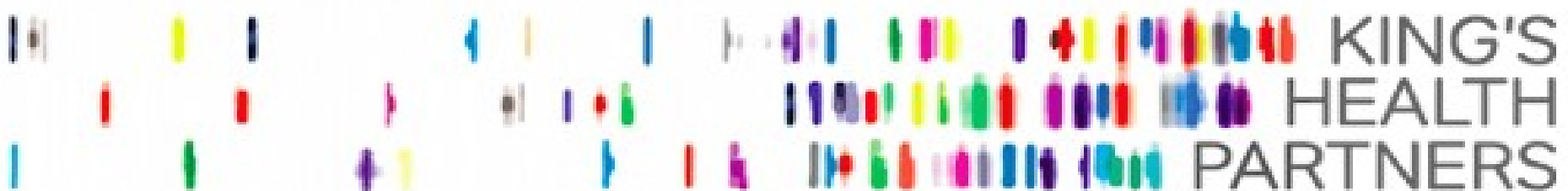


An Introduction to Genes, Genomes and genetic changes in the Myelodysplastic syndromes (MDS)

Dr Nicholas Lea

Laboratory For Molecular Haemato-Oncology (LMH)

Kings College hospital

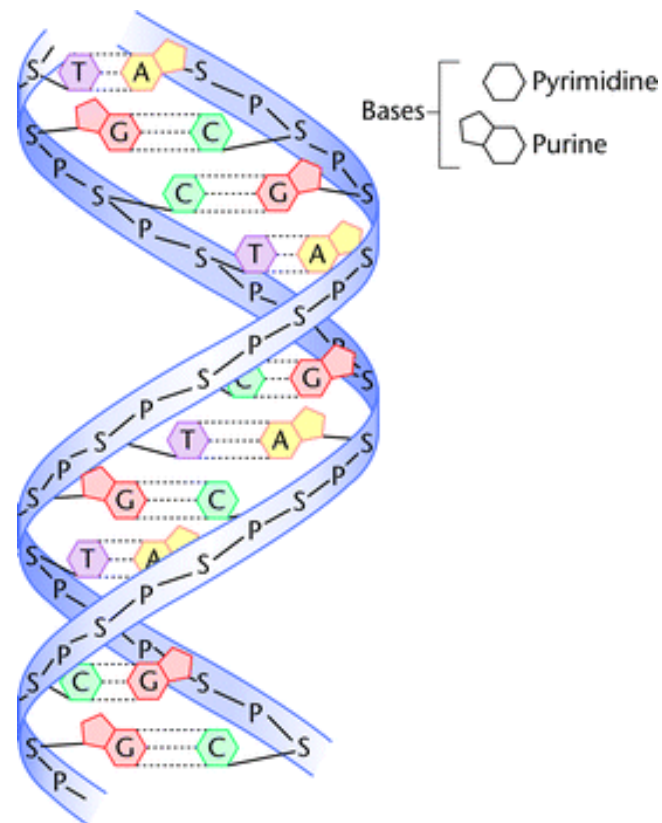
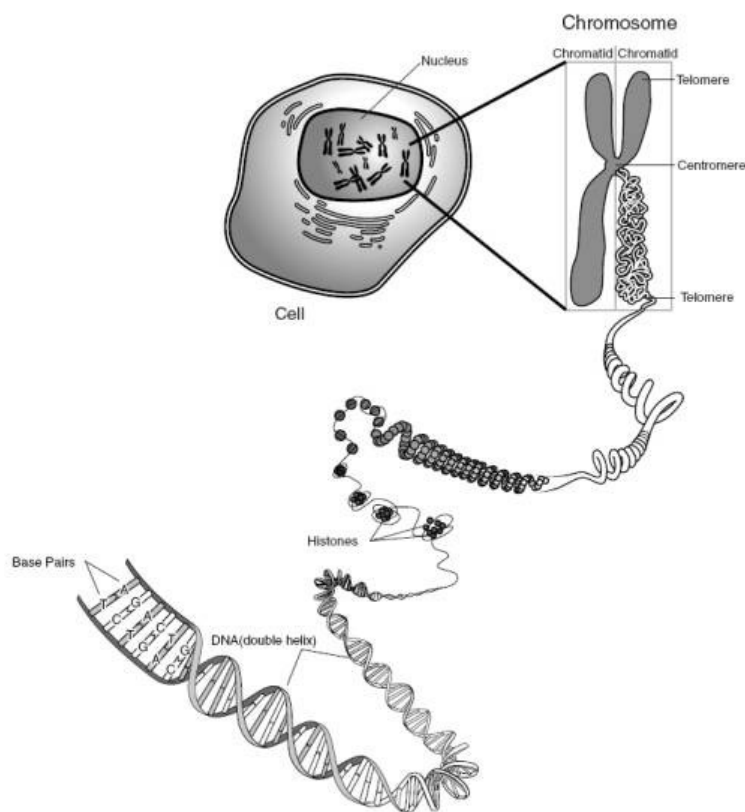


