platforms exist
- CTC enumeration is prognostic
- CTC characterization of patient samples is imminent
- Non-blood CTC applications hold promise
- CTC specimens are cytology!
Important Information Regarding CME/SAMs

The Online CME/Evaluations/SAMs claim process will only be available on the USCAP website until September 30, 2017.

No claims can be processed after that date!

After September 30, 2017 you will NOT be able to obtain any CME or SAMs credits for attending this meeting.