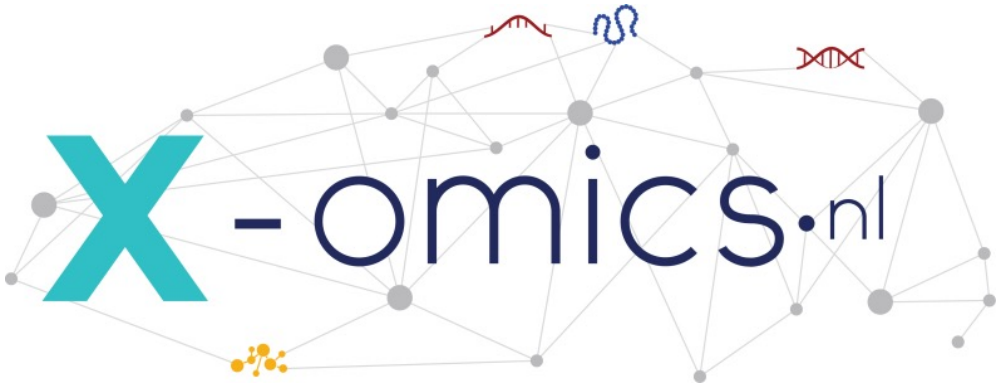
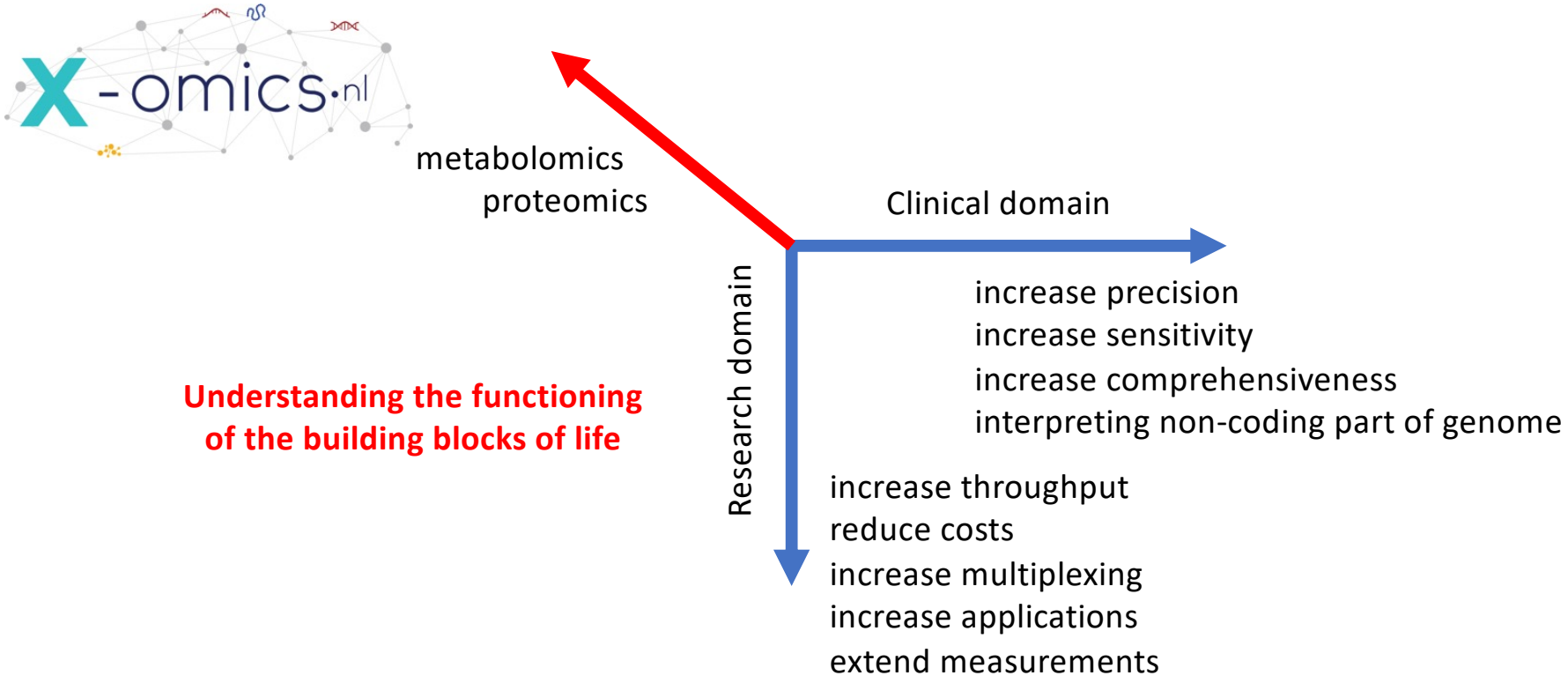
X-omics festival