Objectives

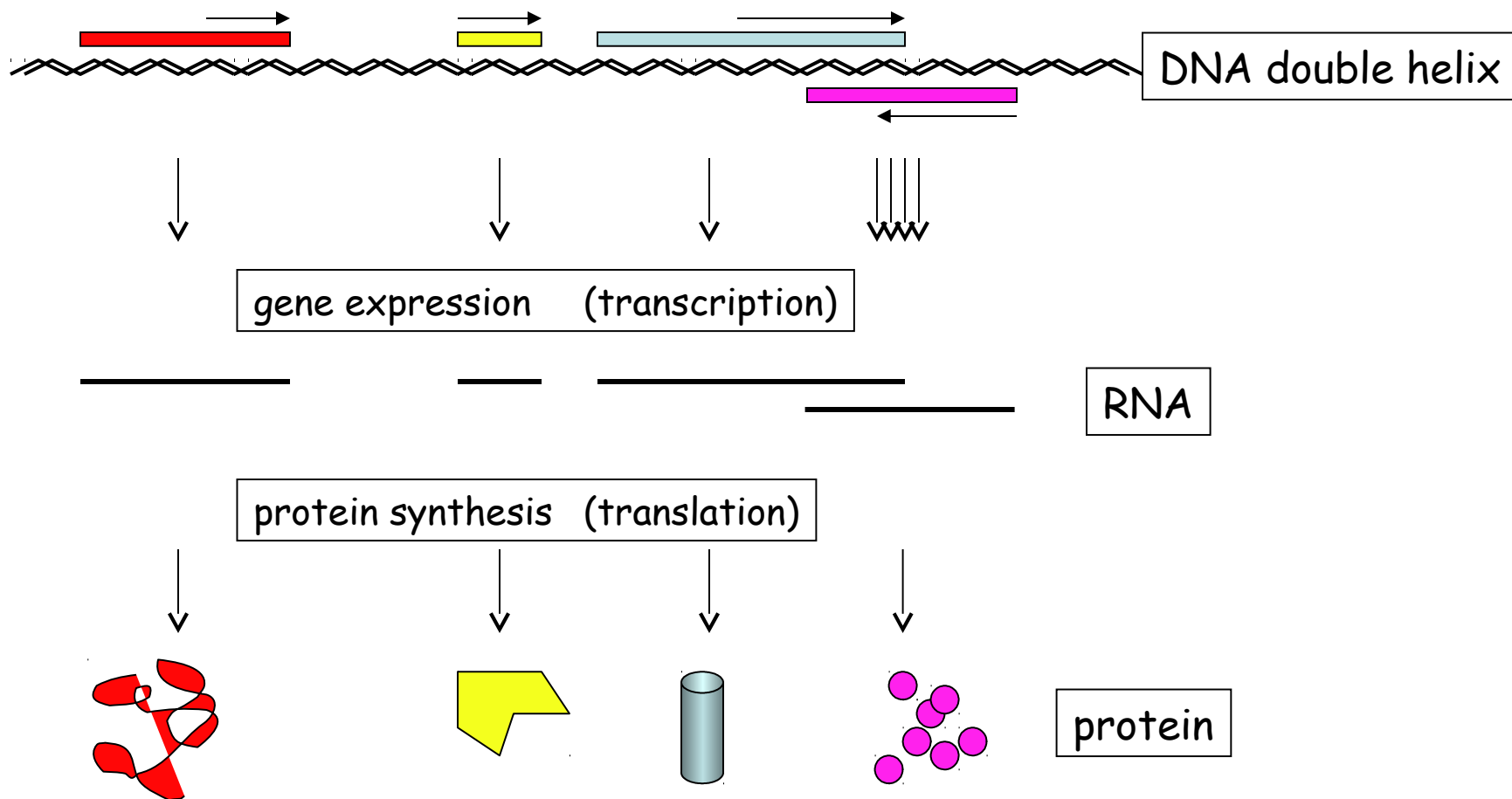
- 1: Genomic organisation, Structure and Genes
- 2: Interrogating our genome: advances in DNA sequencing
- 3: Genomic changes in MDS

