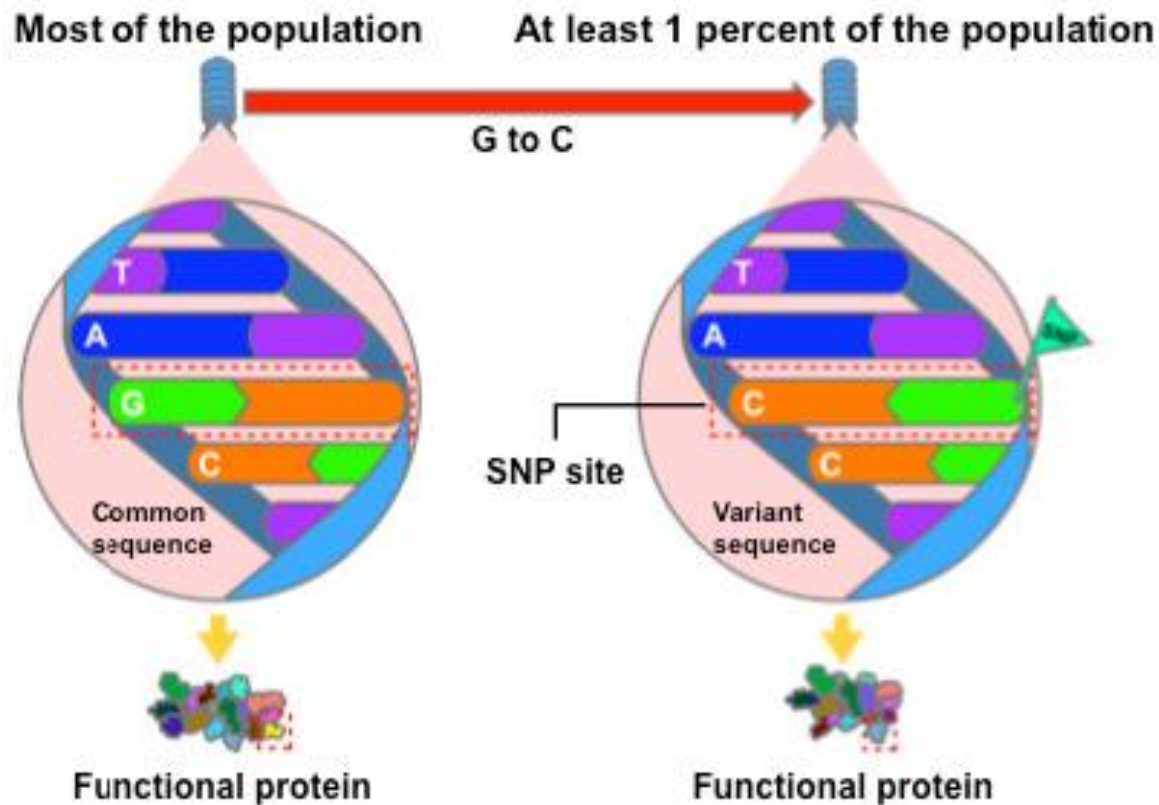# Treatment is chosen based on characteristics of the individual and the disease

