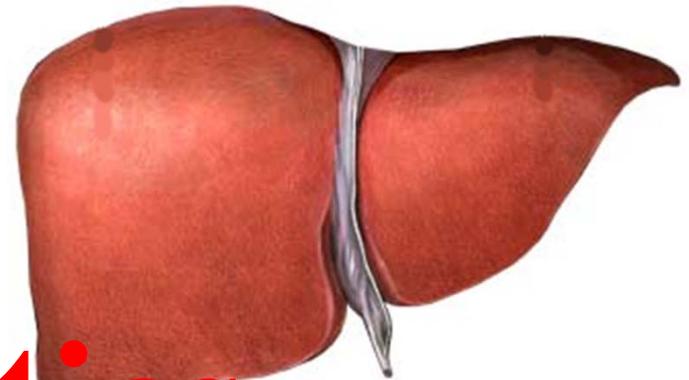
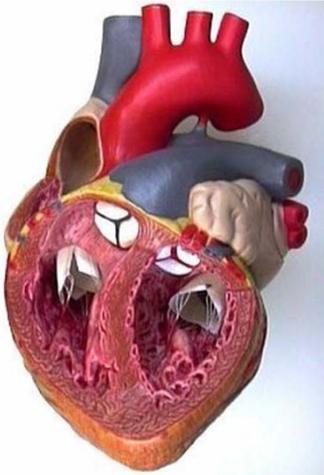