what is our genome ?

Our genes carry biological information encoded in the order or sequence of nucleotides which make up the DNA double helix



From DNA to Protein



Translation

from DNA sequence to protein: the *genetic code*

		Second Letter					
		T	C	A	G		
First Letter	T	TTT } Phe TTC } TTA } Leu TTG }	TCT } TCC } Ser TCA } TCG }	TAT } Tyr TAC } TAA Stop TAG Stop	TGT } Cys TGC } TGA Stop TGG Trp	T	C
	C	CTT } CTC } Leu CTA } CTG }	CCT } CCC } Pro CCA } CCG }	CAT } His CAC } CAA } Gln CAG }	CGT } CGC } Arg CGA } CGG }	T	C
	A	ATT } ATC } Ile ATA } ATG Met	ACT } ACC } Thr ACA } ACG }	AAT } Asn AAC } AAA } Lys AAG }	AGT } Ser AGC } AGA } Arg AGG }	T	C
	G	GTT } GTC } Val GTA } GTG }	GCT } GCC } Ala GCA } GCG }	GAT } Asp GAC } GAA } Glu GAG }	GGT } GGC } Gly GGA } GGG }	T	C
						Third Letter	

The genetic code...

start codon



stop codon



Met	Lys	Leu	His	His	Trp	Lys	Phe	Asp	*
ATG	AAG	TTA	CAT	CAT	TGG	AAA	TTT	GAT	TAA



13,937



32,998



18,759



57,386



20,364



20,962

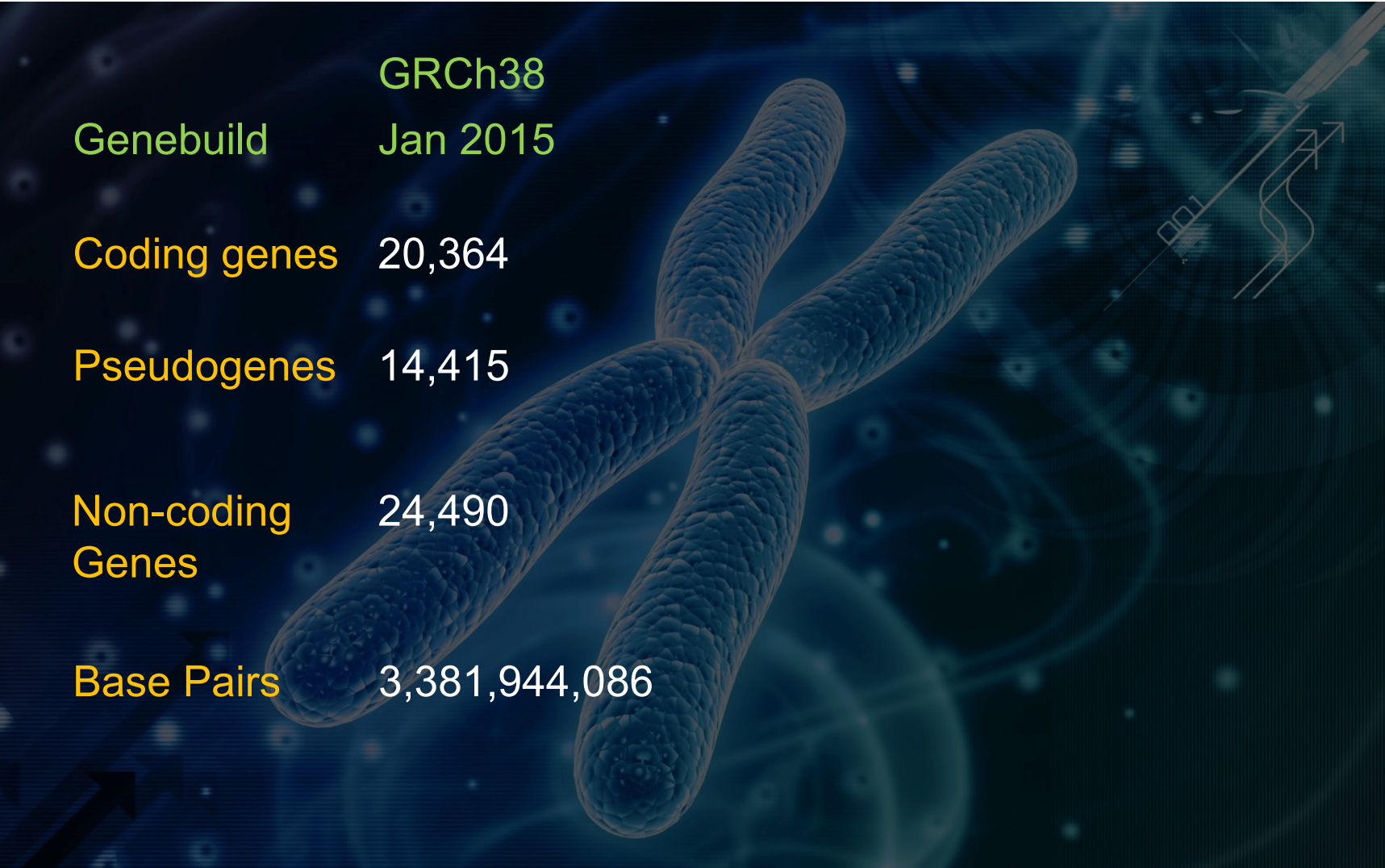


