



JISTOTA MODERNÍ MEDICÍNY

Biological significance of circulating tumor cells in cancers

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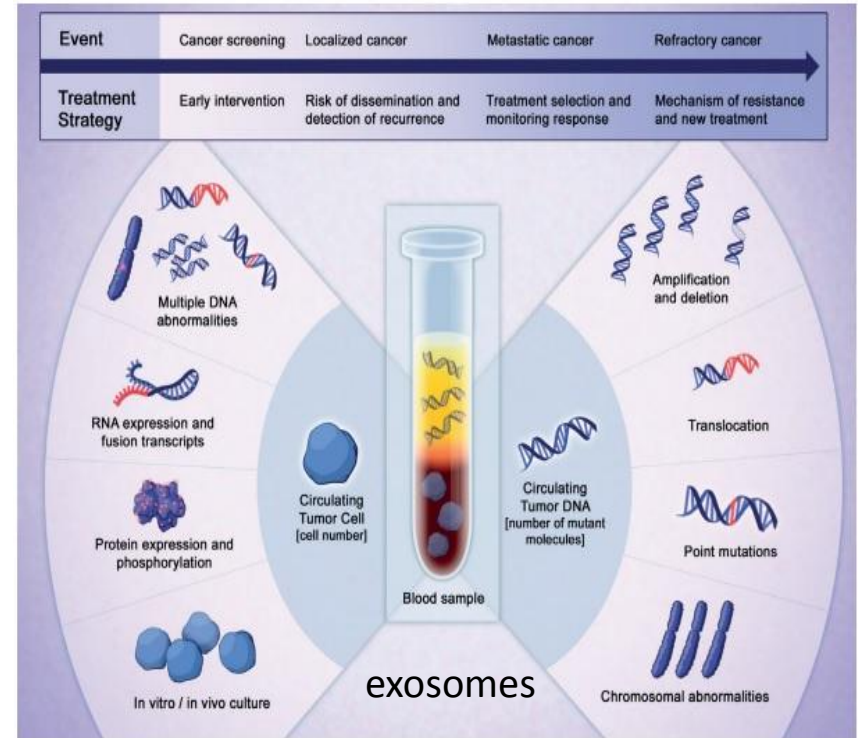
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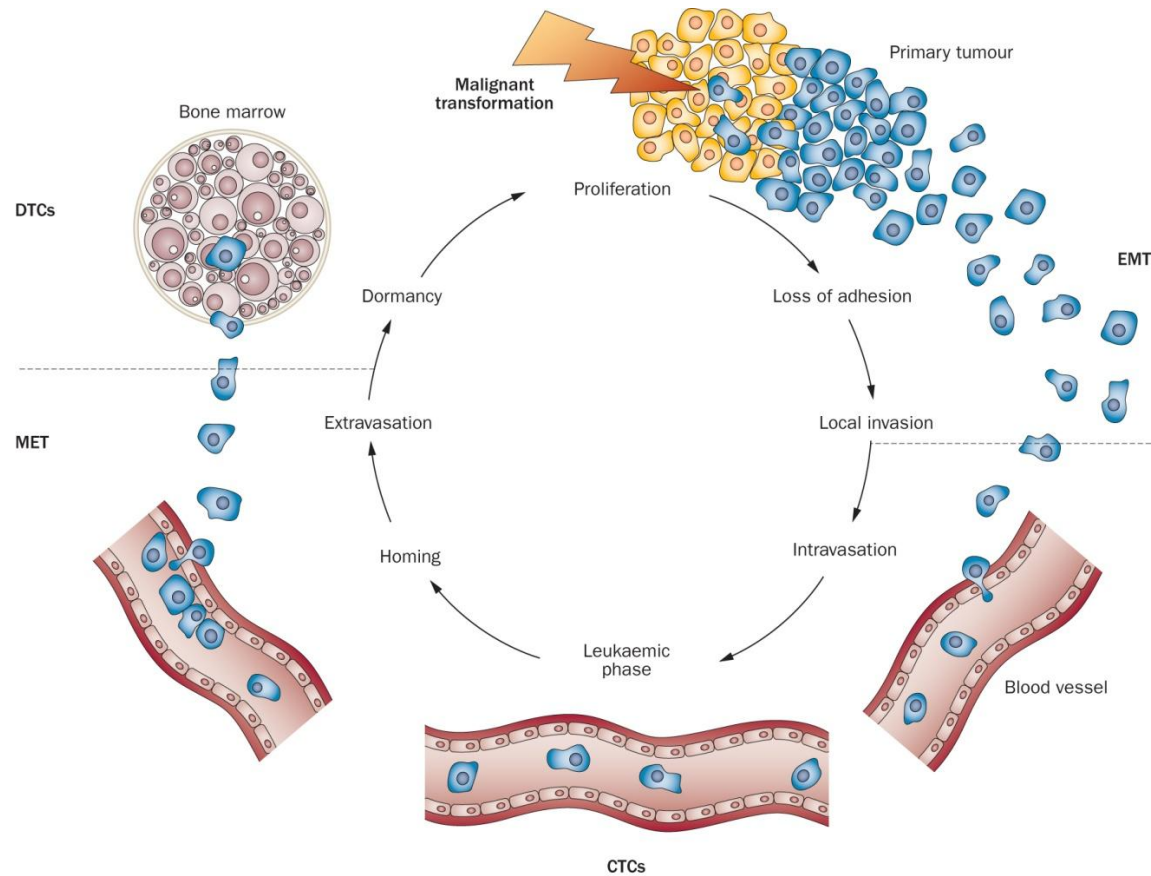
Liquid biopsy