Epigenomics and Cancer

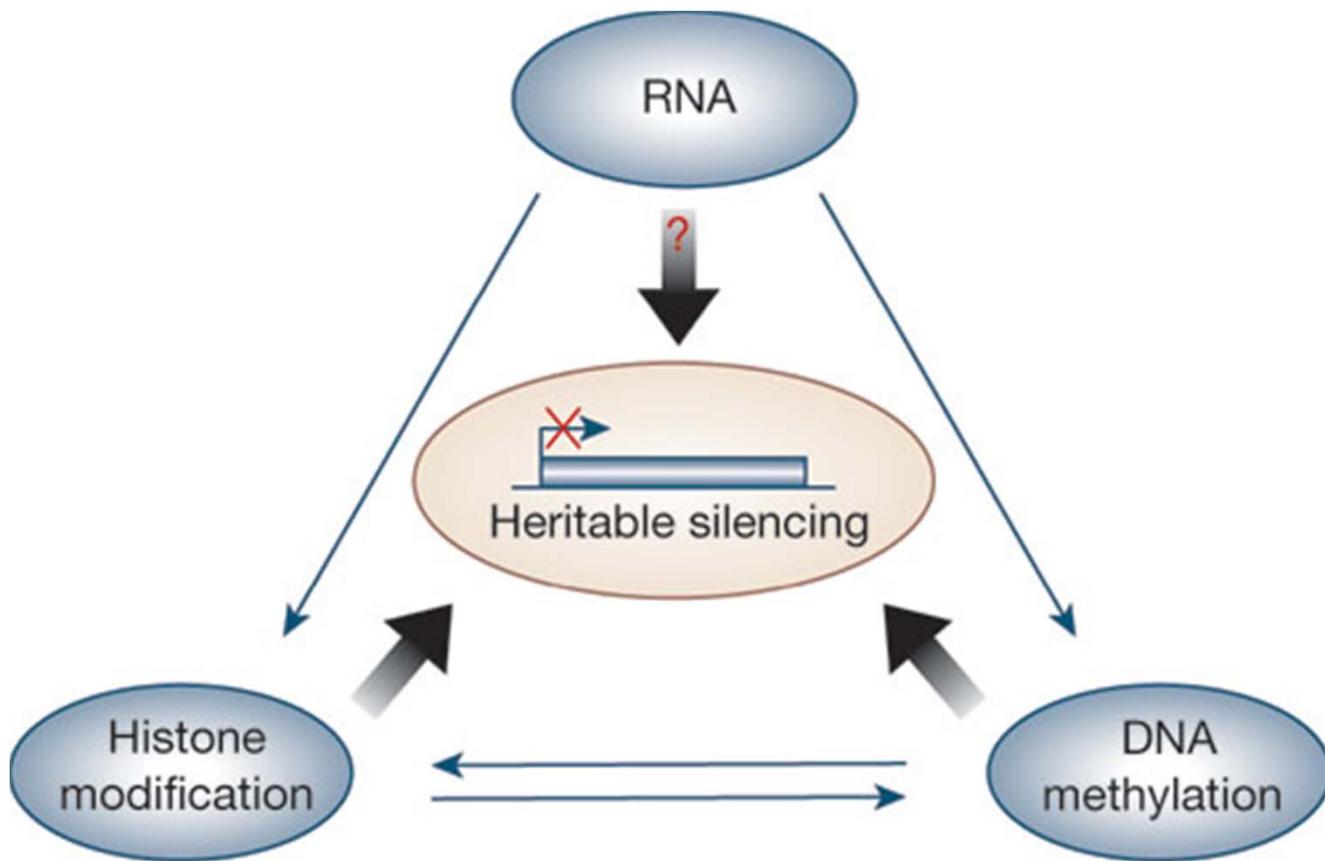
- Peter Jones USC



Genetics



Epigenetics

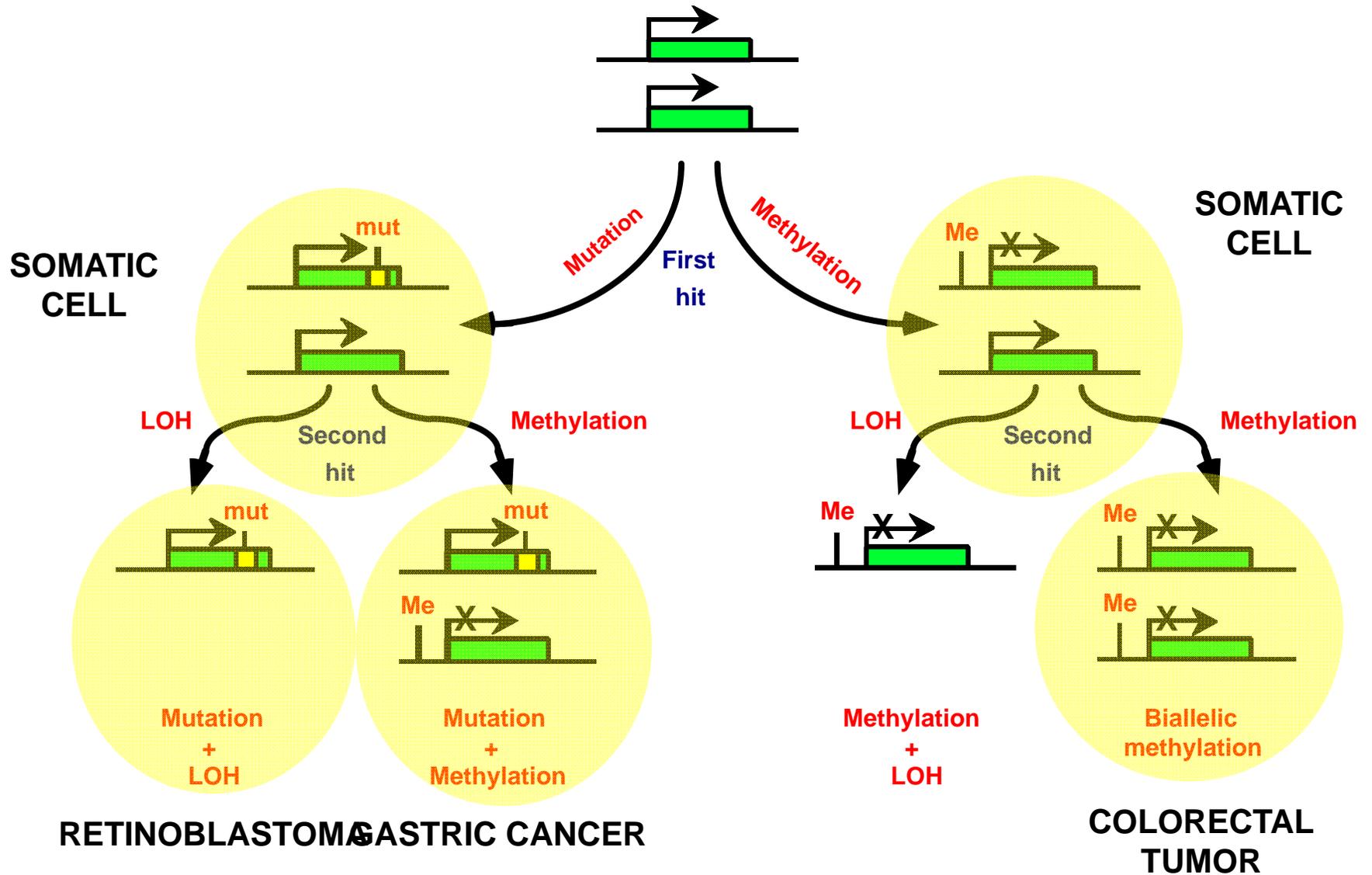


Nature 429 457- 463 (2004)