Tumor   Germline

SNP's or Single Nucleotide Polymorfisms

Most of the population

At least 1 percent of the population

G to C

SNP site

Common sequence

Variant sequence

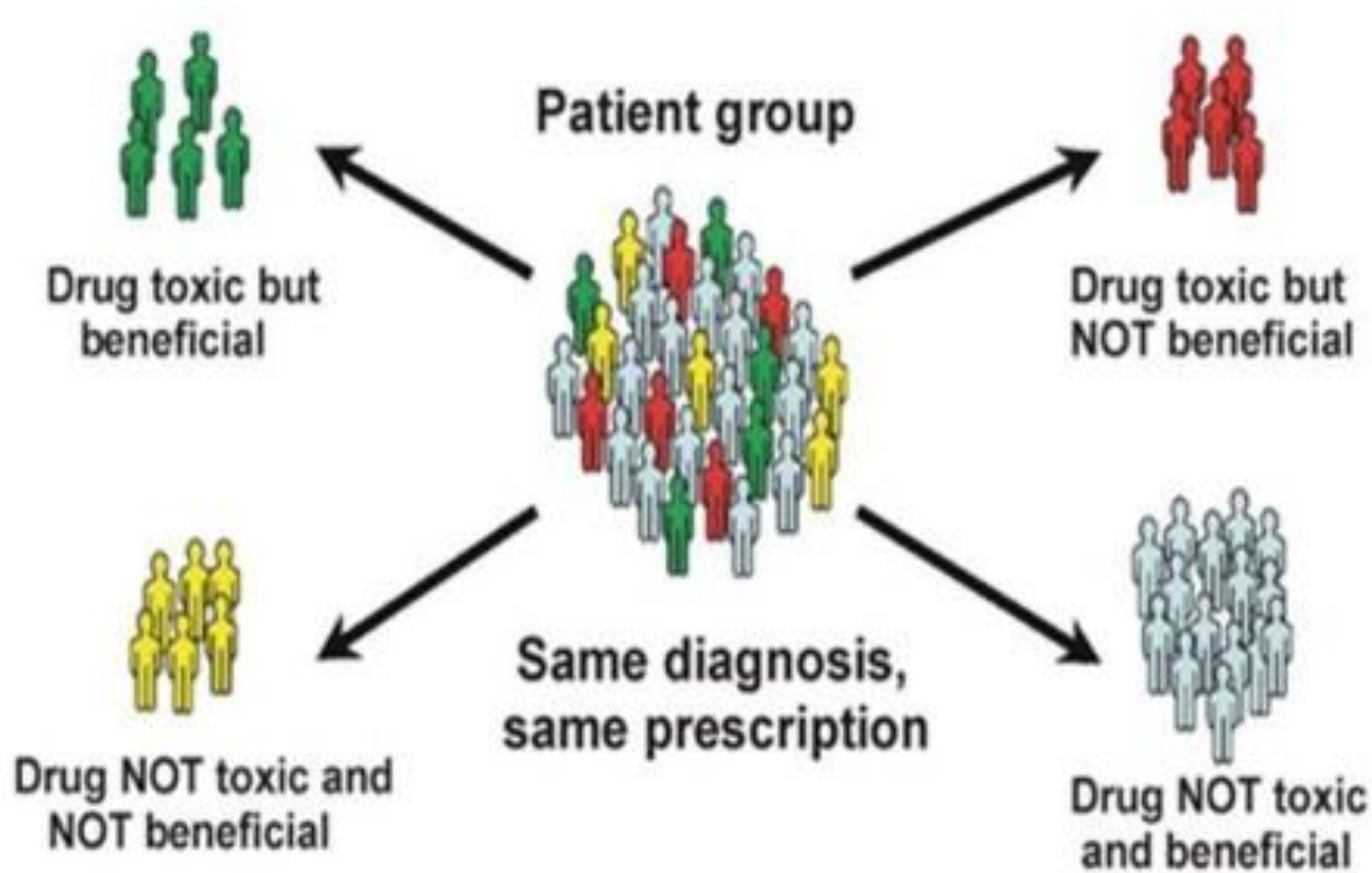Functional protein

Functional protein
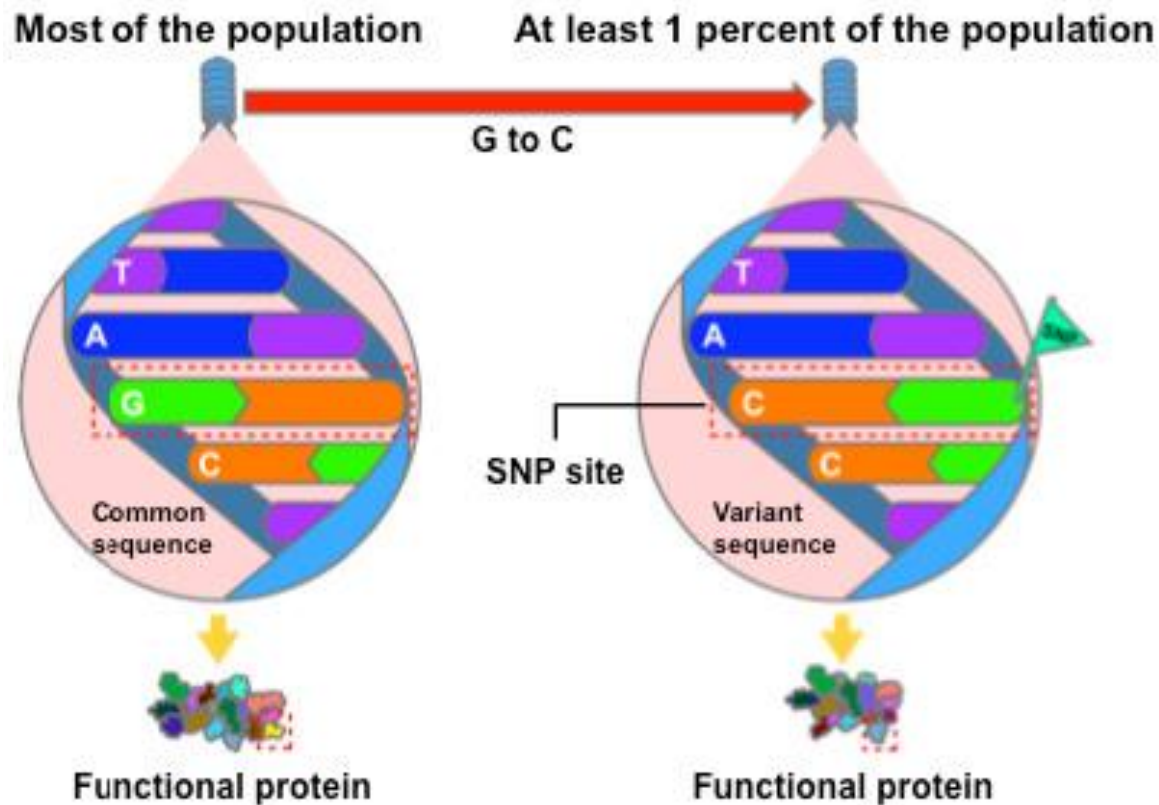
- Host

Germline: Pharmacogenomics

- How do host germline factors influence outcome of drug treatment?

- Variations in the way drugs are metabolized
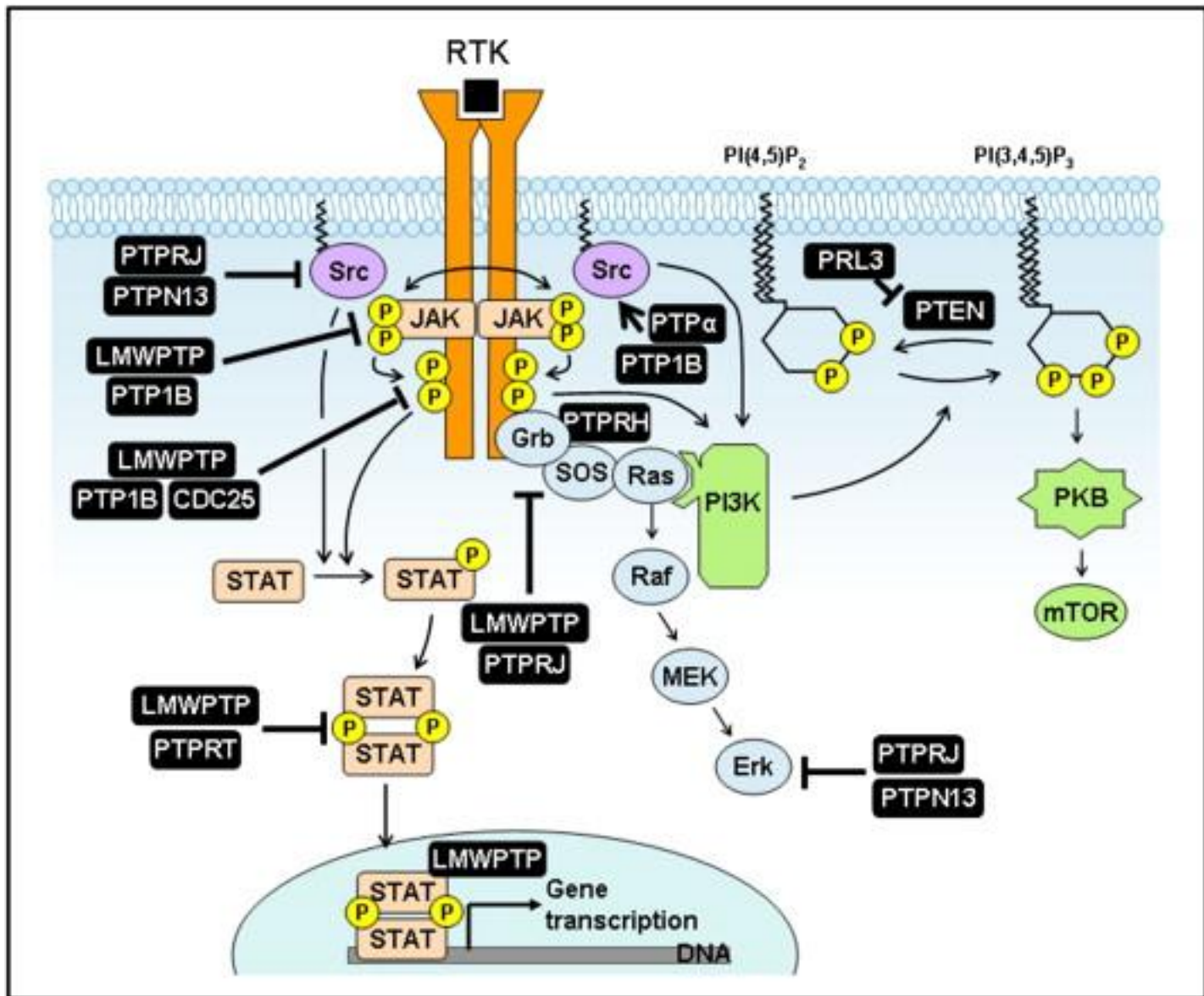
Germline: Pharmacogenomics

