Genomics and cancer a moving landscape

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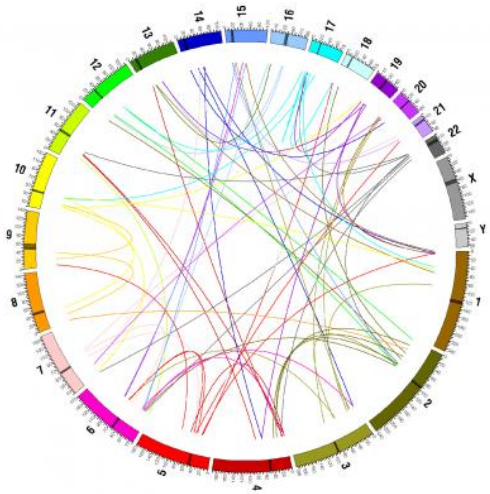
Start of the Genomic Medicine Era

Human genome took about 23 years and several billion dollars to start the project and to publish the draft sequence (finishing is still in progress).

But this is not the end of the story
This is only the beginning



Nature, 2009

"REVOLUTIONARY GENOME SEQUENCING TECHNOLOGIES THE $1000 GENOME"

(Department of Health and Human Services (DHHS))

2004 - develop novel technologies that will enable extremely low-cost, high quality DNA sequencing

2009 - the cost to sequence an entire individual human genome to be $1,000 by the end of 2009 and the time required for sequencing less than one week

we are not their yet but very close – it is about $5000 these days

2012 - The NIH plans to award $5.7 million in funding for research projects that explore ways to use genome sequencing in clinical care, and $800,000 to fund a coordinating center to support these studies.

Clinical sequencing

But even at this stage DNA sequencing is already a very attractive tool that can be used not only for the purpose of conducting research, but also for clinical studies and, most importantly, to improve the quality of clinical diagnosis and the selection of treatments for individual patients.

CANCER BIOLOGY

Sequencing guides cancer treatment

HIGHLY READ on genome-biology.com in the last 30 days

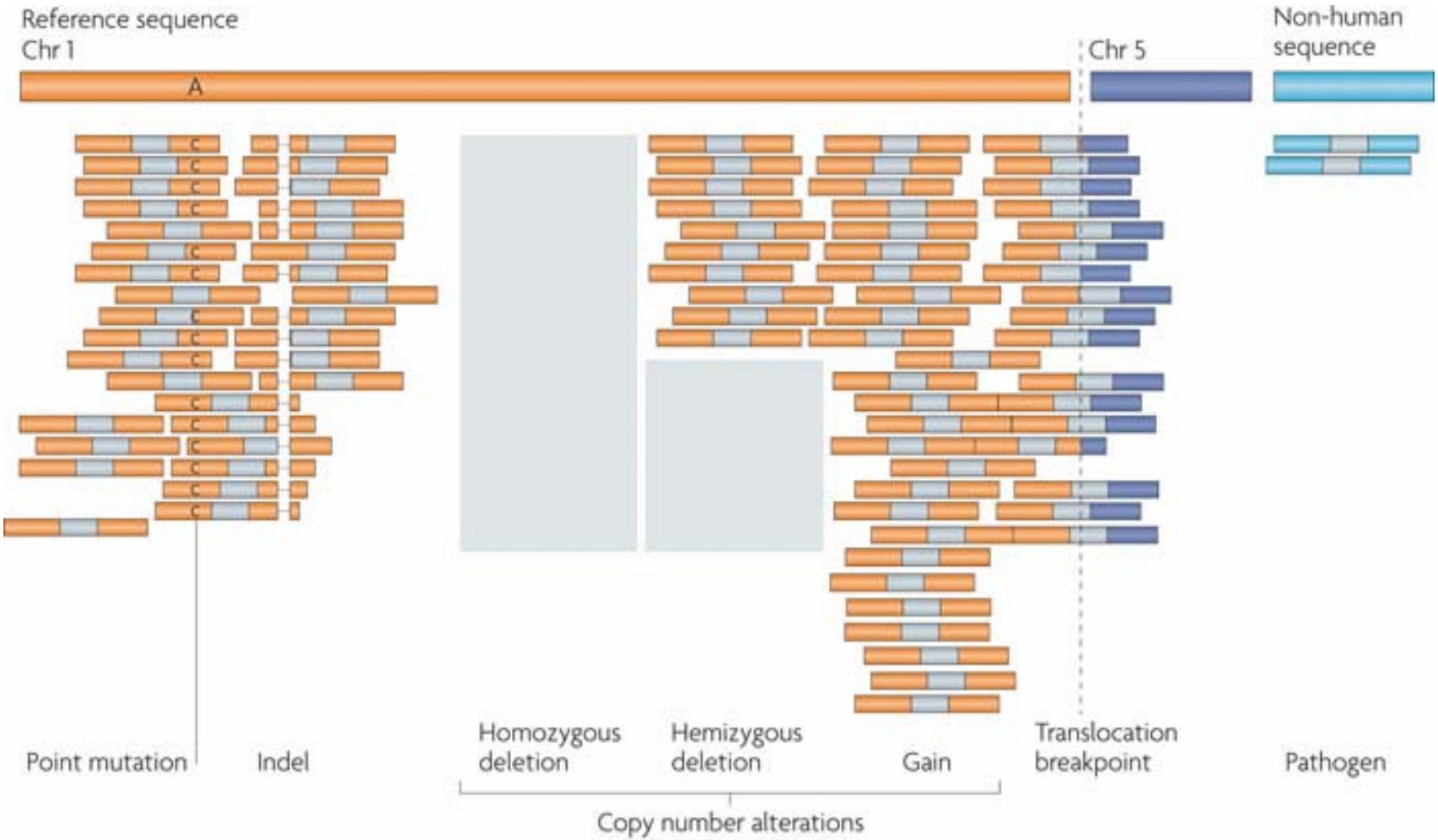
The full genome sequence of a rare tongue tumour has allowed physicians to draw up a personalized treatment plan where no established protocol existed.