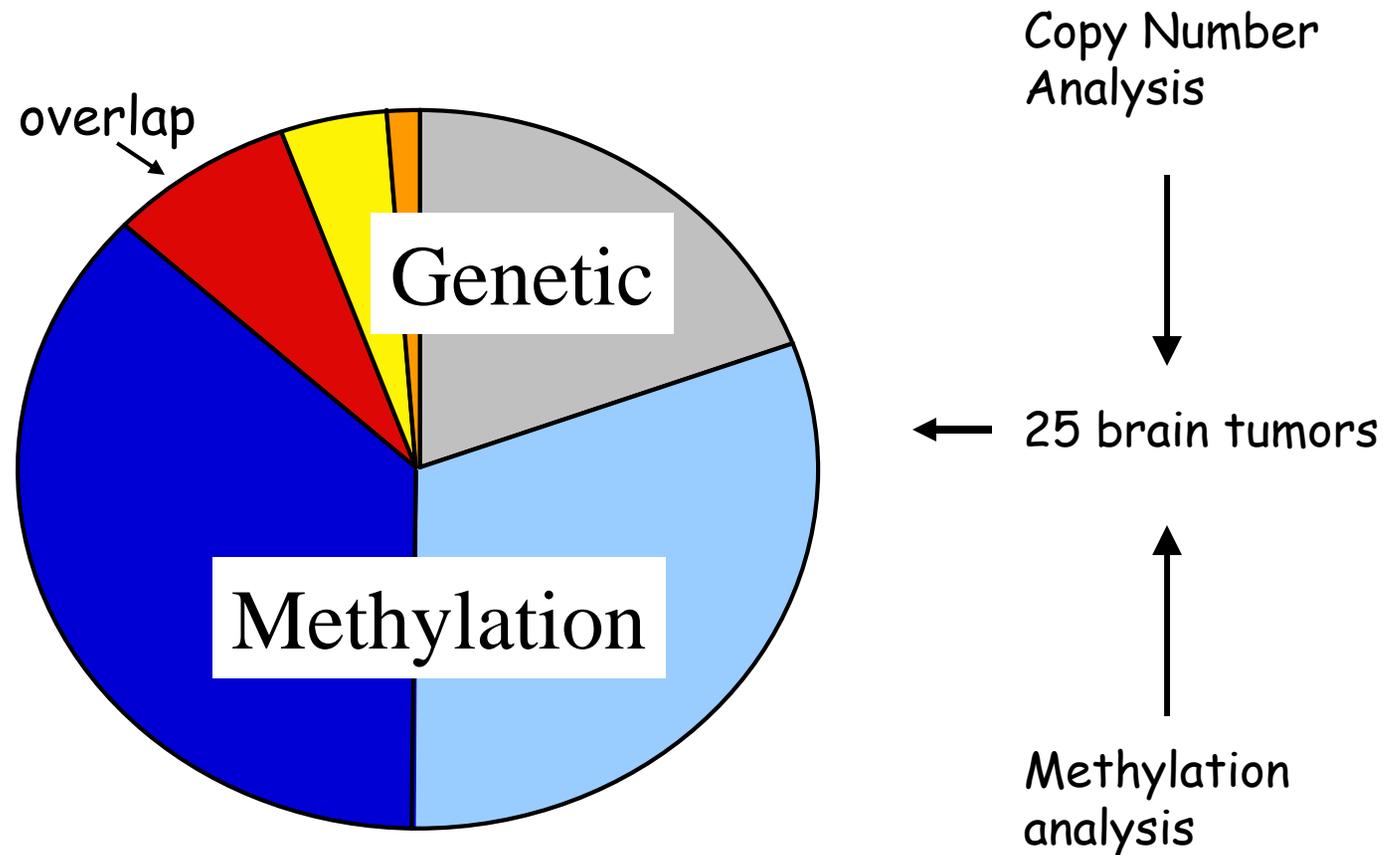
Transcriptional Silencing by DNA Methylation