Developments and trends in the genomics domain



Kick-off September 2018



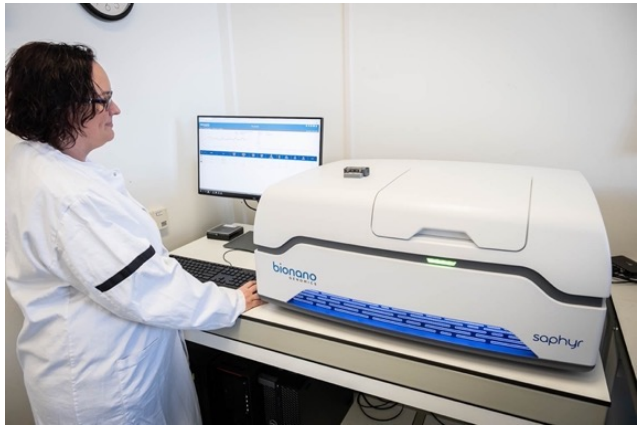
Understanding the functioning of the building blocks of life

Increased precision and comprehensiveness

- From short reads to long reads (next speaker Marcel Neelen)
- Available innovative platforms within X-omics

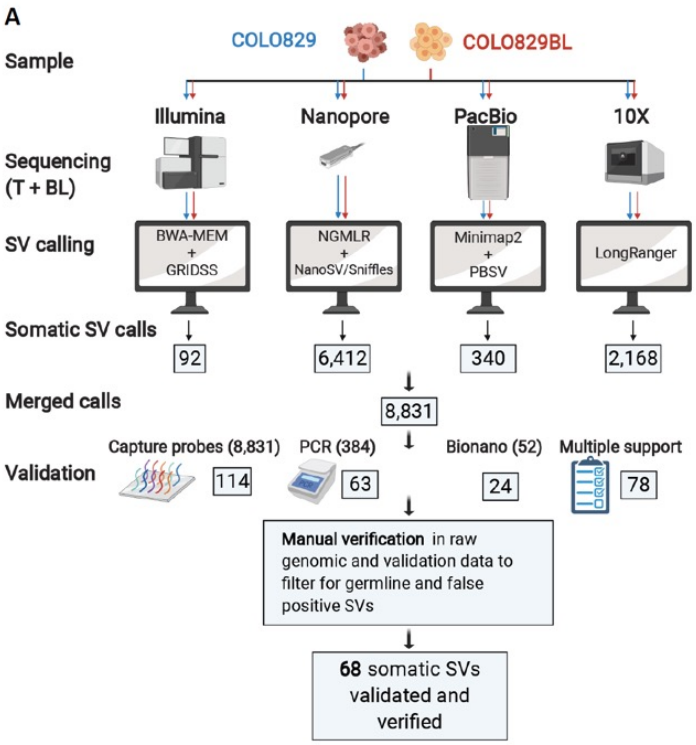
Oxford Nanopore Promethion

PacBio Sequel II

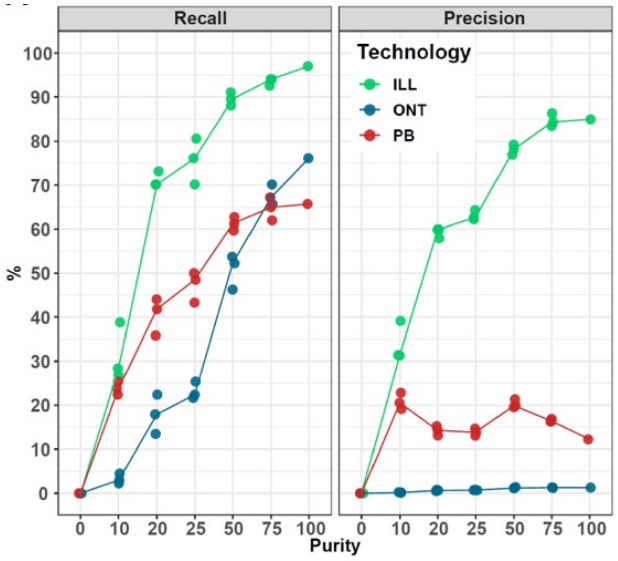


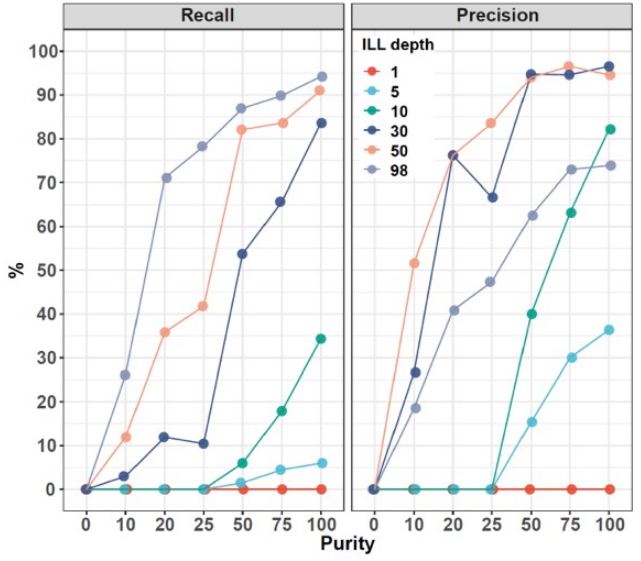
BioNano Saphyr

Multiplatform comparison for somatic SV detection



COLO829 tumor-normal pair (90x, 30x)