SNP's or Single Nucleotide Polymorfisms

- **Host impact on tumor**

Treatment is chosen based on characteristics of the individual and the disease
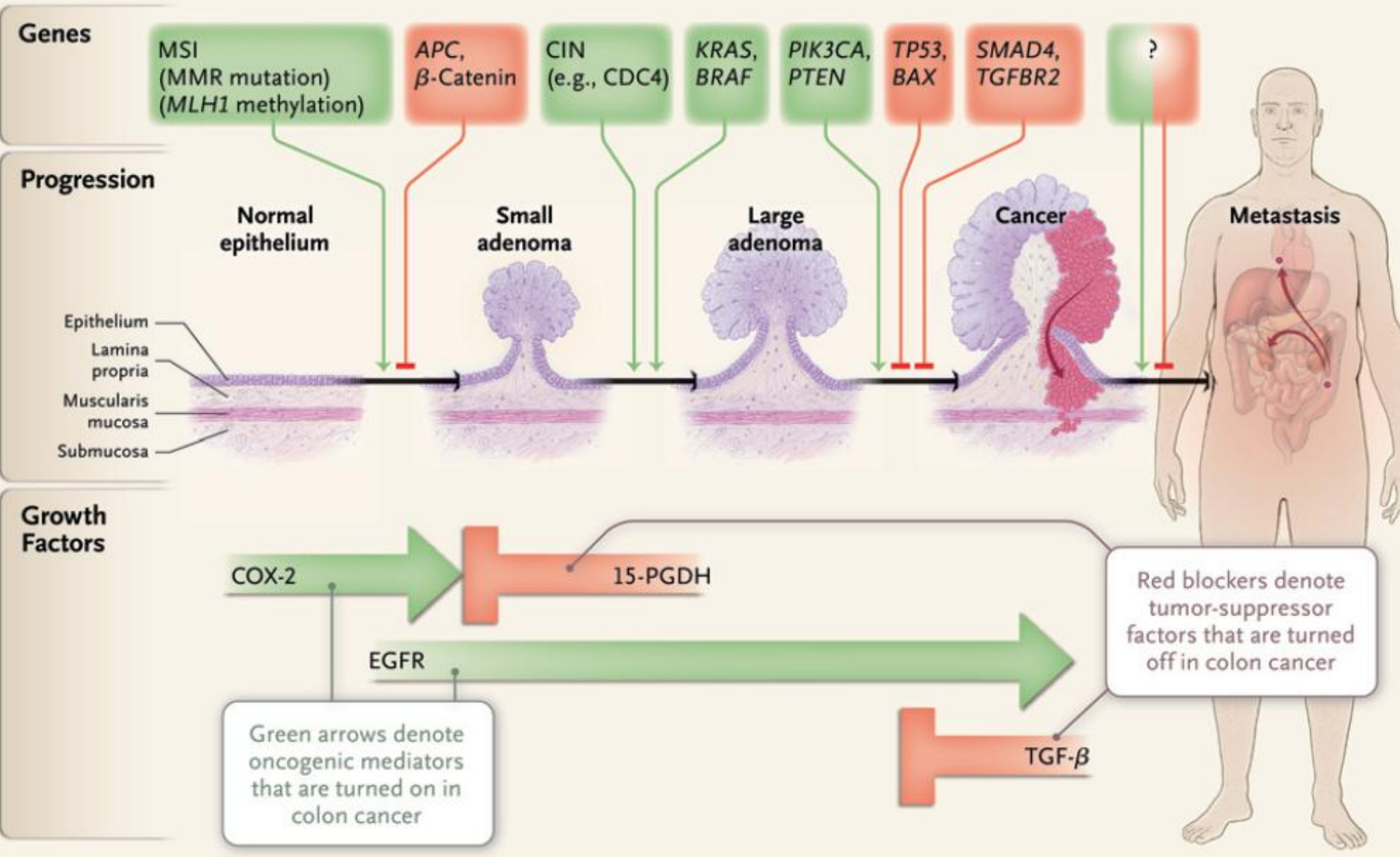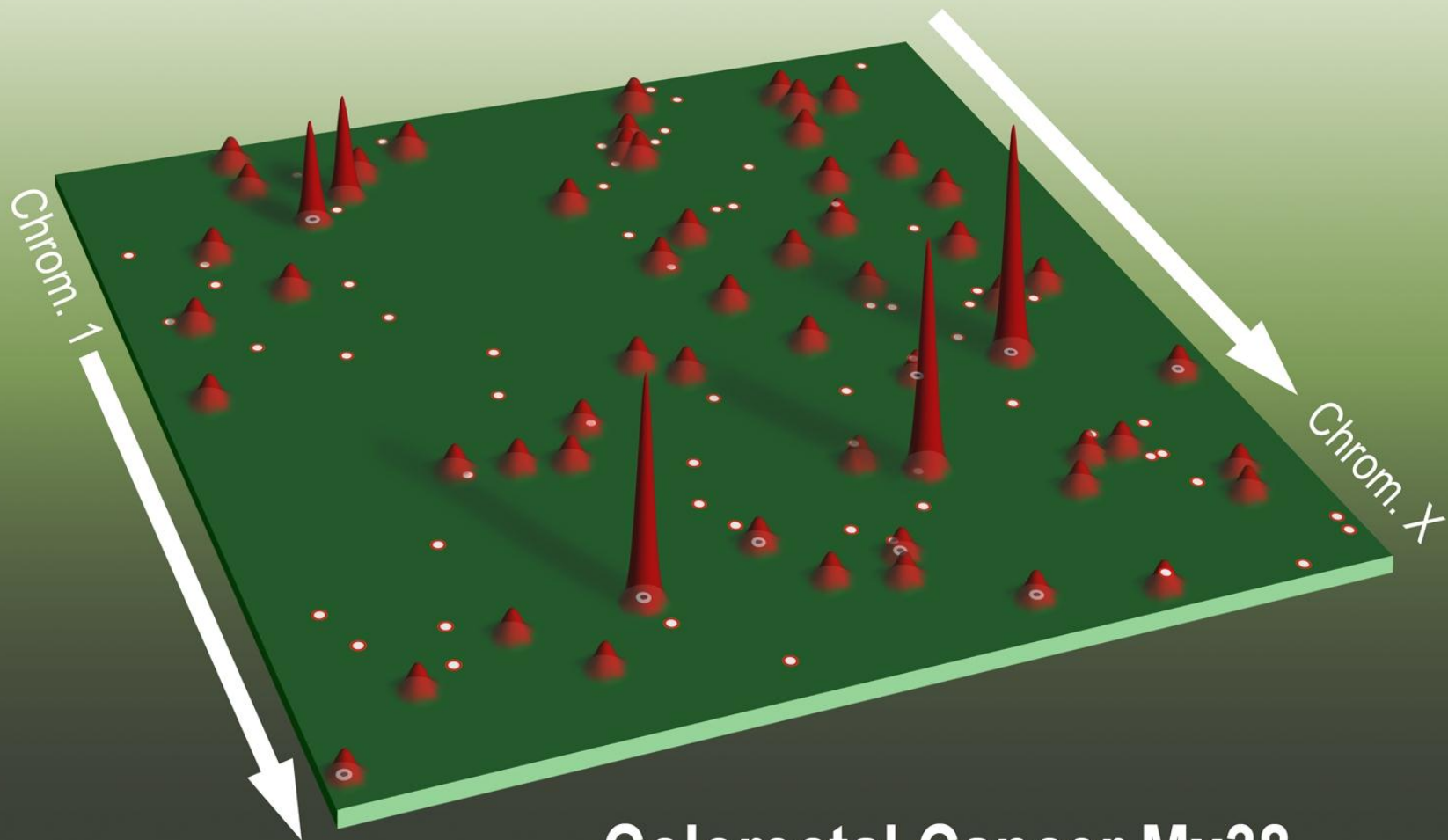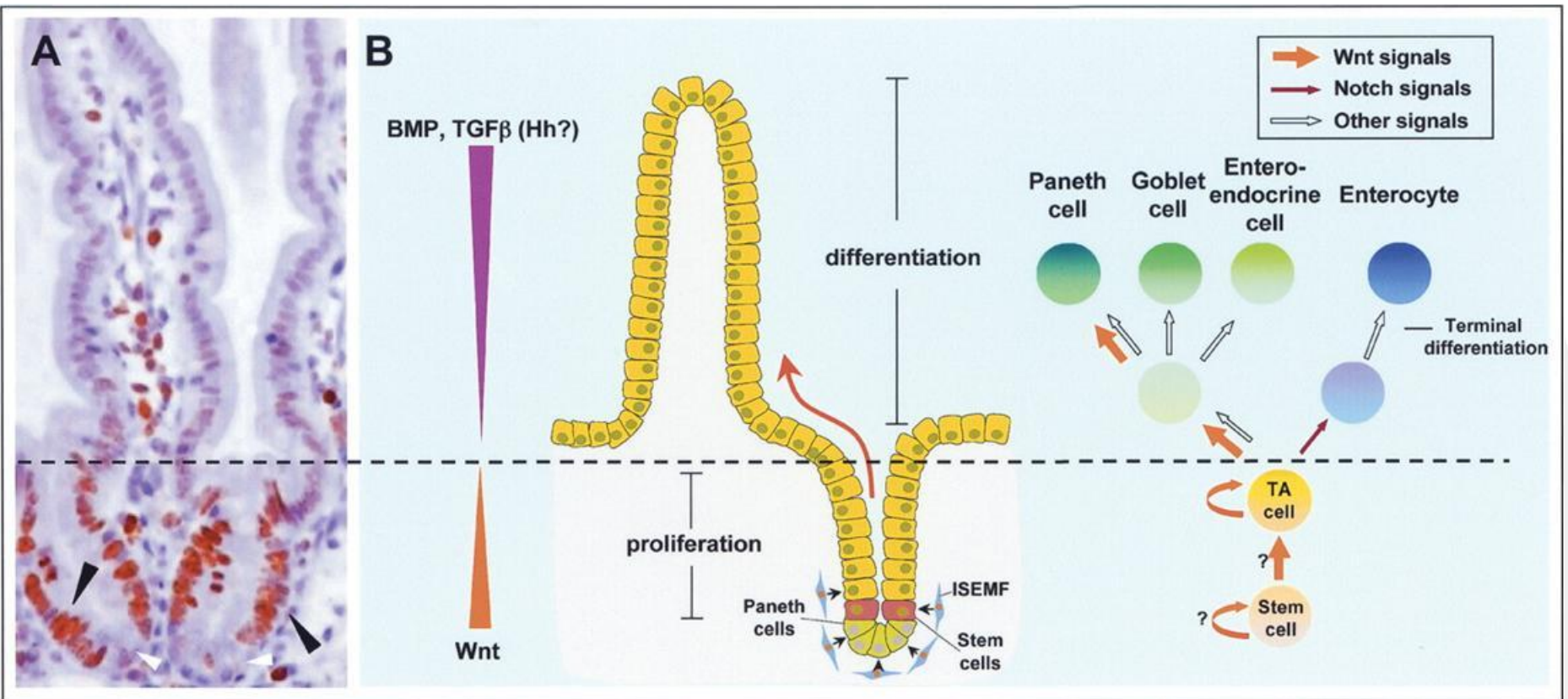
Tumor   Germline