Knudson's Hypothesis



Loci affected by epigenetic mechanisms are often independent of those affected by genetic mechanisms



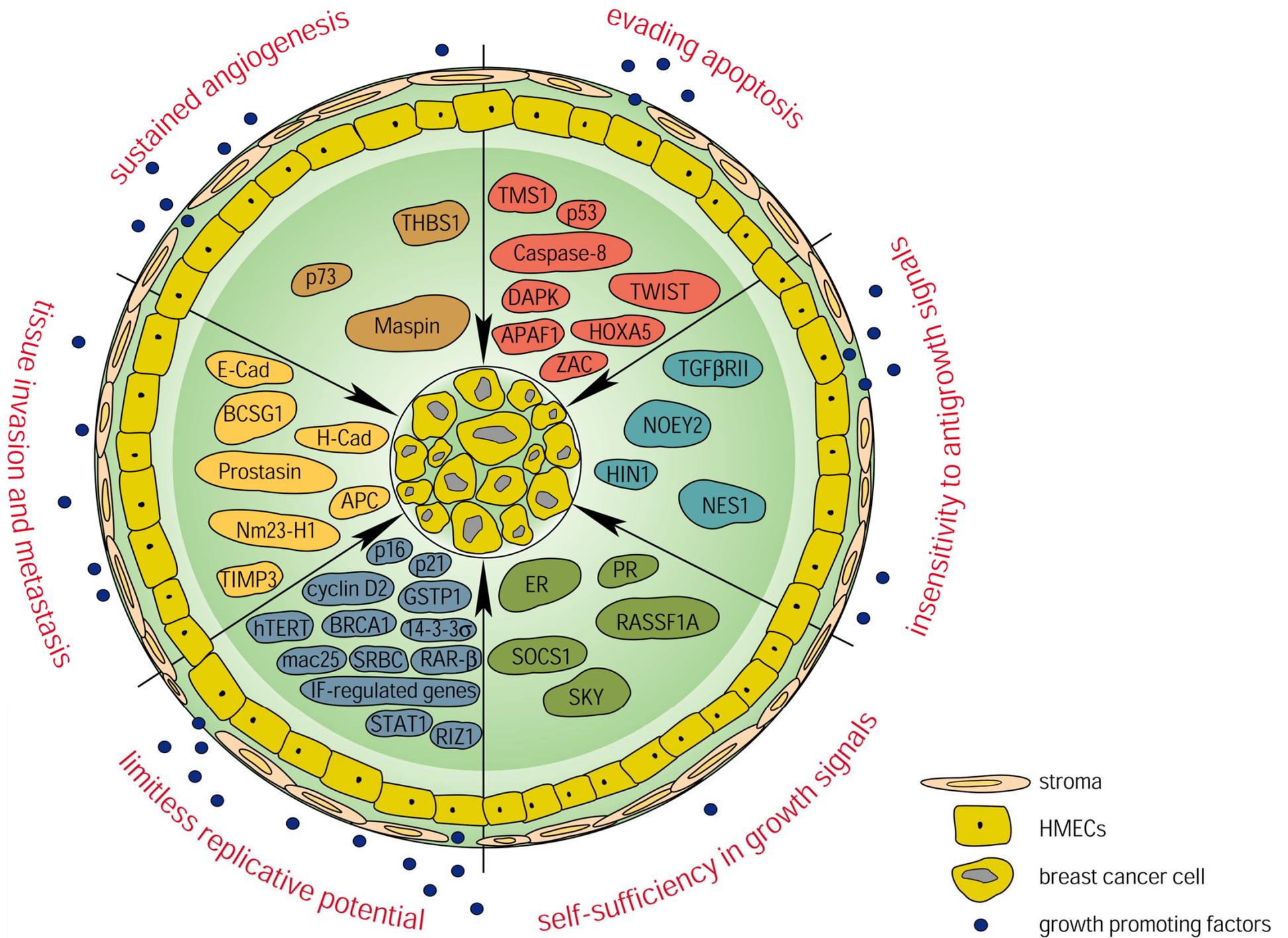
Zardo, Nature Genetics, 2002

Hypermethylated Genes Re-activated by 5-Aza-C or DNMT DKO in HCT 116 Cells

