

# MOLECULAR PATHOLOGY STANDARDIZATION: TISSUE TREATMENT AND PRESERVATION

Olli Carpén

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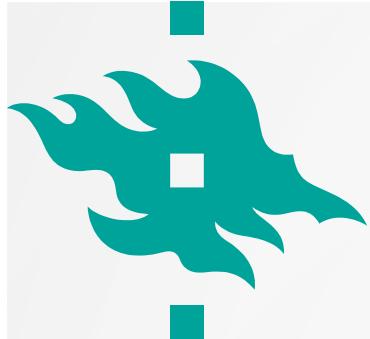
HELSINGIN BIOPANKKI  
HELSINGFORS BIOBANK  
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HUS & HELSINKIN YLIOPISTO YHTEISTYÖSSÄ  
HUS & HELSINGFORS UNIVERSITET I SAMARBETE  
A COLLABORATION BETWEEN HUS & UNIVERSITY OF HELSINKI



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@OlliCarpen



# A RENAISSANCE FOR FFPE TISSUE SPECIMENS

- Novel technologies expand the use of pathology FFPE specimens
- *Next generation digital pathology*
- *Spatial RNA transcript analysis (combined with image analysis)*
- *DNA analysis (e.g. genotyping)*
- All these technologies require that tissue specimens are collected with high standards – however, they do not need practices beyond routine diagnostic pathology



# H&E-IMAGES CONTAIN IMPORTANT INFORMATION NOT CAUGHT BY HUMAN EYE – AI CAN HELP TO CAPTURE SUCH INFORMATION



## Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning

Nicolas Coudray<sup>1,2,9</sup>, Paolo Santiago Ocampo<sup>3,9</sup>, Theodore Sakellaropoulos<sup>4</sup>, Navneet Narula<sup>3</sup>, Matija Snuderl<sup>3</sup>, David Fenyö<sup>5,6</sup>, Andre L. Moreira<sup>3,7</sup>, Narges Razavian<sup>8\*</sup> and Aristotelis Tsirigos<sup>1,3\*</sup>

tissues, formalin-fixed paraffin-embedded tissues and biopsies. Furthermore, we trained the network to predict the ten most commonly mutated genes in LUAD. We found that six of them—STK11, EGFR, FAT1, SETBP1, KRAS and TP53—can be predicted from pathology images, with AUCs from 0.733 to 0.856 as measured on a held-out population. These findings suggest that deep-learning models can assist pathologists in the detection of cancer subtype or gene mutations. Our approach can be applied to any cancer type, and the code is available at <https://github.com/ncoudray/DeepPATH>.

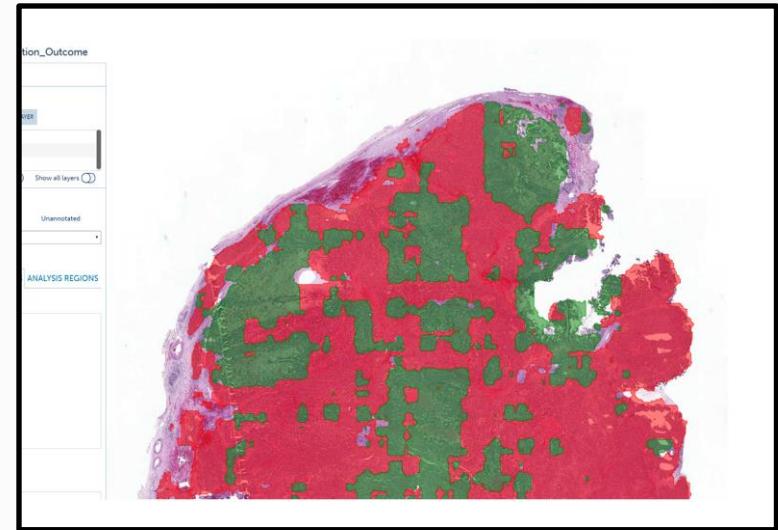
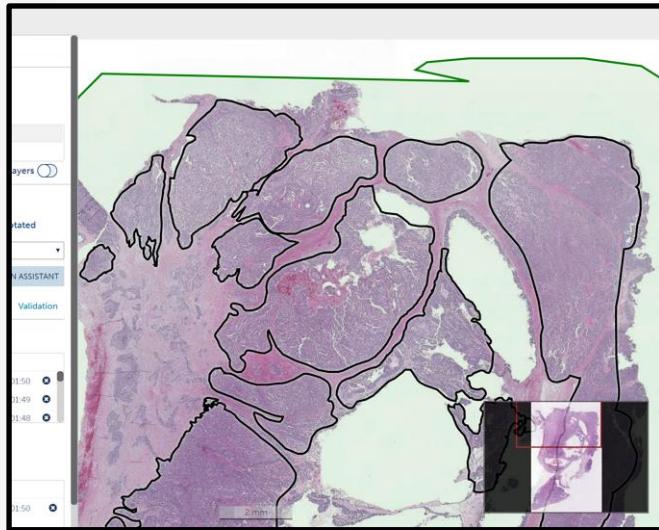
**“** A computer can learn patterns in images so that it can make predictions based on those patterns – this is the essence of deep learning.

