Tissue Heterogeneity

Getting patients on the right treatment, faster.

CIRCULOGENE
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Tissue is imperative to diagnose a cancer. However, tissue has many limitations when it comes to fully reflecting tumor biology and guiding the best treatment for each individual with cancer. Clonal heterogeneity of cancer drives a dynamic tumor biology. This heterogeneity is the biggest limitation of tissue biopsies. Multiple sites of metastatic disease can have diverse inter-tumoral heterogeneity. Even within a single tumor there can be marked intra-tumoral heterogeneity. A tissue biopsy at one site will not reflect the molecular tumor biology of other sites. A tissue biopsy reflects just one small area within that tumor at one static point in time. Every time a cancer metastasizes, there is clonal evolution with increasing tumor biology heterogeneity.

Biopsy accessibility and adequate sampling often preclude full tissue molecular testing. Tissue acquisition costs and complications can also negatively impact time-to-treatment. Plasma NGS with ctDNA/RNA can overcome this limiting barrier of tissue heterogeneity and can dynamically reflect the "'future" tumor biology of the most aggressive clone. Tissue to diagnose the cancer; liquid biopsy to know and treat the tumor biology.

CIRCULOGENE'S *complete gene panel is a noninvasive technique that can be combined with traditional tissue biopsy to track cell-free DNA and detect disease biomarkers in blood faster and more accurately.*

J Thorac Oncol.

2018 Oct;13(10):1496-1507
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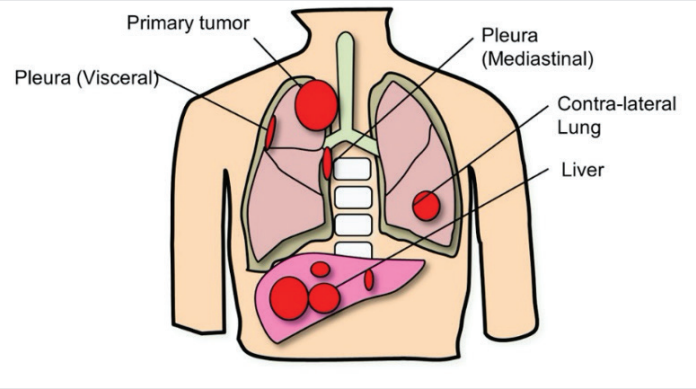
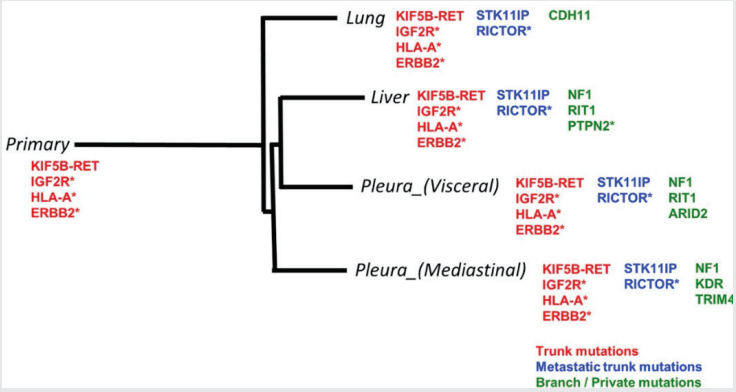
Innate Genetic Evolution of Lung Cancers and Spatial Heterogeneity: Analysis of Treatment-Naïve Lesions

- **Tissue molecular testing is limited by inter/intra-tumoral heterogeneity**
- **Different tumors…different branch/private mutations**
- **A tissue biopsy at one site…only assesses that one site**



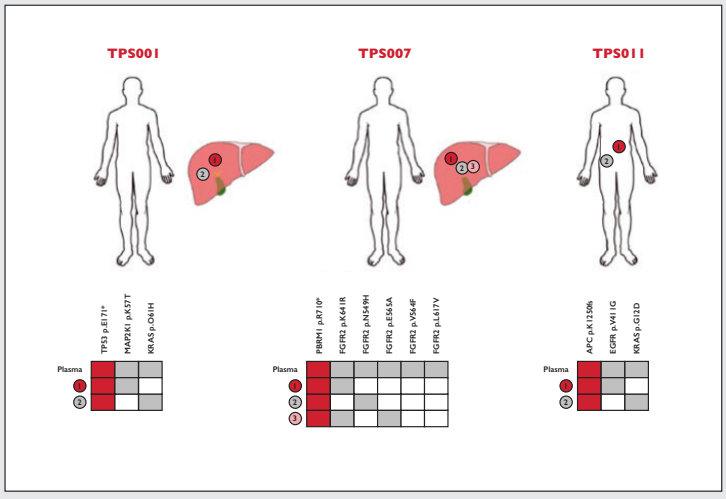


Nat Med.