A 78-year-old patient had his cancer sequenced after initial treatments failed to slow tumour growth, which had spread to his lungs. When Steven Jones of the British Columbia Cancer Agency in Vancouver, Canada, and his colleagues analysed the sequence and compared it with that of his normal cells, they determined that tumour growth was probably driven by overexpression of a cancer-promoting gene called *RET*.

A combination of drugs that target *RET* held back the cancer for seven months, until the tumours became drug-resistant. The team sequenced the cancer again and identified new mutations that had activated the AKT and MAPK pathways, which are often upregulated in cancer. The results provide a snapshot of how tumours evolve to evade treatment.

Genome Biol. 11, **R82 (2010)**

Cancer is a disease of genome alterations. Which alterations can be detected:

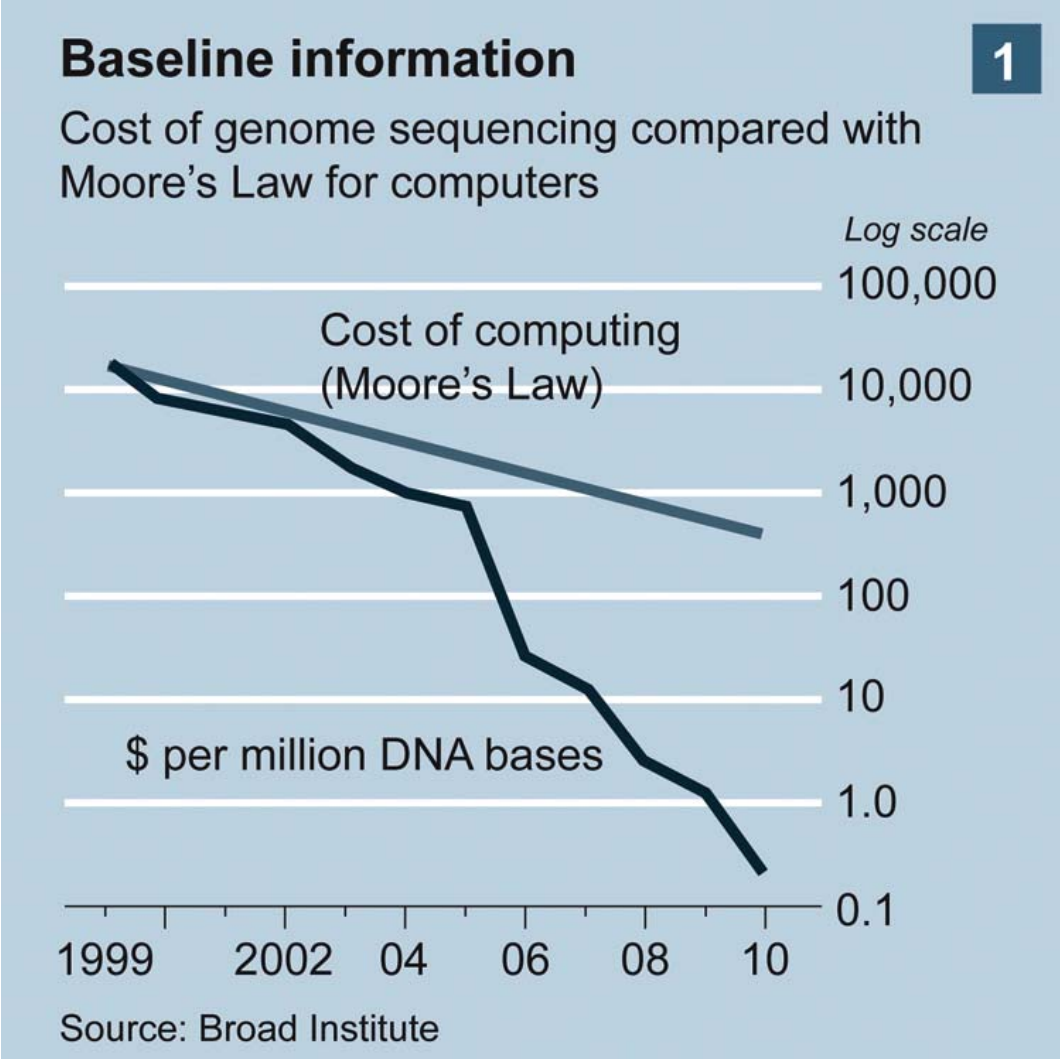


M. Meyerson, S.Gabriel, G.Getz, Nature Reviews Genetics 11, 685-696

Cost of computing vs sequencing cost

Moore's law: computers double in power roughly every two years—an increase of more than 30 times over the course of a decade, with reductions in cost.

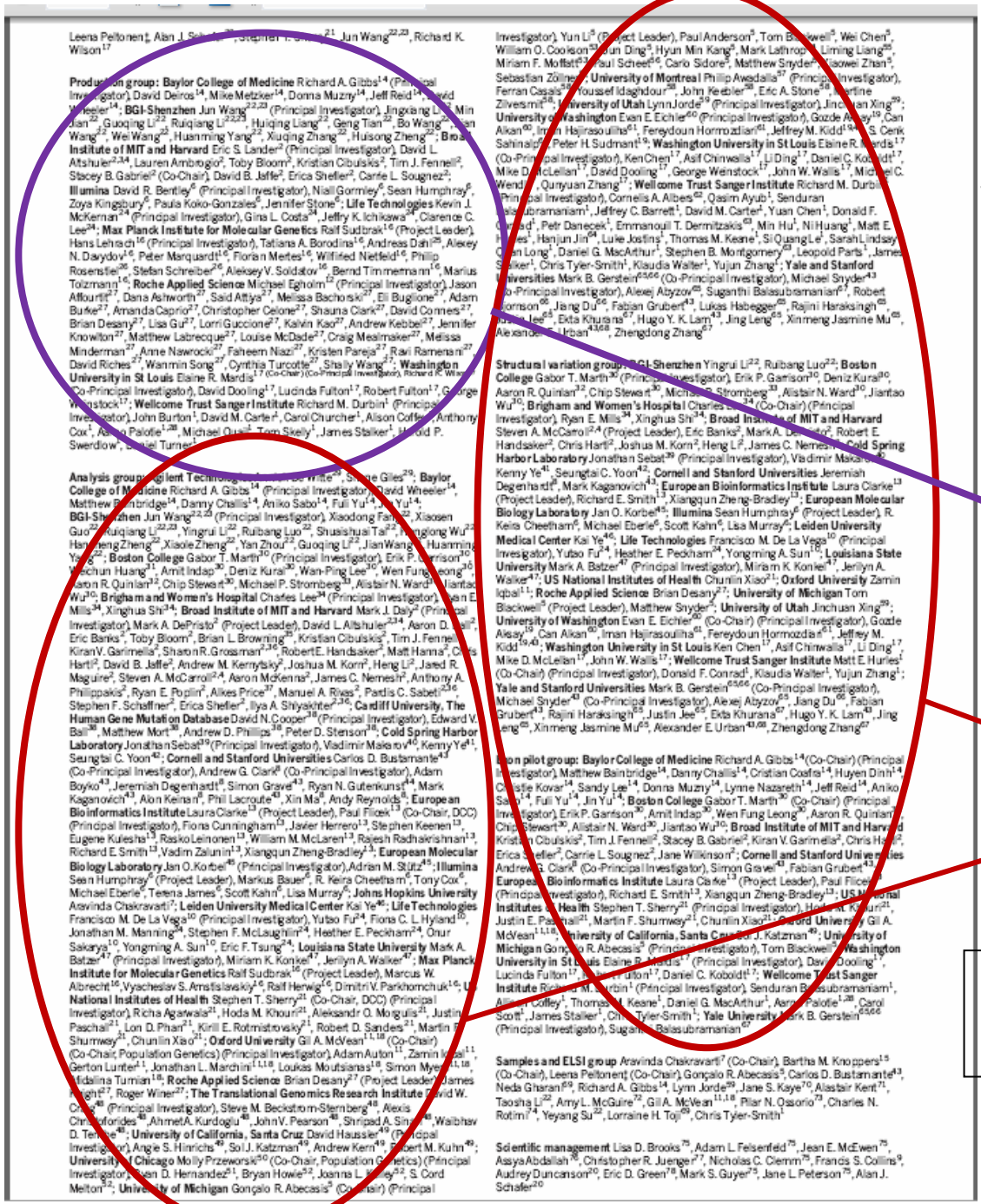
(Moore's law describes a long-term trend in the history of computing hardware. The number of transistors that can be placed inexpensively on an integrated circuit has doubled approximately every two years. The trend has continued for more than half a century and is not expected to stop until 2015 or later.)