**”**

**“** A deep learning network can learn highly complex visual features from image data, achieving performance that may even equal that of a human expert.

**”**

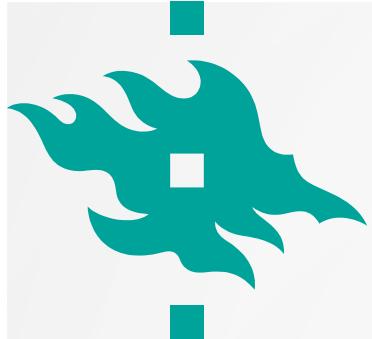
# IMAGE ANALYSIS CAN IDENTIFY SPECIFIC AREAS WITHIN CANCERS THAT DEFINE THE OUTCOME



- Correlation with tumor heterogeneity?

Artificial intelligence-based image analysis can predict outcome in high-grade serous carcinoma via histology alone

**scientific reports**



# QUALITY ASPECTS FOR AI-GUIDED DIGITAL PATHOLOGY

- Slide preparation parameters: e.g. *embedding, cutting, staining*
- Scanning parameters: *focus, color spectrum, completeness of scan, resolution*
- *Annotation, metadata, ontology*
- A standard *data format and normalization method* of data sets from different sources (e.g. **DICOM**)
- **Protocols and systemic quality control should be standardized to reduce the system errors and random errors**



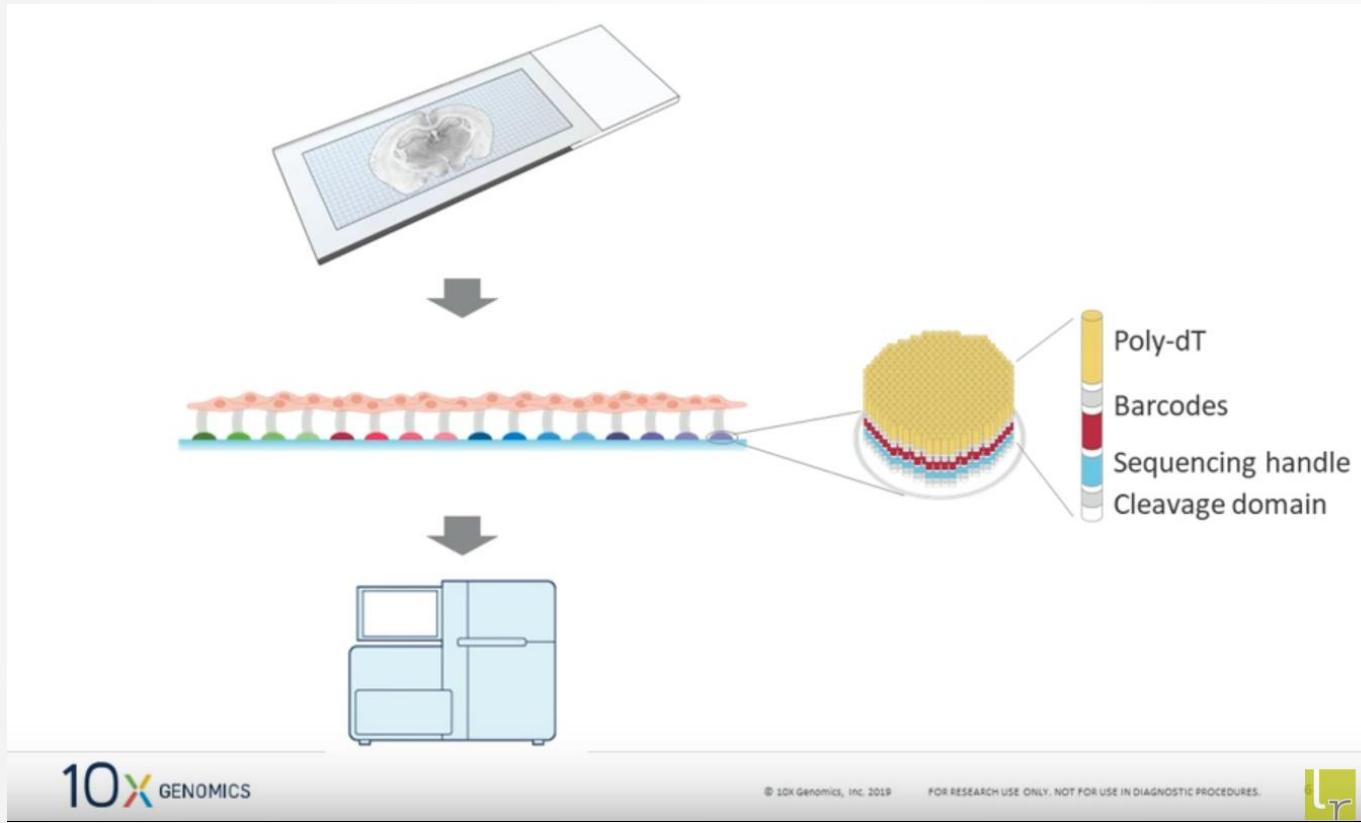
# SPATIAL TRANSCRIPTOMICS – METHOD OF THE YEAR – IS NOW AVAILABLE FOR FFPE SPECIMENS