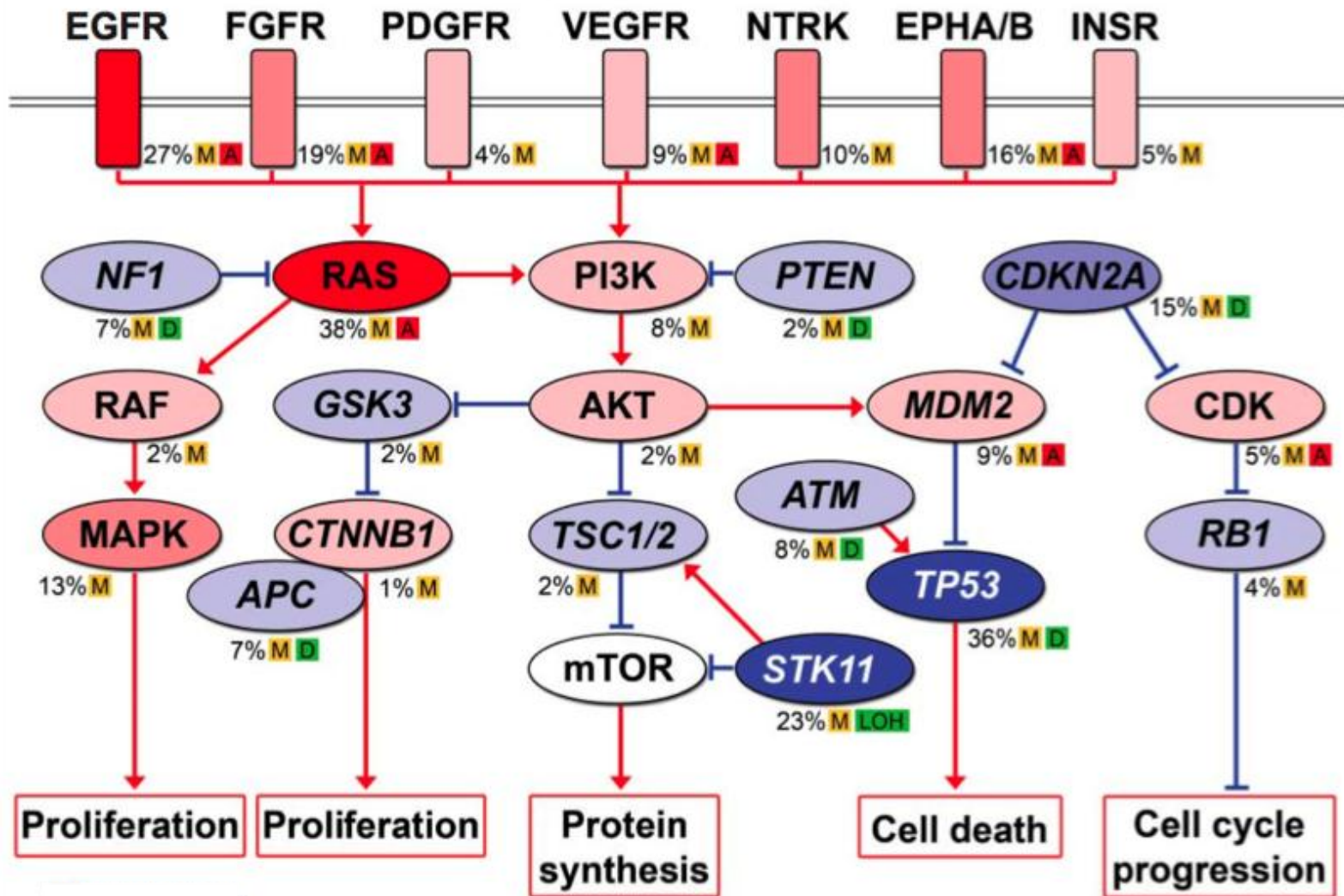**Figure 2.** Genes and Growth Factor Pathways That Drive the Progression of Colorectal Cancer.

ESMO

Chrom. 1

Chrom. X

Colorectal Cancer Mx38

B Vogelstein, 2007, Science
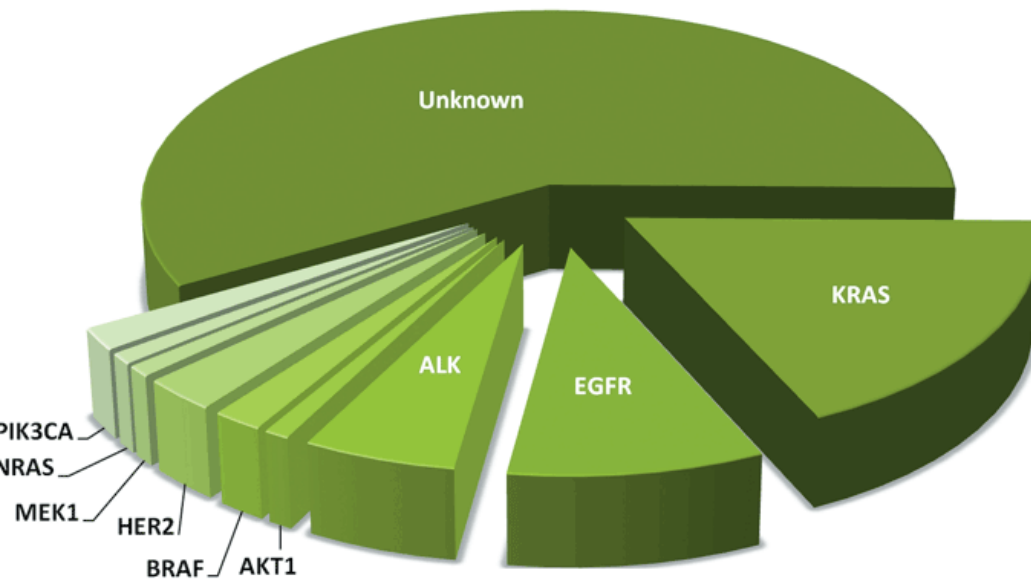Average of 71 mutations in a colorectal cancer