- describes a new diagnostic approach based on CTC analysis
- noninvasive tests using blood or fluids that can detect circulating tumor cells (CTC), circulating tumor free DNA (cfDNA), and exosomes
- in comparison with standard biopsy:
 - Quick
 - Comprehensive tissue profile
 - Easily obtained
 - Minimal risk and invasiveness



cancerworld.org

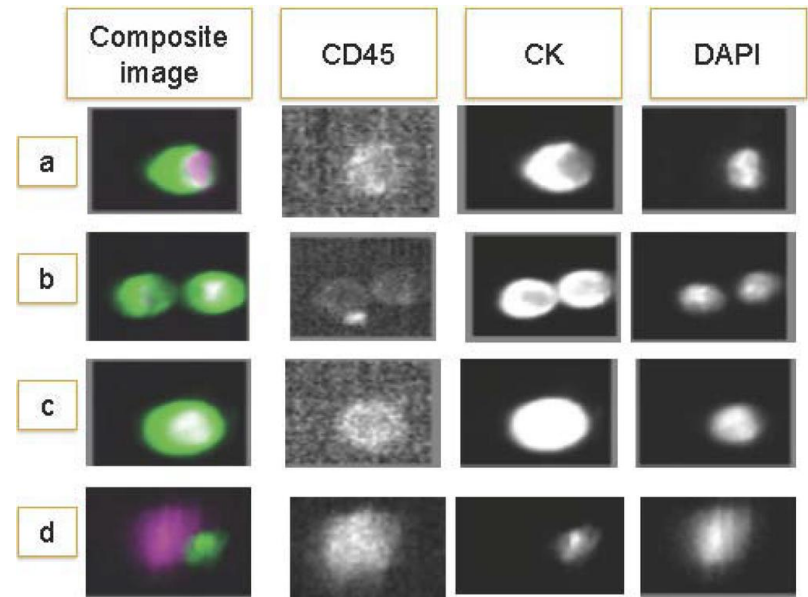
Malignant transformation



Schilling, D. et al.
(2012) Nat. Rev. Urol.