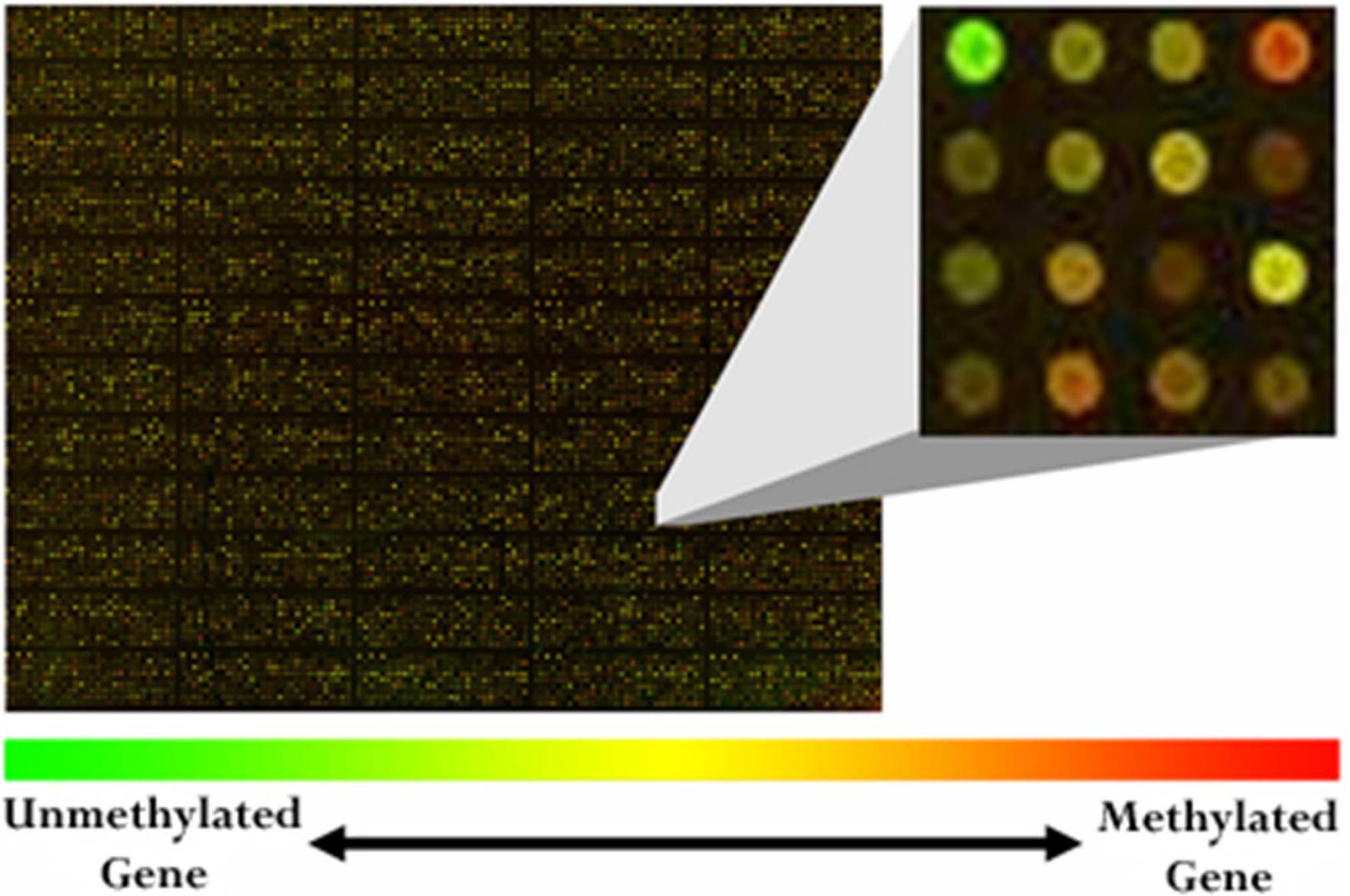
Mutations in:

- *β-catenin*
- *TGF-β receptor*
- *MLH1*
- *p16*
- *MLH1*
- Wild type *p16* allele
- *HIC-1*
- *SFRP 1*
- *SFRP2*
- *SFRP4*
- *SFRP5*
- *GATA 4*
- *GATA-5*
- *Timp-3*
- *TFF1*
- *TFF2*
- *TFF3*
- *Inhibin α*