Generation truth set
Benchmark: technology, sequencing depth, tumor purity
Reference for platform and bioinformatic tool improvements



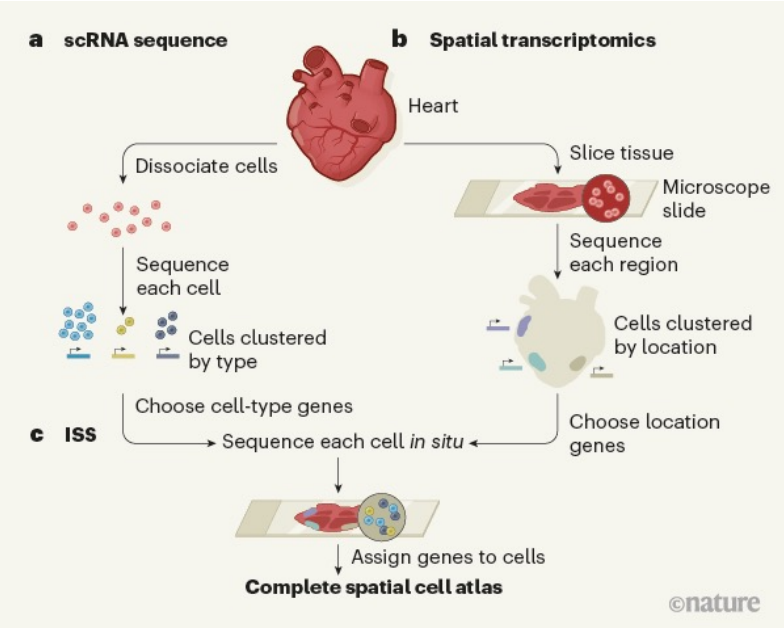


Espejo Valle-Inclan et al. A multi-platform reference for somatic structural variation detection. https://www.biorxiv.org/content/10.1101/2020.10.15.340497v1

Increase throughput and reduce costs

Needs driven by:

- single cell profiling: DNA (CNA), RNA, modifications, combinations
- spatial profiling



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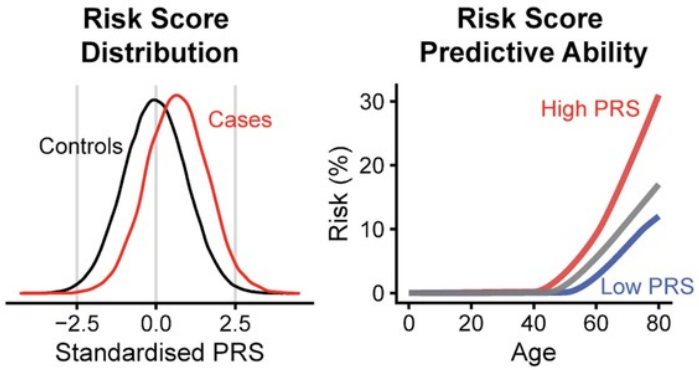