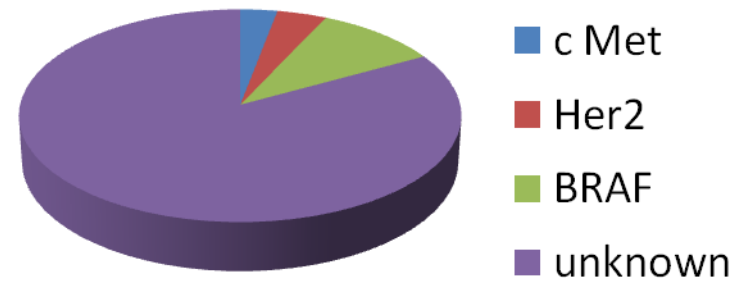# Many faces to a tumor from a given organ

Oncogenic drivers

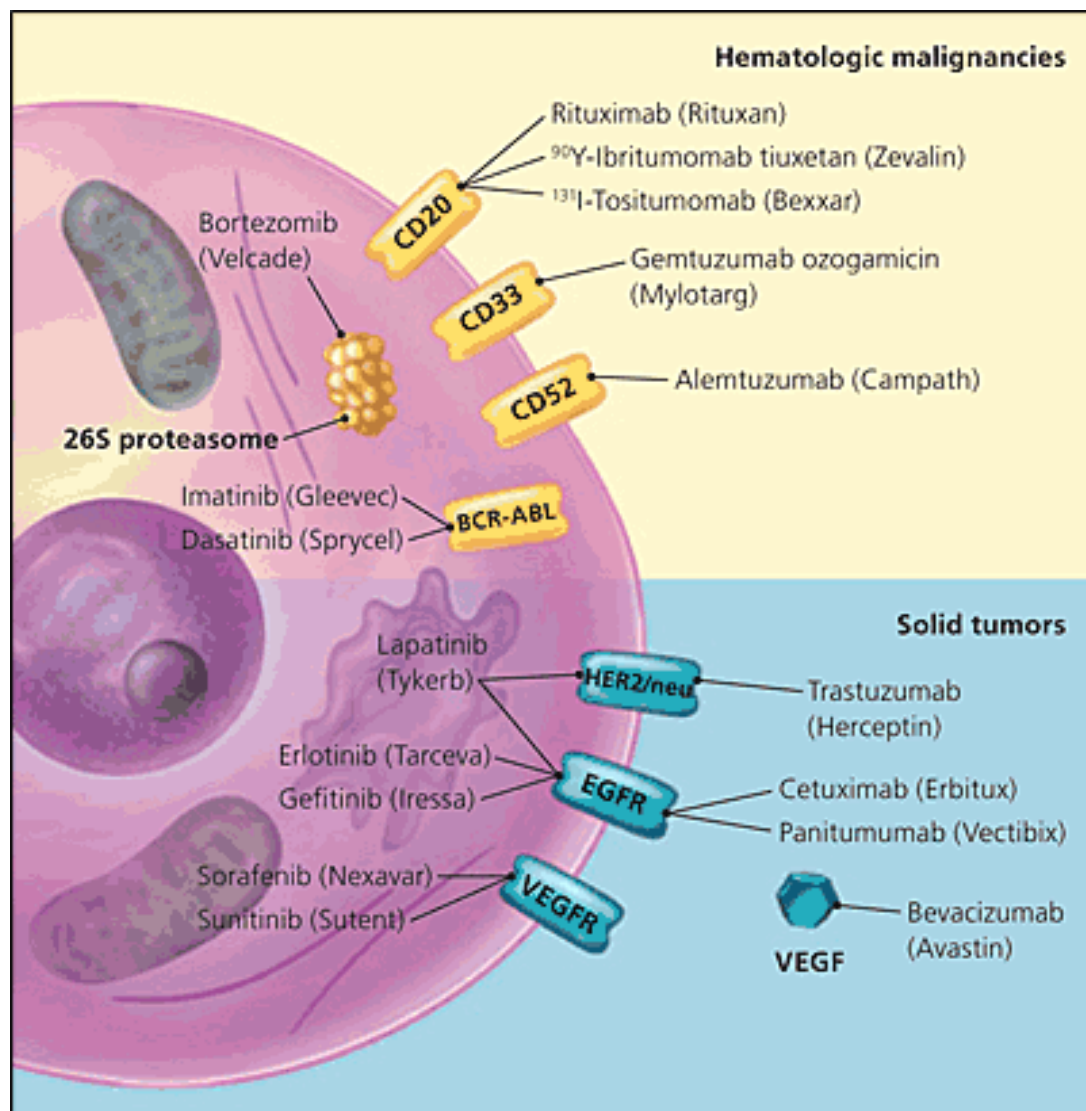**MAJOR advances in differentiating tumors for different cancer types**
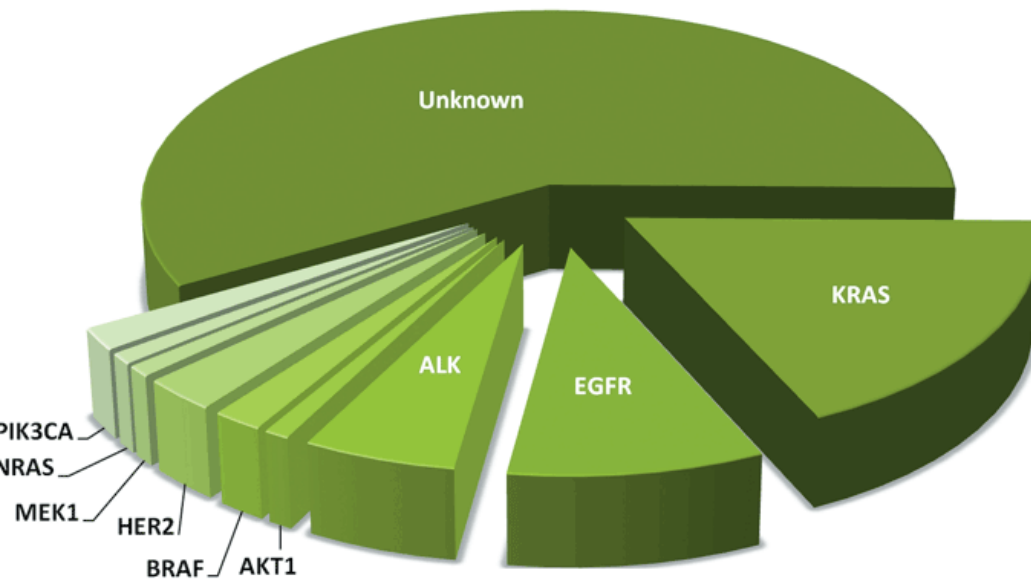
- Lung cancer