A groundbreaking molecular profiling method → allows measurement of gene activity in a tissue sample → maps where the activity occurs

The screenshot shows the nanoString website. At the top, there's a navigation bar with links for PRODUCTS, RESEARCH FOCUS, RESOURCES, SUPPORT, and COMPANY. Below the navigation is a large image of a tissue section with green and purple staining patterns. Overlaid on this image is a green location pin icon with a small circular inset showing a map. In the bottom left corner of the image area, the text "CONTACT US" is visible. On the far left, the nanoString logo is displayed. In the center-left, the text "GeoMx® Digital Spatial Profiler" is prominently featured. Below it, a smaller line of text reads "Discover Where Biology Happens". At the very bottom of the screenshot, there are three small links: "Products", "GeoMx Digital Spatial Profiler", and "GeoMx® DSP Overview".

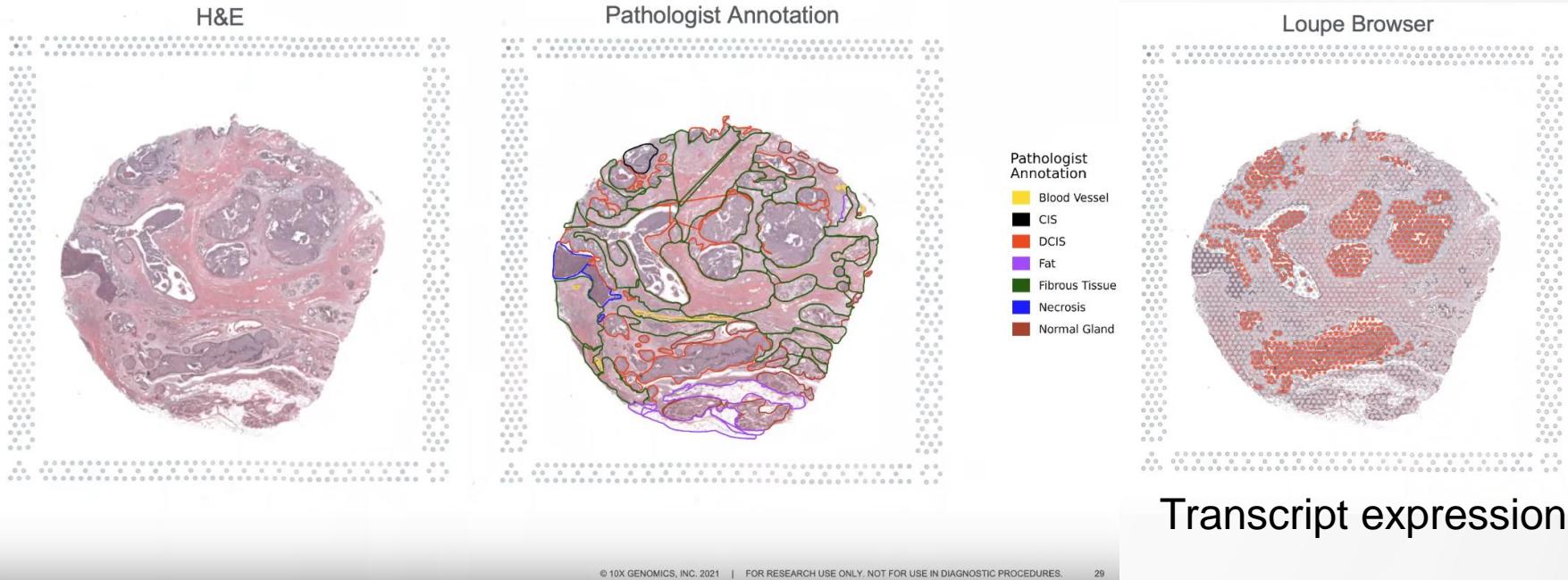
The screenshot shows the 10X Genomics website for the Visium Platform. The top right corner features the text "Visium Platform". The main title "10X GENOMICS" is centered at the top. Below the title, the text "Inside Visium spatial capture technology" is displayed in large white letters. In the bottom right corner, there is a 3D perspective view of a tissue sample, showing a grid-like pattern of colored dots (blue, yellow, red) representing spatially resolved data points.