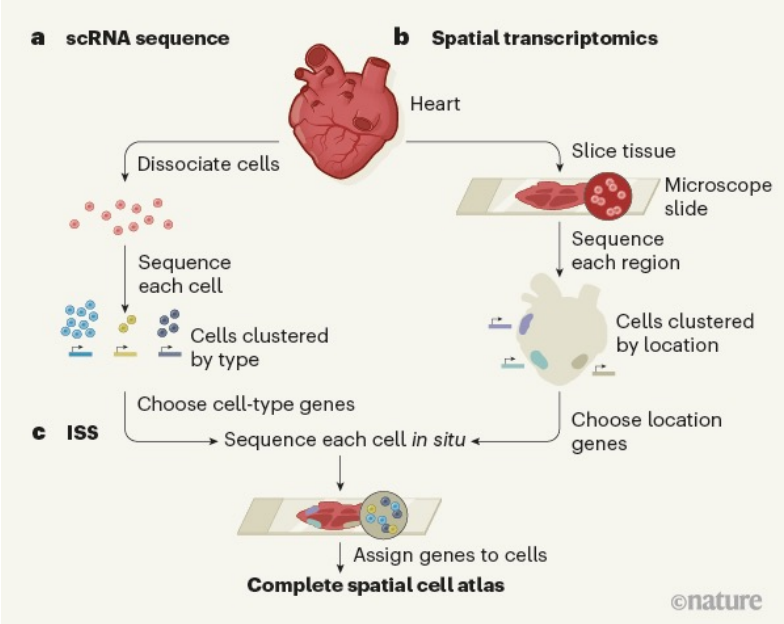

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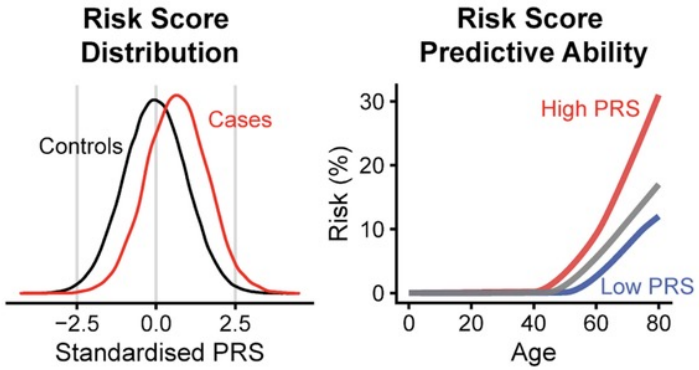
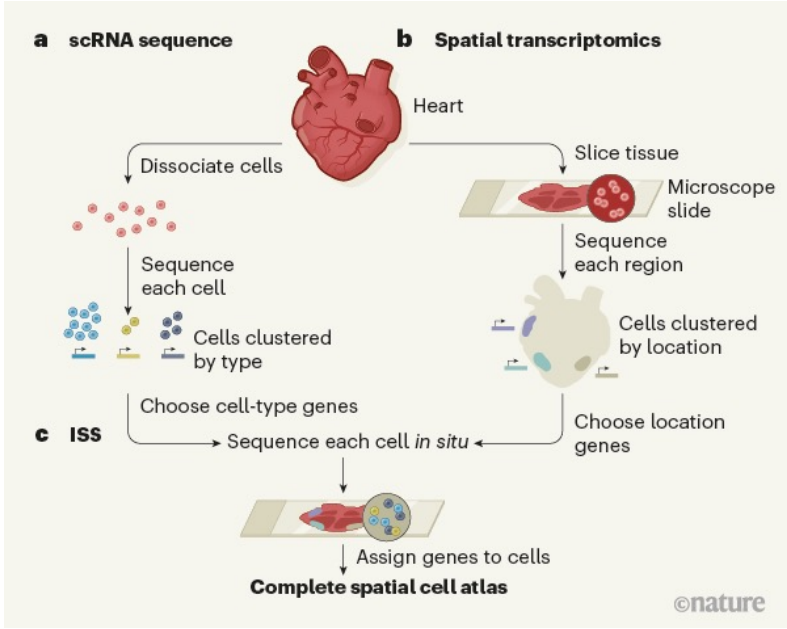
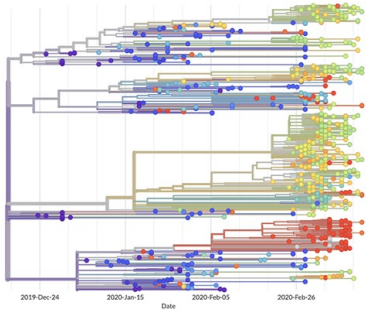
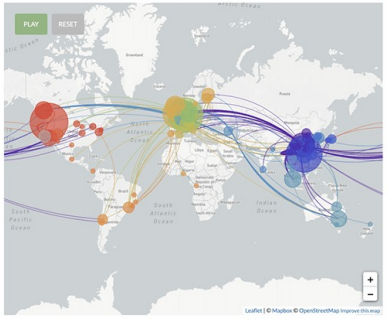




- COVID





Increase throughput and reduce costs

Developments to meet these demands:

- Dual index and Unique Molecular Identifiers allow unprecedented multiplexing (implemented)