A map of human genome variation from population-scale sequencing

The 1000 Genomes Project Consortium*

28 OCTOBER 2010 | VOL 467 |
NATURE | 1061



Production group

People in different aspects of data analysis

- wgs of 179 individuals from 4 populations
- 2 mother-father-child trio (high coverage)
- Exone-targeted sequencing of 697 individuals

Huge need in bioinformatics tools: Simple pipelines/protocols and easy to read reports

Sample sequencing

Data Analysis

Patients treatment

Doctors simple life = Hard work for programmers and bioinformatitions

Team work to set up cancer sequencing facility

statistician

statistician

molecular biologist

mathematician

data processing specialist

molecular oncologists
(pathway analysis)

data analysis automation

pathologists

data bases specialist

oncologists
(treatment selection)

user friendly interfaces

IT infrastructure (compute power,
data storage, updates etc)

Routine diagnostics of cancer patients

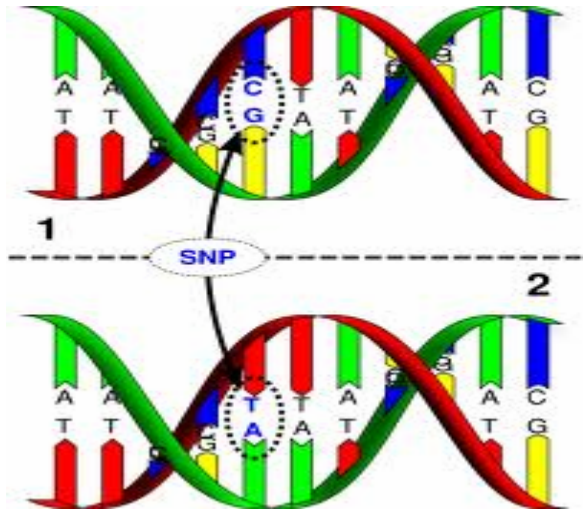
Step by step plan

- Stage 1 - sequence of panel of well characterized onco-specific genes and gene onco-suppressors
- Stage 2 - Sequence and analysis of all coding regions of the genome (full exome sequence) together with the analysis of gene expression level (transcriptome)
- Stage 3 - Sequence and analysis of the complete genome of each patient