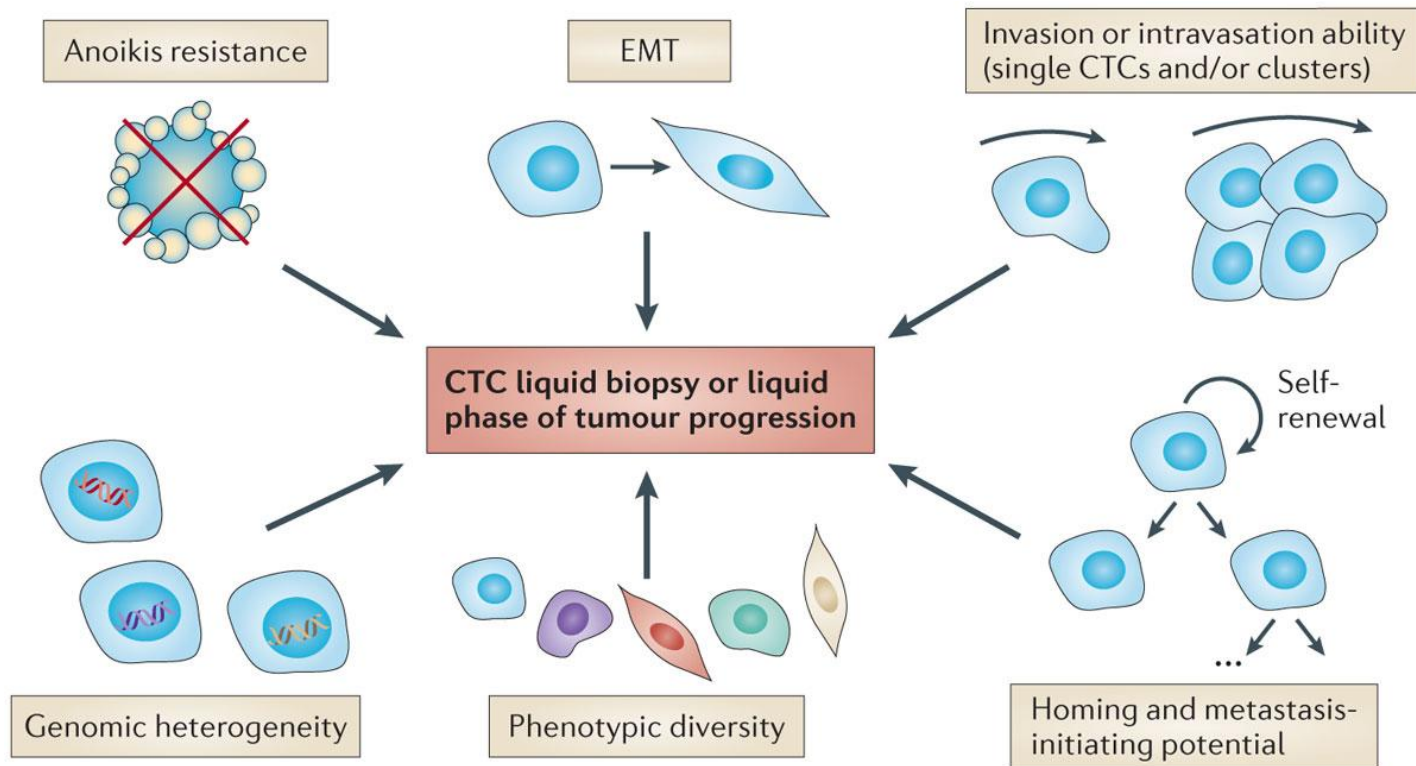
Circulating tumor cells

- CTCs are extremely rare
(1 cell per 10^{6-7} leukocytes)
- BC CTCs have a mean diameter of 13.1. μm
(leukocytes $10\mu\text{m}$)
- accepted CTC characteristics:
 - presence of nucleus
 - visible cytoplasm
 - expression of cytokeratin
 - absence of CD45 expression