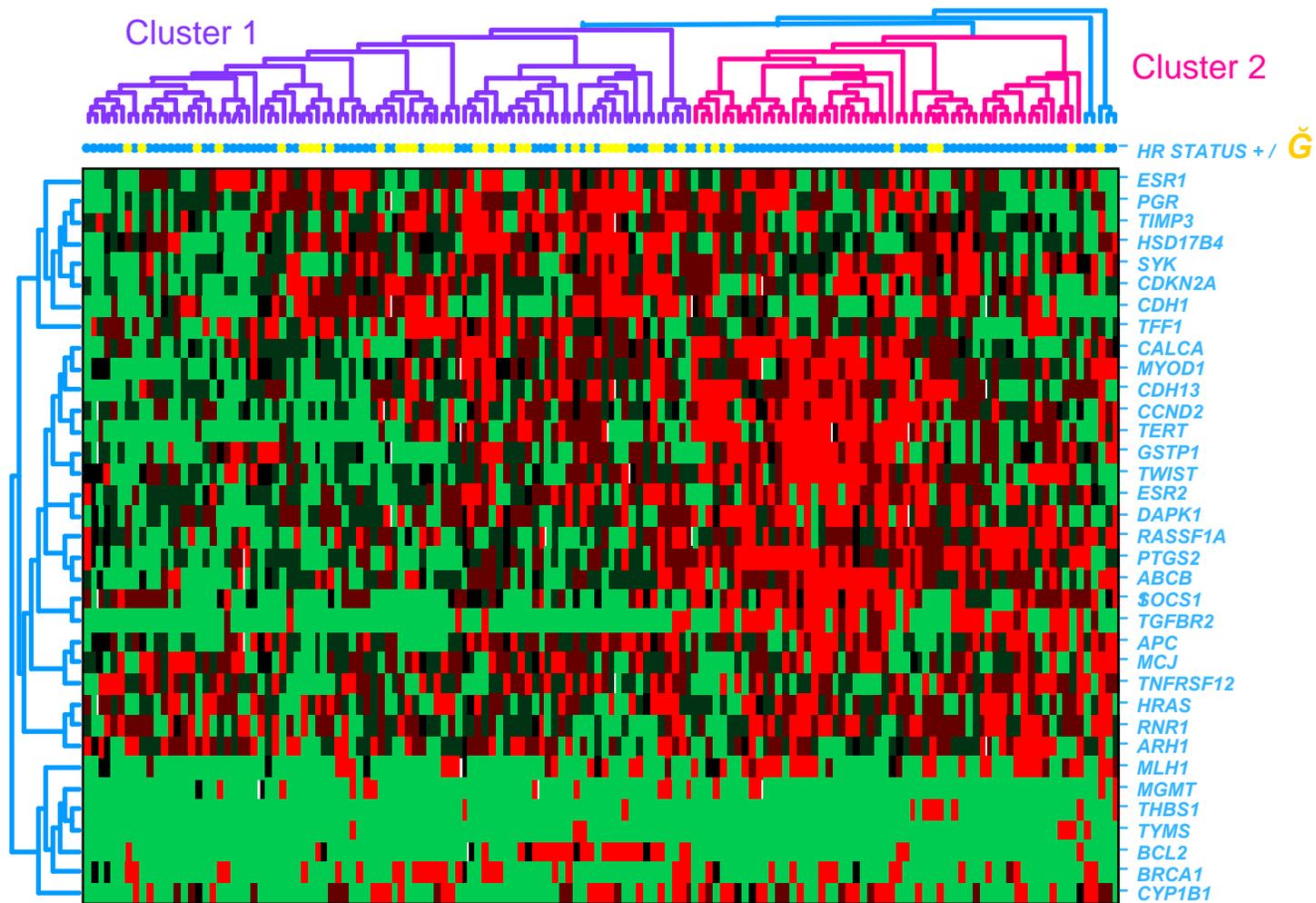
Groups of silenced genes?



Orion Genomics MethylScope



MethyLight Analysis of 35 Genes in 148 Human Breast Carcinomas



Widschwendter et al. (2004) Cancer Research 4, 3807

**AACR Workshop on
the Human Epigenome
June 2005**

Human Epigenome Project

“The goal of the Human Epigenome Project is to identify all the chemical changes and relationships among chromatin constituents that provide function to the DNA code, which will allow a fuller understanding of normal development, aging, abnormal gene control in cancer and other diseases and the role of the environment in human health.”