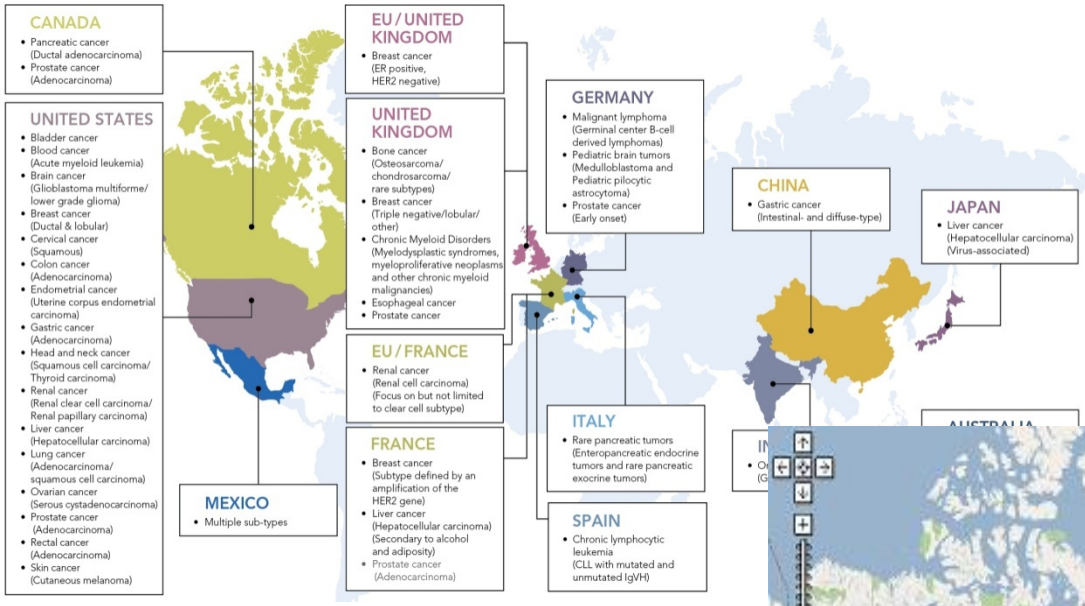
The ethical, legal, and social issues

- data to be released to the patient
- data release and identifiability
- data that can be released into the public domain
- protection of patient confidentiality
- sharing and understanding data (what to do with all the findings for the individual patient etc.)
- data storage security, confidentiality and reliability
- how long to store data?
- sequencing service cost
- insurance
- ……

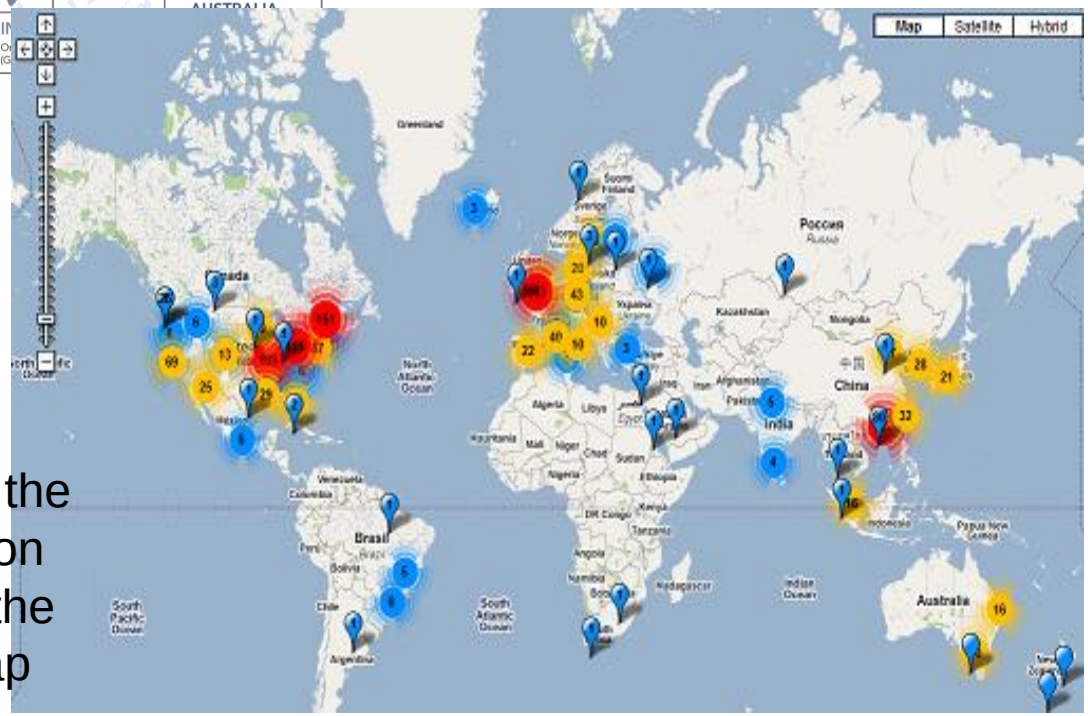
Each baby to be sequenced at birth: personal reference



The International Cancer Genome Consortium (ICGC)



BGI genomics map



My dream is to see Russia as one of the countries that are well represented on maps like these, and to take part in the creation of a Russian genomics map

THANK YOU!