Cancers **2010**, 2(2), 1221-1235

Cellular and molecular characteristics of CTCs

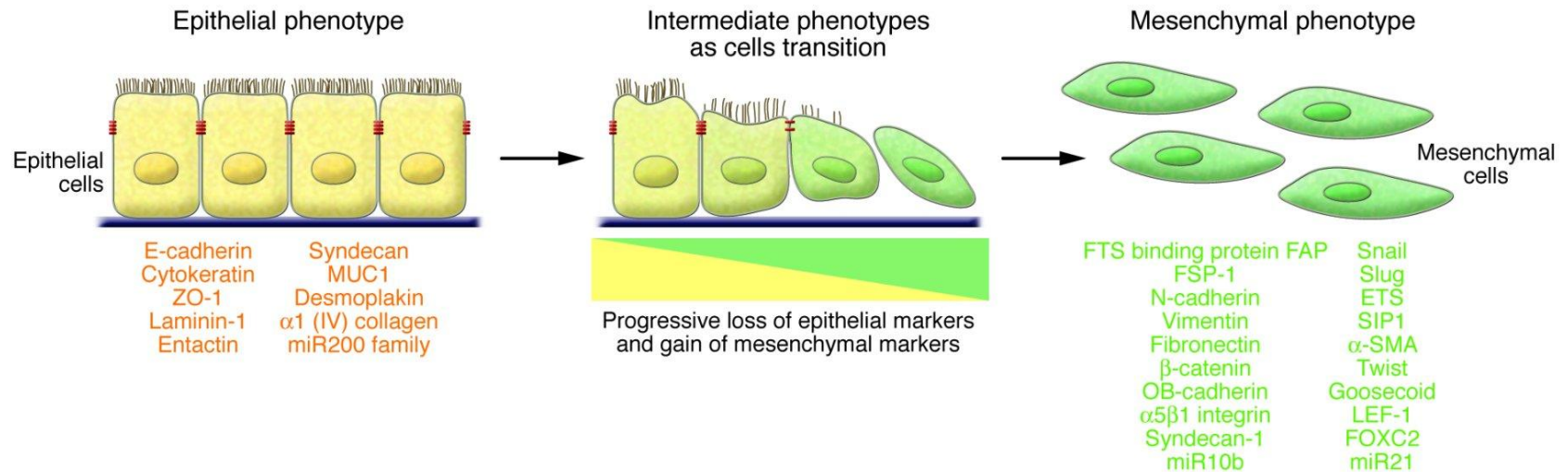


Nature Reviews Cancer (2014): 14: 623 -631.