Human Epigenome Project

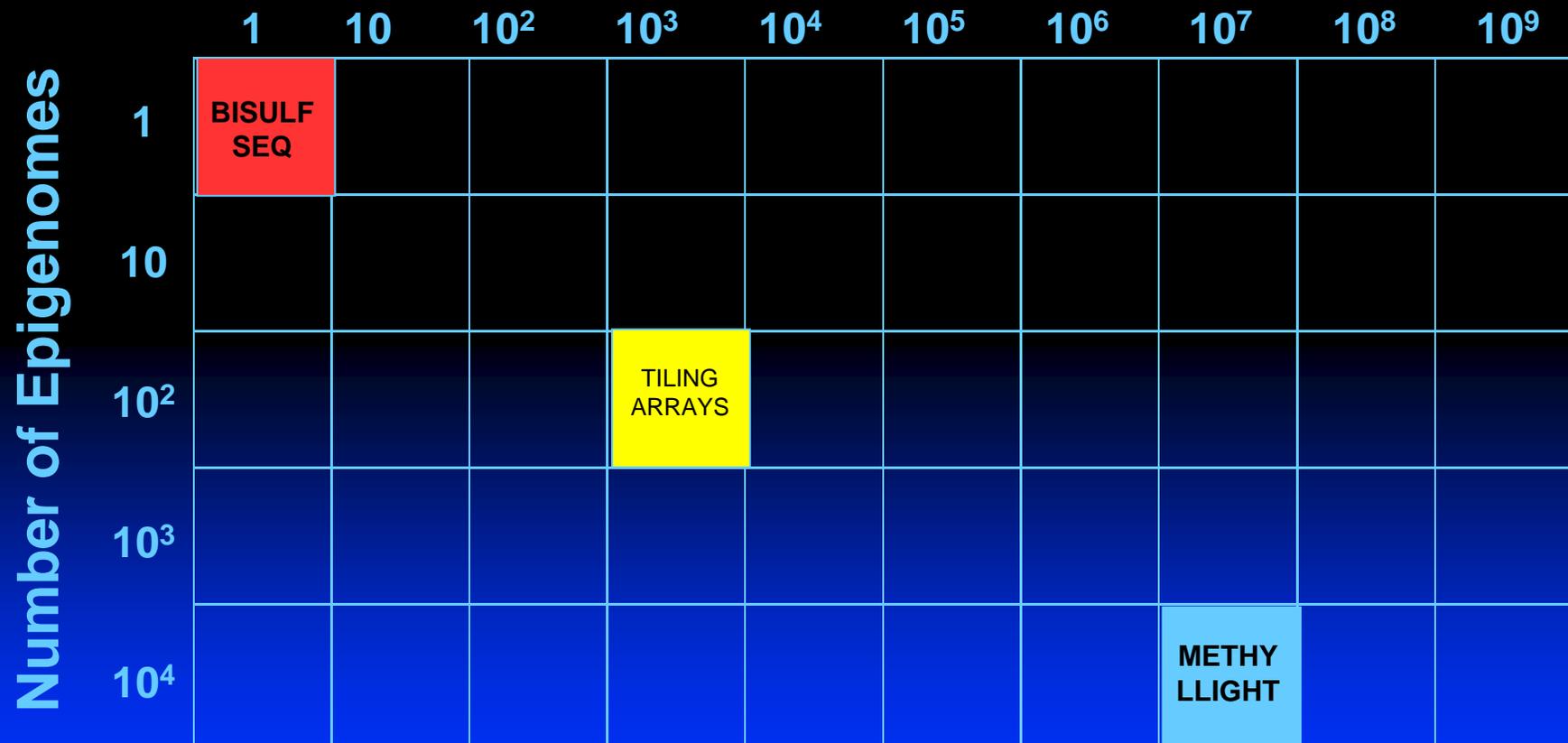
Technology to do it is ready

Epigenetic changes probably outnumber genetic changes in cancer

Start with a reference Epigenome
(Fibroblasts?)

Epigenome Analysis

Assay Resolution (bp)



AACR Action Plan

- Scientific collaborations. AACR will form a Human Epigenome Task Force and collaborate with NCI
- International partnerships. Any U.S. epigenome effort should coordinate with, and take into account, projects currently underway in other parts of the world.
- Communications. The AACR will coordinate efforts to keep the general public informed about the importance of a Human Epigenome Project to the conquest of cancer.