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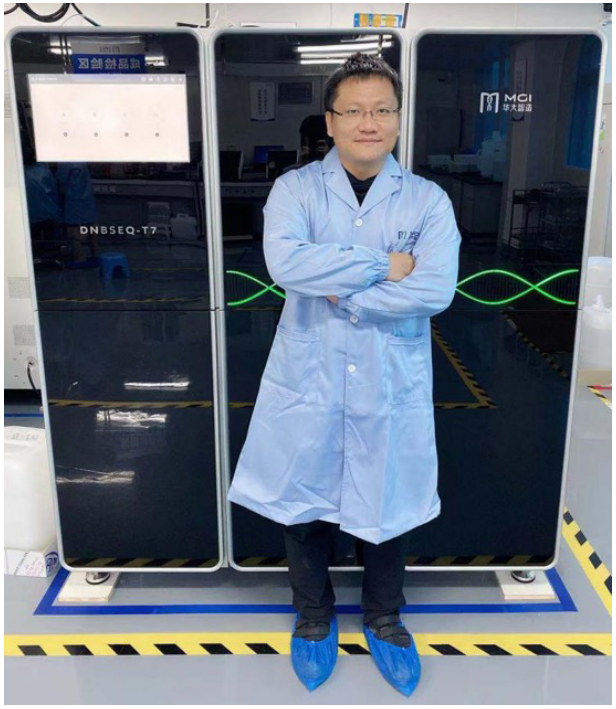
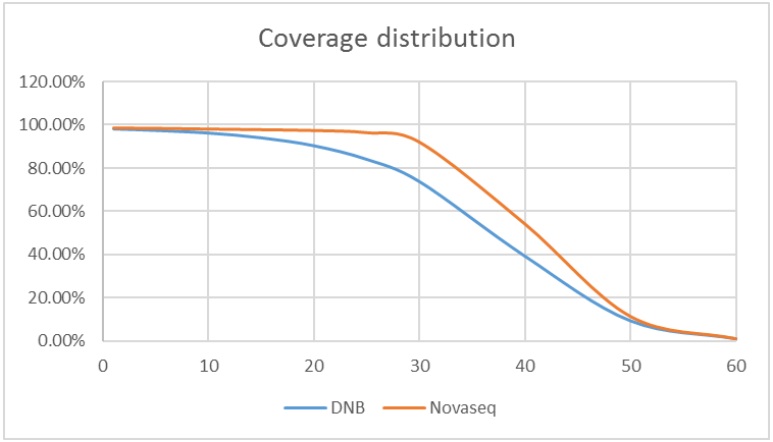
- Short-read platform innovations: Novaseq6000, NextSeq2000, MGI DNBseq (explored)

Short read competition is closing in (MGI DNBSEQ-T7)



	DNB1	Novaseq1	Novaseq2	Novaseq3	Novaseq4
True Pos SNVs	3053824	3068040	3068122	3068456	3067833
False Pos SNVs	5040	4284	4370	4105	4298
False Neg SNVs	100435	86219	86137	85803	86426
Precision SNVs	0.998	0.999	0.999	0.999	0.999
Sensitivity SNVs	0.968	0.973	0.973	0.973	0.973
F-score SNVs	0.9830	0.9855	0.9855	0.9856	0.9854

Sensitivity for INDEL in DNB data is slightly lower than SNV



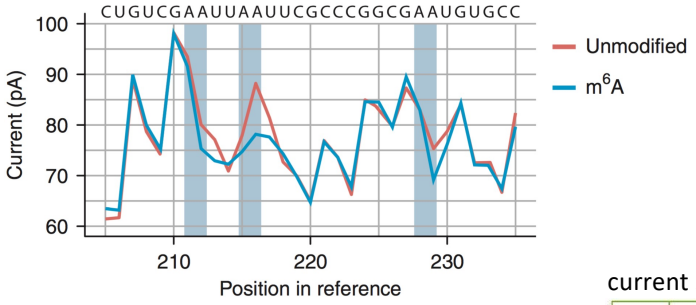
MGI versus Illumina:

- small variant detection on par
- higher percentage of reads passing QC (less duplicates)
- more variation in coverage depth
- (somatic) structural variant calling needs optimization
- costs per genome in same range

Increase applications and extend measurements

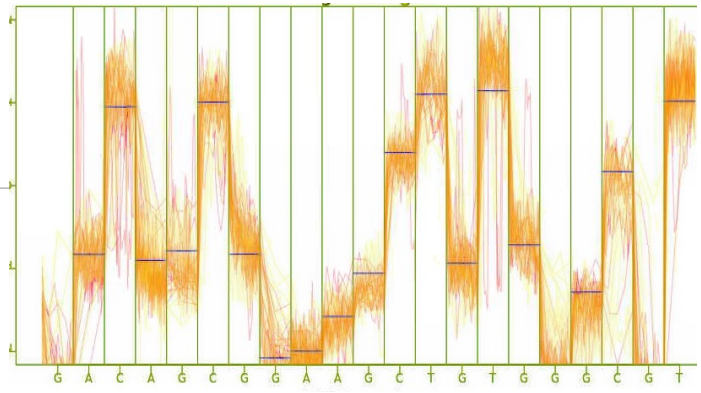
- reading base modifications from nanopore reads-