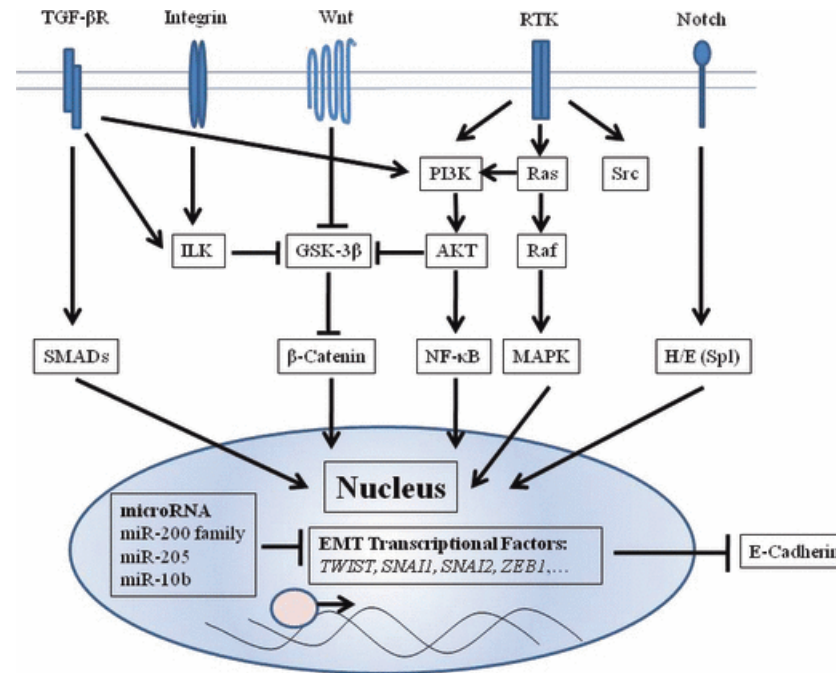
Anoikis

- 1994 by Frisch and Francis (Journal of Cell Biology)
„state of being without a home“
- form of programmed cell death that occurs in anchorage-dependent cells when they detach from surrounding ECM
- In rat model, shedding $3.2 - 4.1 \times 10^6$ cells per day per gram of tissue
- some cells are resistant to anoikis
- in mouse model, approximately 2.5% of CTCs formed micrometastases and 0.01% of CTCs progressed to form macrometastases

Epithelial-mesenchymal transition

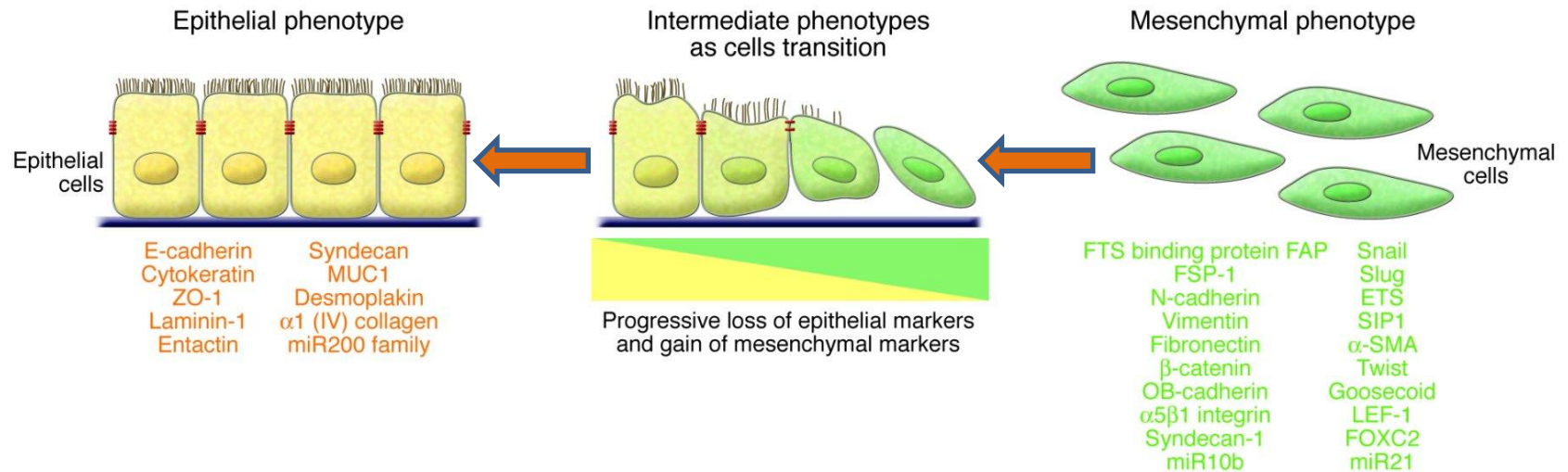


Epithelial–mesenchymal transition regulation in cancer



Cancer Science (2009): 101 (2): 293-299.