30,074



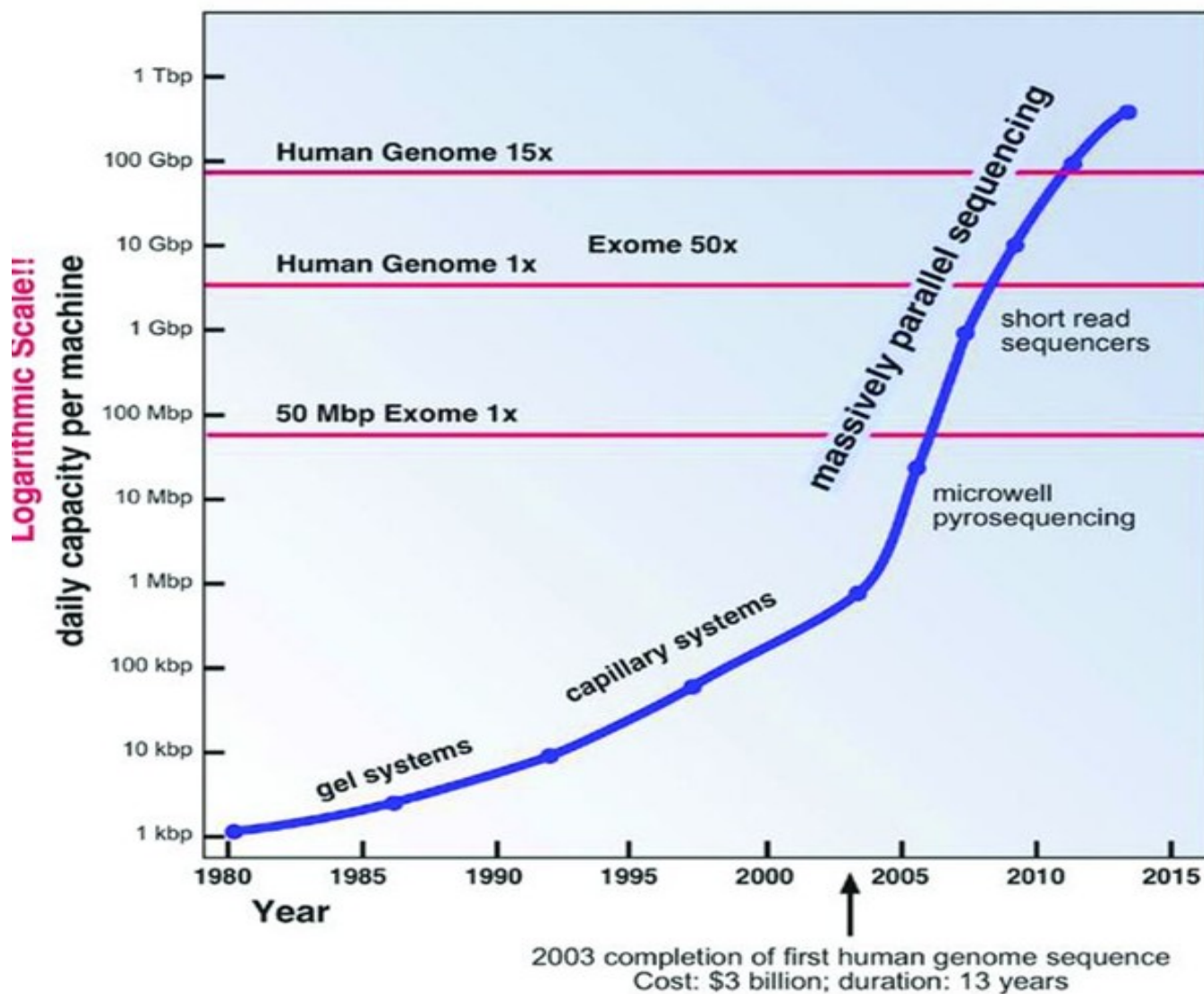
41,019

The Human Genome



	GRCh38
Genebuild	Jan 2015
Coding genes	20,364
Pseudogenes	14,415
Non-coding Genes	24,490
Base Pairs	3,381,944,086

Sequencing technology improvements

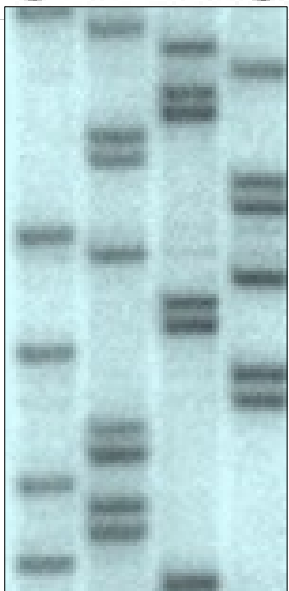


Next Generation Sequencing

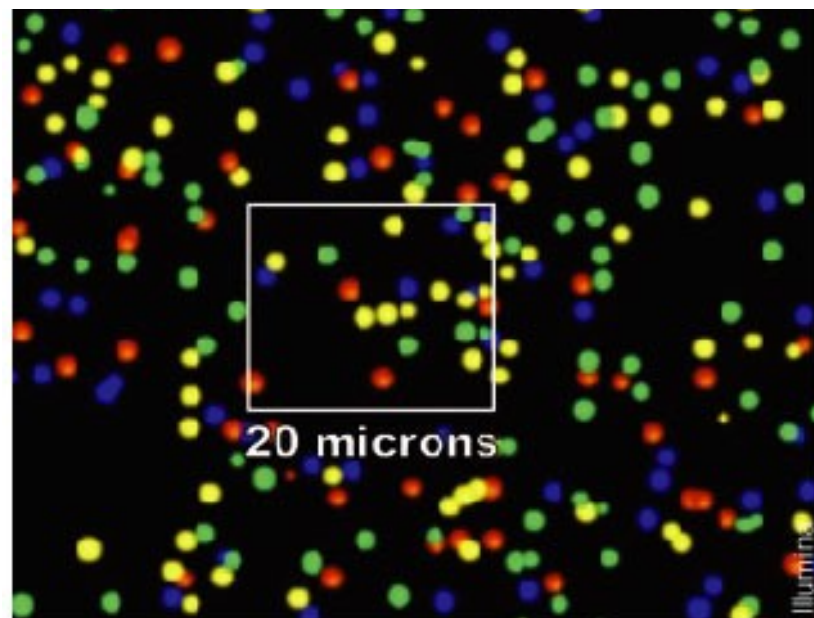
- Sanger sequencing the human genome cost \$3 billion and took more than a decade – completed in 2003.
- NGS - 5 Human genomes per week for around \$5000 per genome.