- Colon cancer

Targeted therapy

Hematologic malignancies

- CD20
  - Rituximab (Rituxan)
  - ^{90}Y-Ibritumomab tiuxetan (Zevalin)
  - ^{131}I-Tositumomab (Bexxar)
- CD33
  - Gemtuzumab ozogamicin (Mylotarg)
- CD52
  - Alemtuzumab (Campath)
- Bortezomib (Velcade)
- 26S proteasome
- BCR-ABL
  - Imatinib (Gleevec)
  - Dasatinib (Sprycel)

Solid tumors

- HER2/neu
  - Lapatinib (Tykerb)
  - Trastuzumab (Herceptin)
- EGFR
  - Erlotinib (Tarceva)
  - Gefitinib (Iressa)
  - Cetuximab (Erbitux)
  - Panitumumab (Vectibix)
- VEGFR
  - Sorafenib (Nexavar)
  - Sunitinib (Sutent)
- VEGF
  - Bevacizumab (Avastin)
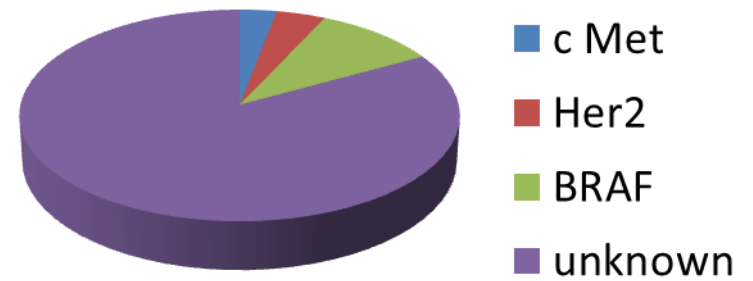
© 2008 RENEE CANNON