- Single, native DNA or RNA molecules sequenced up to tenths of kbs
- Base-modifications modelled from raw signal (algorithms need training on known data)
  - Signal differences small and fuzzy

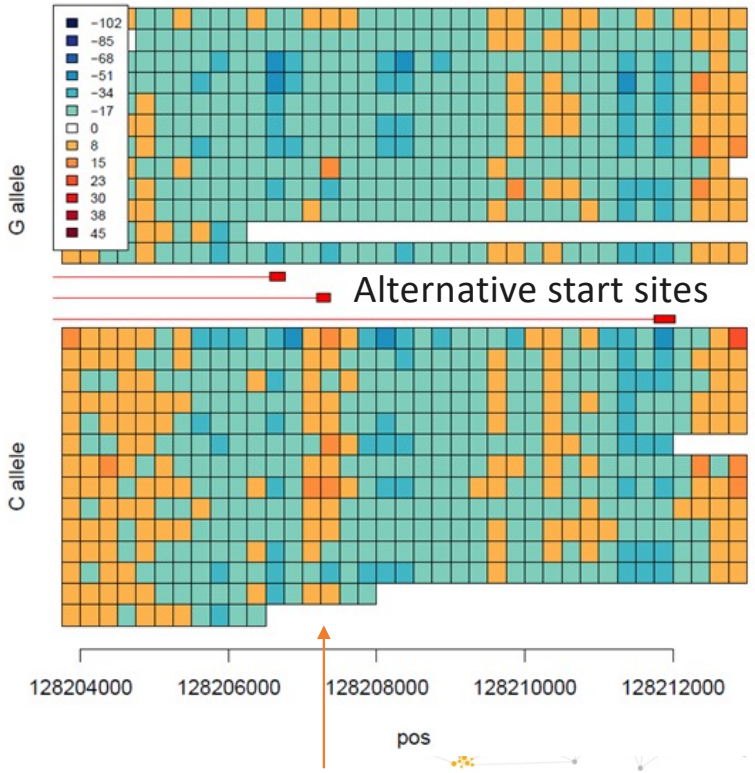


Garalde et al. nature methods 2018

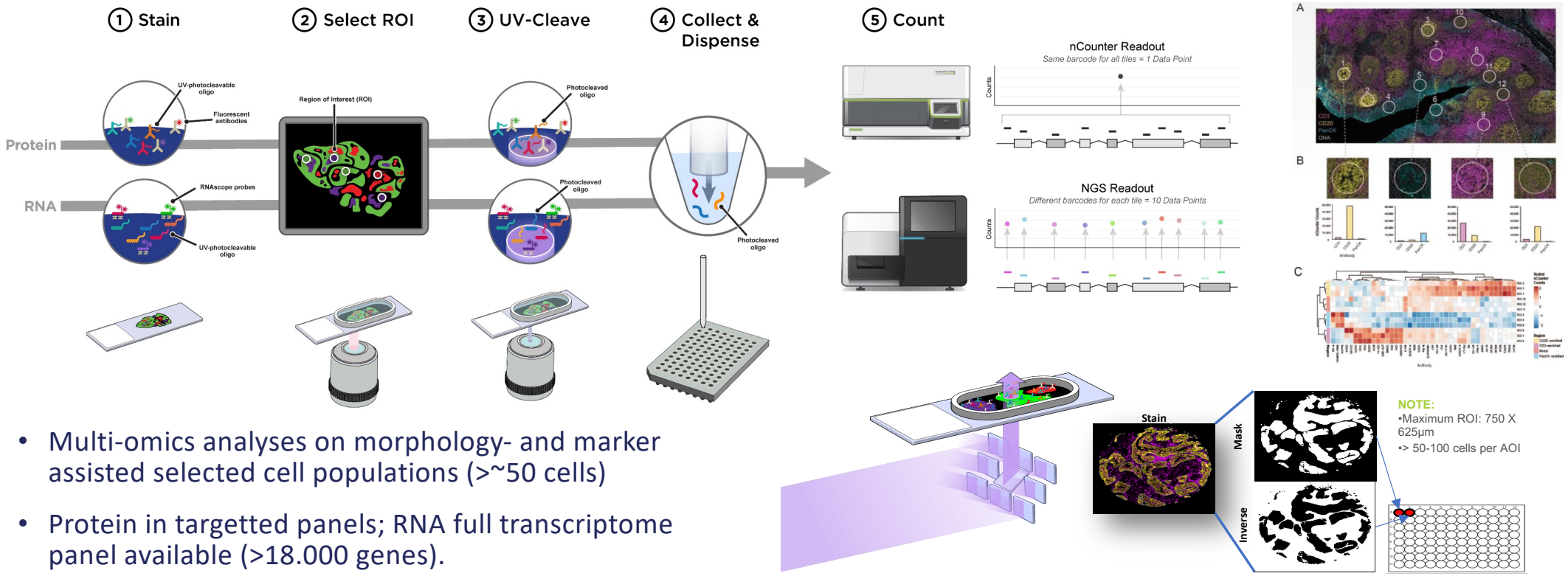
current signal: yellow methylated; red - unmeth