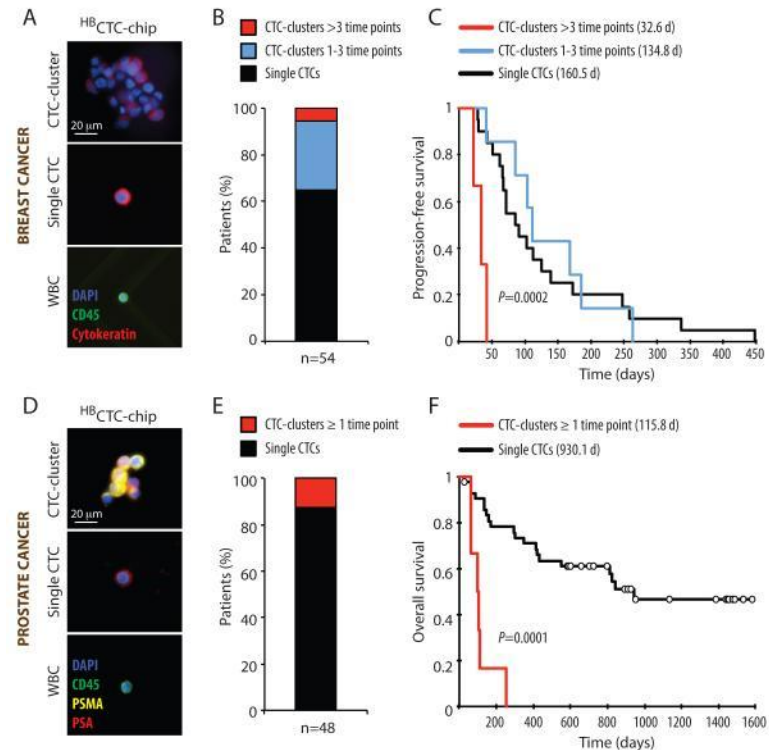
Mesenchymal-epithelial transition



Single CTC or clusters ?

- Clusters

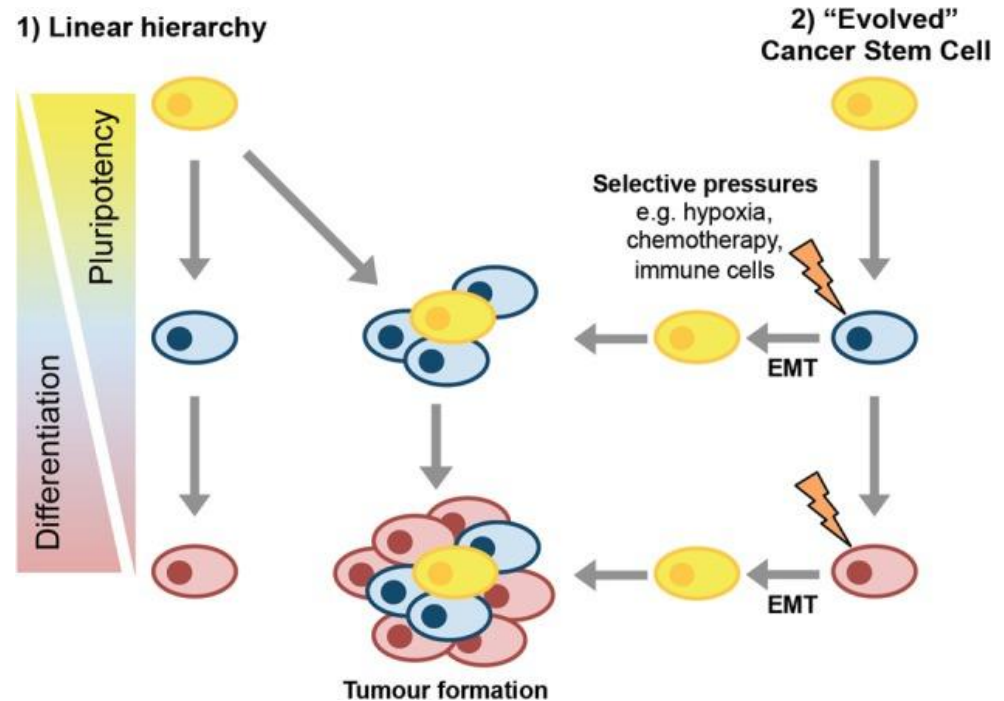
- tumor microemboli form before entering the circulation
- more malignant potential
- correlation with poor prognosis



Cell (2014), 158(5): 1110–1122.