ESMO

Oncogenic drivers

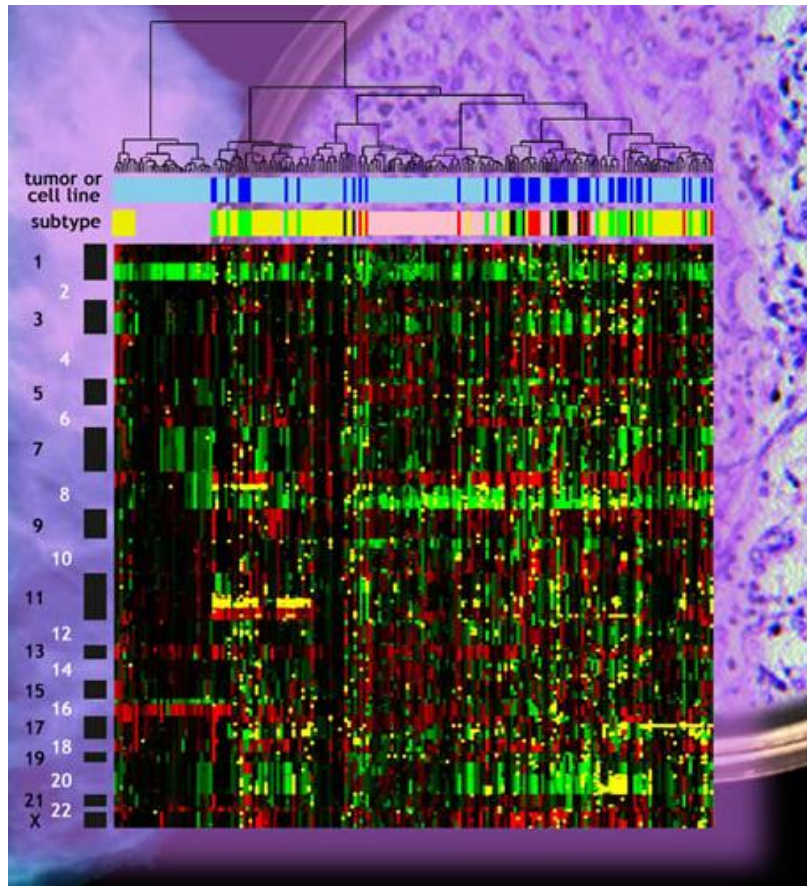**MAJOR advances in differentiating tumors for different cancer types**
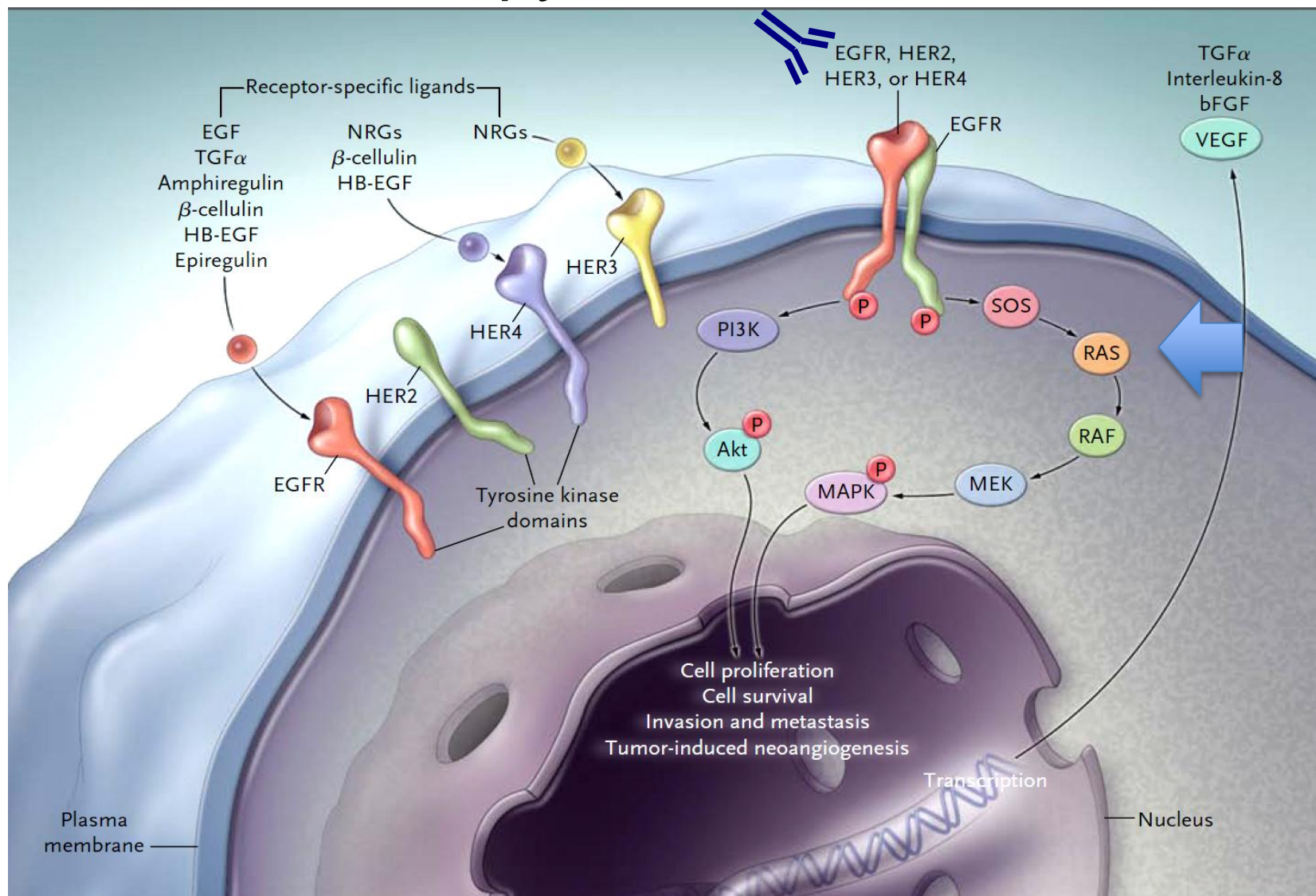
- Lung cancer

- Colon cancer

Subtypes

MAJOR advances in differentiating tumors for different cancer types
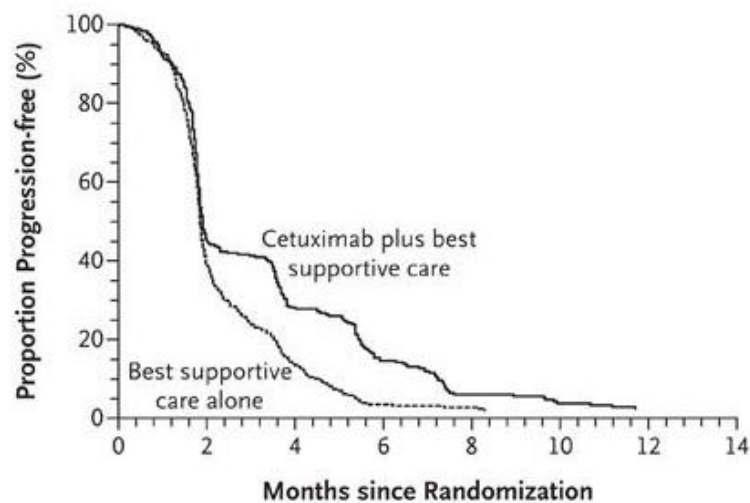

- **Breast cancer**
- **Lung Cancer**
- **Colon cancer**
- **Brain tumors**
- **….**

- **Provide a framework of the disease, match drug efficacy in the different groups**

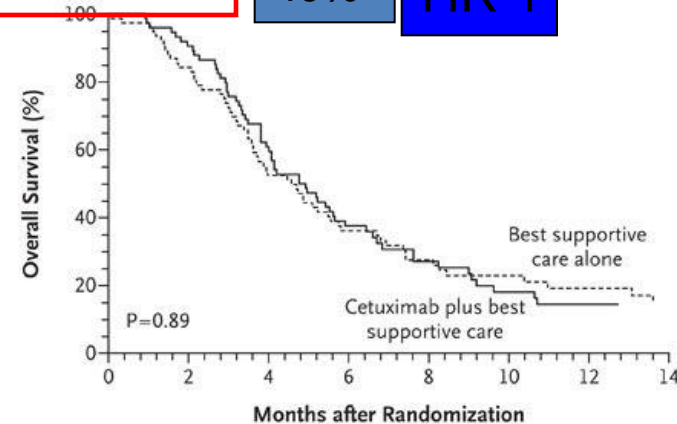# Anti EGFR therapy and colorectal cancer

Adapted from Ciardiello F. and Tortora G. NEJM 2008;358:1160-74

Monotherapy Erbitux Unselected patients
NEJM 2007

Monotherapy Kras selected patients
NEJM 2008

Biomarker enriched trials   ISPY2

Personalized treatment

requirements

•Background knowledge on the disease biology

•Targetted drugs

•Trials to prove the efficacy of the approach

•An in depth knowledge on the biology of the individual patients tumor, baseline and over time

•Banking samples, repeat biopsies, consent

Thank You