Carlo Vermeulen: DNA methylation



Spatial multi-omics

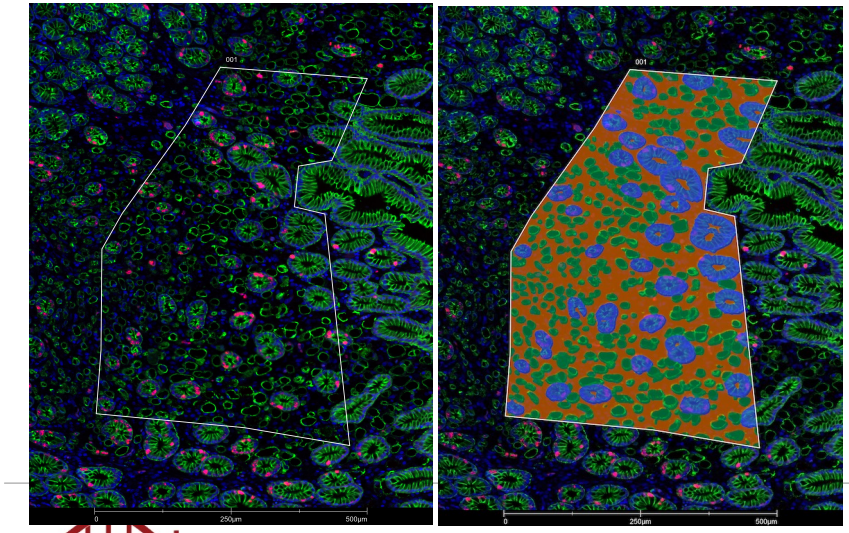


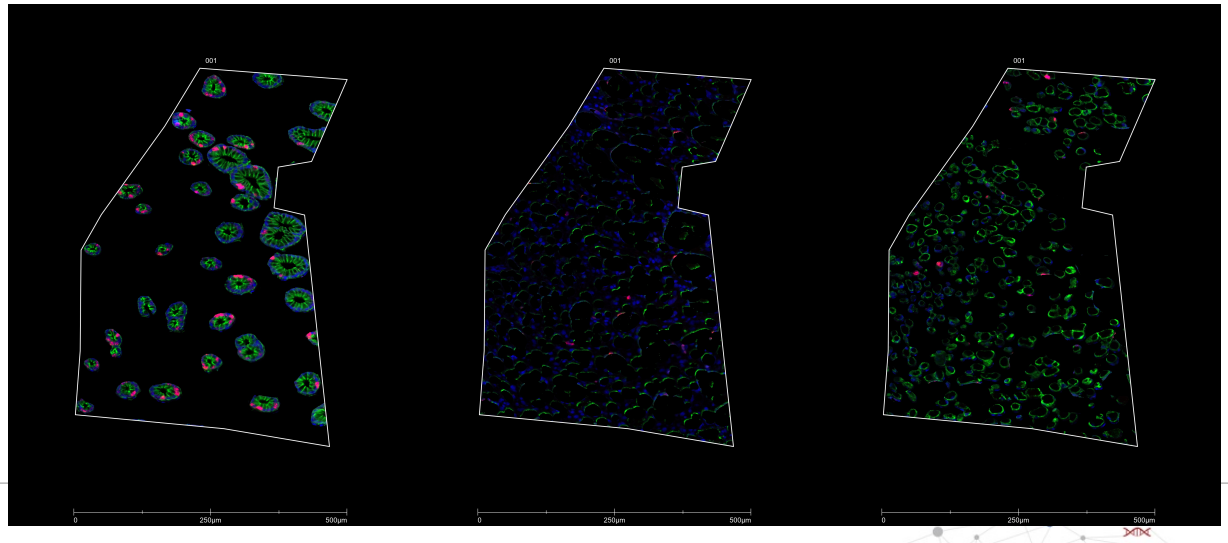
- Multi-omics analyses on morphology- and marker assisted selected cell populations (>~50 cells)
- Protein in targetted panels; RNA full transcriptome panel available (>18.000 genes).

gastric signet ring cell carcinoma: custom segmentation

- Fully customized, external deep learning based segmentation used to select cells
- Imported in GeoMX to harvest bound RNA probes and analyse RNA cancer panel profiles.