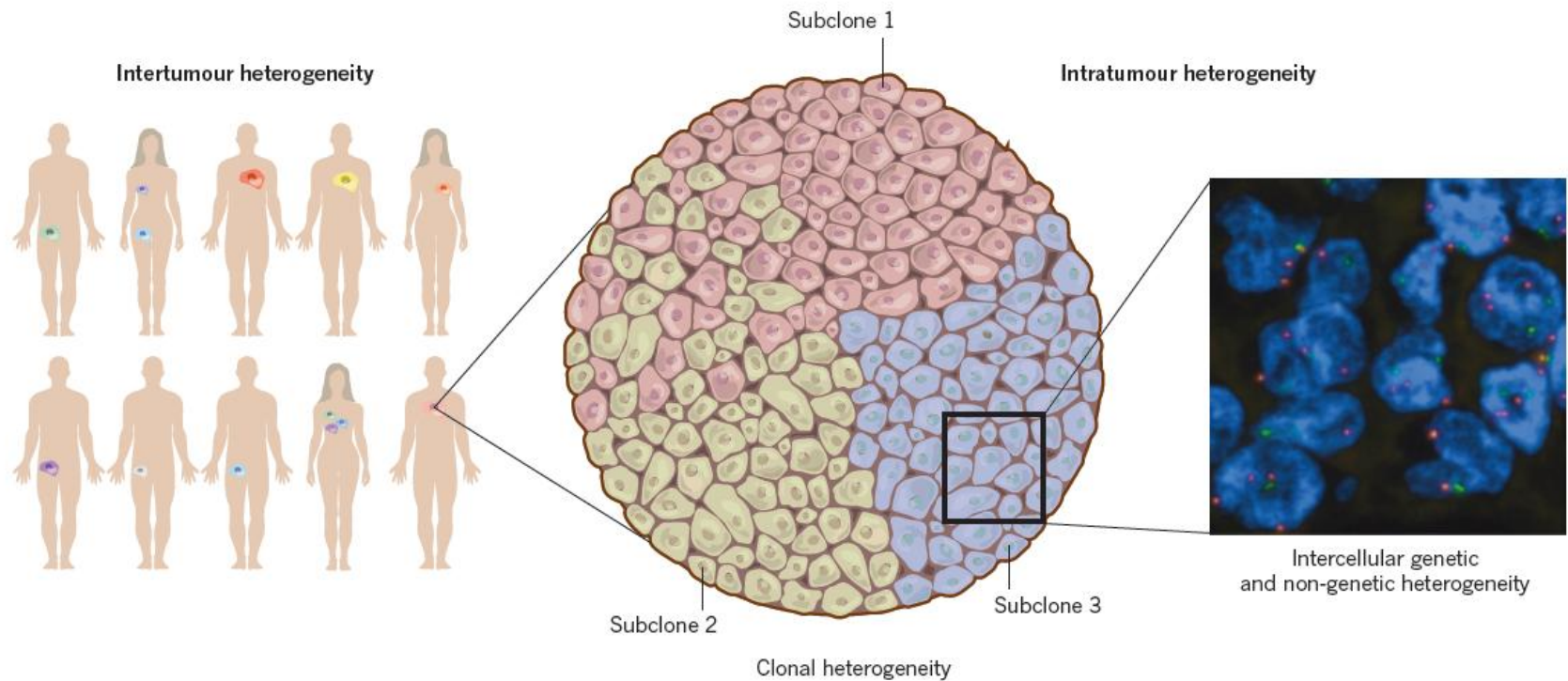
Cancer „stem cell“ (CSC)

- attributes as:
 - quiescence
 - self-renewal
 - asymmetric division
 - drug resistance
 - resistance to radiation
- markers of CSC:
 - CD44+/CD24-
 - ALDH1



Front Physiol (2013); 4: 225.

Heterogeneity



Aims of research on CTC

- estimation of the risk for **metastatic relapse or metastatic progression**
- **stratification** and real-time **monitoring** of therapies
- identification of **therapeutic targets** and **resistance mechanisms**
- understanding the **biology of metastatic development**

Consortium Cancer ID



Thank you for attention

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