Sequencing technologies

C T A G



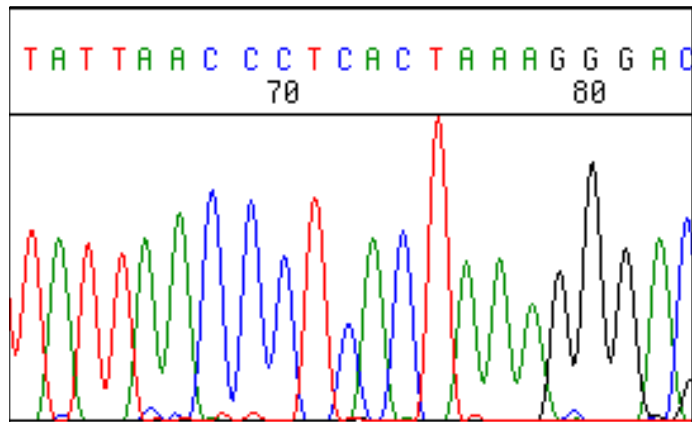
1Kb per
gel 1-2
days



Cluster density ~ 1.4 million / mm^2

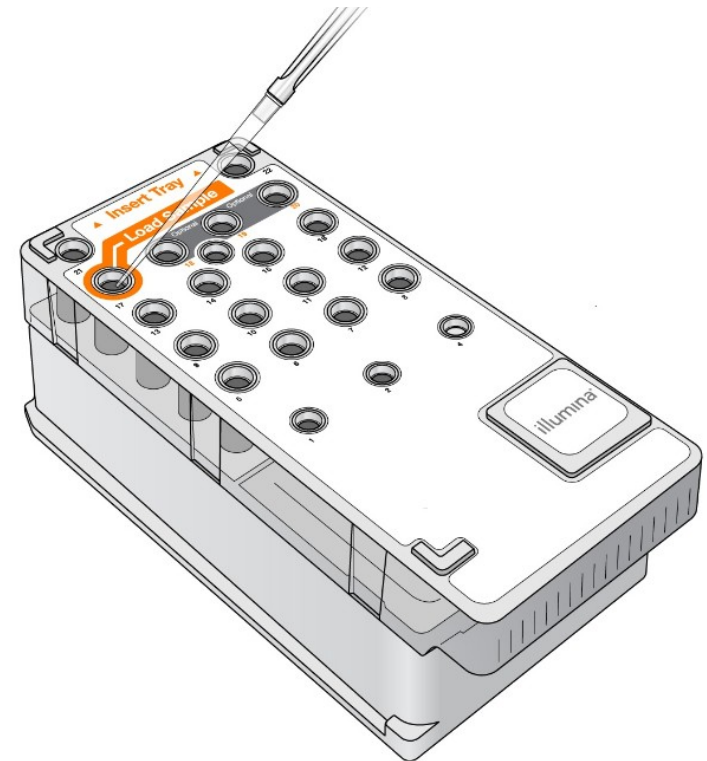
Up to 4 billion reads / run

13-15Gb 2.5 days



20Kb 1 day

Illumina MiSeq Instrument



MiSeq Cluster generation