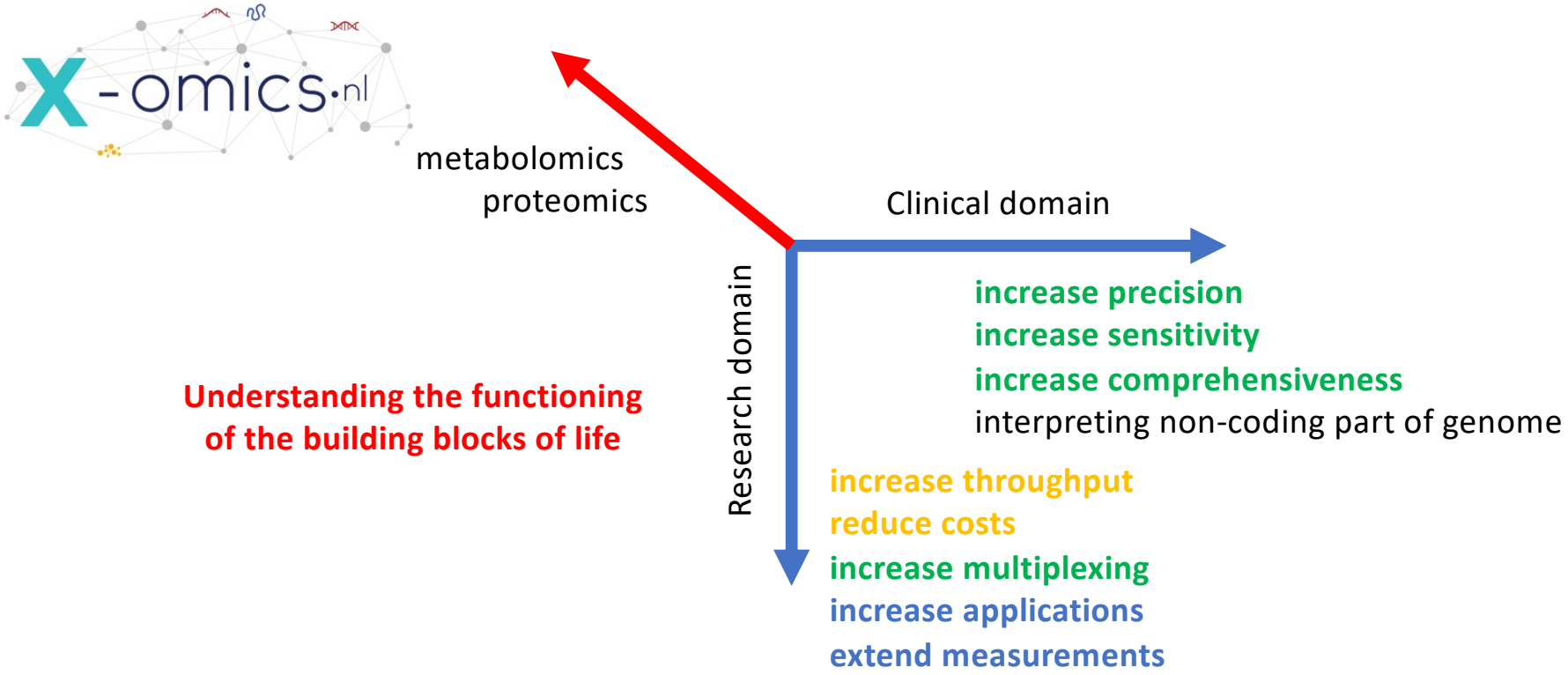
Staining:	Segmentation:
DNA	WT epith: DNA/PanCk
PanCk	Tumor: PanCk
KI67	Other: Microenv.





L. Kemp, M. Gloerich, Center for Molecular Medicine, UMC Utrecht

Progress


metabolomics
proteomics
Clinical domain
Research domain
increase precision
increase sensitivity
increase comprehensiveness
interpreting non-coding part of genome
Understanding the functioning
of the building blocks of life
increase throughput
reduce costs
increase multiplexing
increase applications
extend measurements