2019;25:1415–1421

Liquid versus tissue biopsy for detecting acquired resistance and tumor heterogeneity in gastrointestinal cancers

- **Plasma ctDNA identified the resistance pathway 75% versus tissue only 48%**
- **A tissue biopsy of one site only assesses that one site and may miss aggressive resistant clones**



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Ann Oncol.

2019 Aug 1;30(8):1254-1264
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Towards precision oncology for HER2 blockade in gastroesophageal adenocarcinoma

- Cancers have marked malignant clonal heterogeneity
- Different tumor sites have different clones that evolve and change with growth and metastases
- A liquid biopsy with ctDNA/RNA can dynamically identify this clonal heterogeneity and evolution

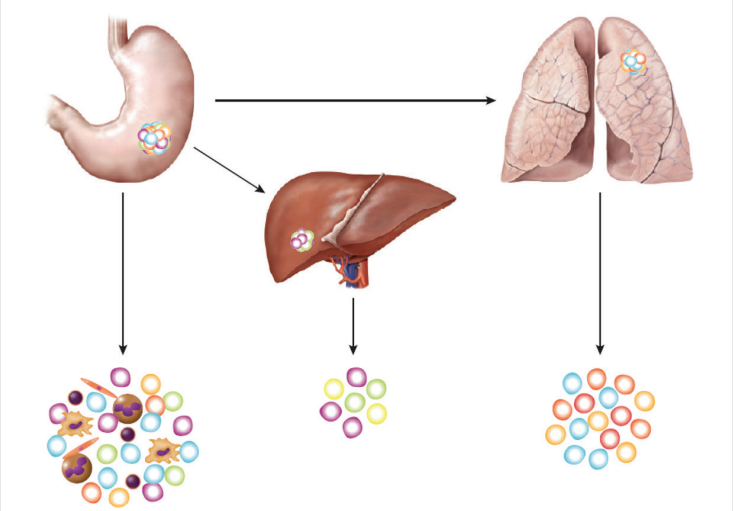
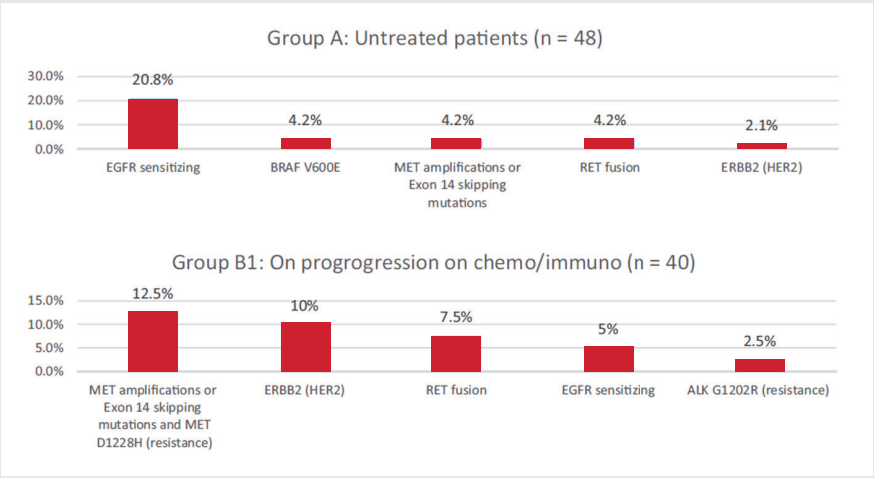


Figure 2. Intra-tumour heterogeneity: a role for clonal evolution. Primary tumours are made up by different cell populations bearing diverse molecular alterations. Those molecular changes can be reproduced or not in metastatic sites. Moreover, some specific molecular abnormalities can be found only in metastatic spots. HER2 amplification may be heterogeneously distributed in different areas of the primary tumours. This feature can be weakened or lost in metastatic sites. Some other molecular alterations may exclusively appear in metastasis (as EGFR amplification and PIK3CA mutations).



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The Clinical Impact of Comprehensive Genomic Testing of Circulating Cell-Free DNA in Advanced Lung Cancer

- Every time a cancer recurs, progresses, or metastasizes, there is clonal evolution with increasing tumor biology heterogeneity
- Previous tissue biopsies will not reflect this evolving heterogeneity
- A liquid biopsy with plasma NGS can identify the new tumor biology

Oncologist

2012;17(7):978-85
DOI:10.1634/theoncologist.2011-0385

EGFR Mutation Heterogeneity and the Mixed Response to EGFR Tyrosine Kinase Inhibitors of Lung Adenocarcinomas

- EGFR mutations can be different at different tissue sites
- Primary tumor and matched distant metastases may be different