# SPATIAL TRANSCRIPTOMICS – THE BASICS



Up to 20,000 transcripts can be located at nearly single cell level

# FFPE DATA OVERLAY VISUALIZATION – COMBINING HISTOLOGY AND TRANSCRIPT EXPRESSION



## Benefits:

- Unbiased identification of candidate biomarkers/biomarker clusters
- Understanding on the role of cellular interplay in cancer
- Explainable AI – reveals the biology of underlying features identified by AI

# RNA QUALITY CONTROL – AN IMPORTANT STEP IN SPATIAL TRANSCRIPTOMICS

2x 10 $\mu$ m sections



RNA DV200

Automated RNA  
extraction



VISIUM 10x recommends DV200 >50 % (**RNA quality**)

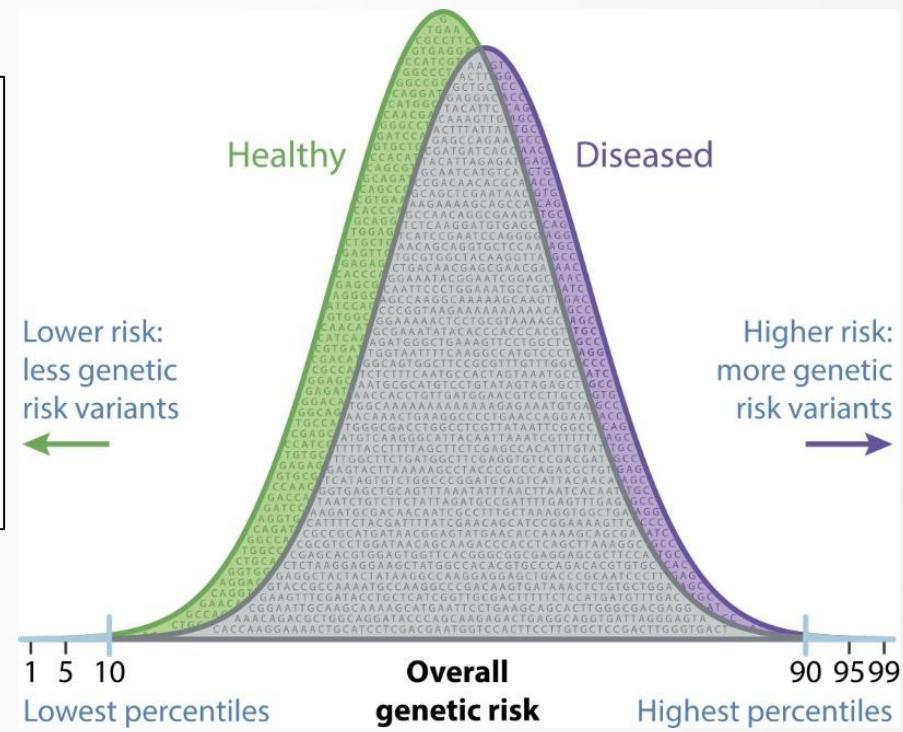
Own experience shows that data quality is reasonable, if DV200 >30 %

Role of sample age (> 5 y) and storage conditions (e.g. temperature)

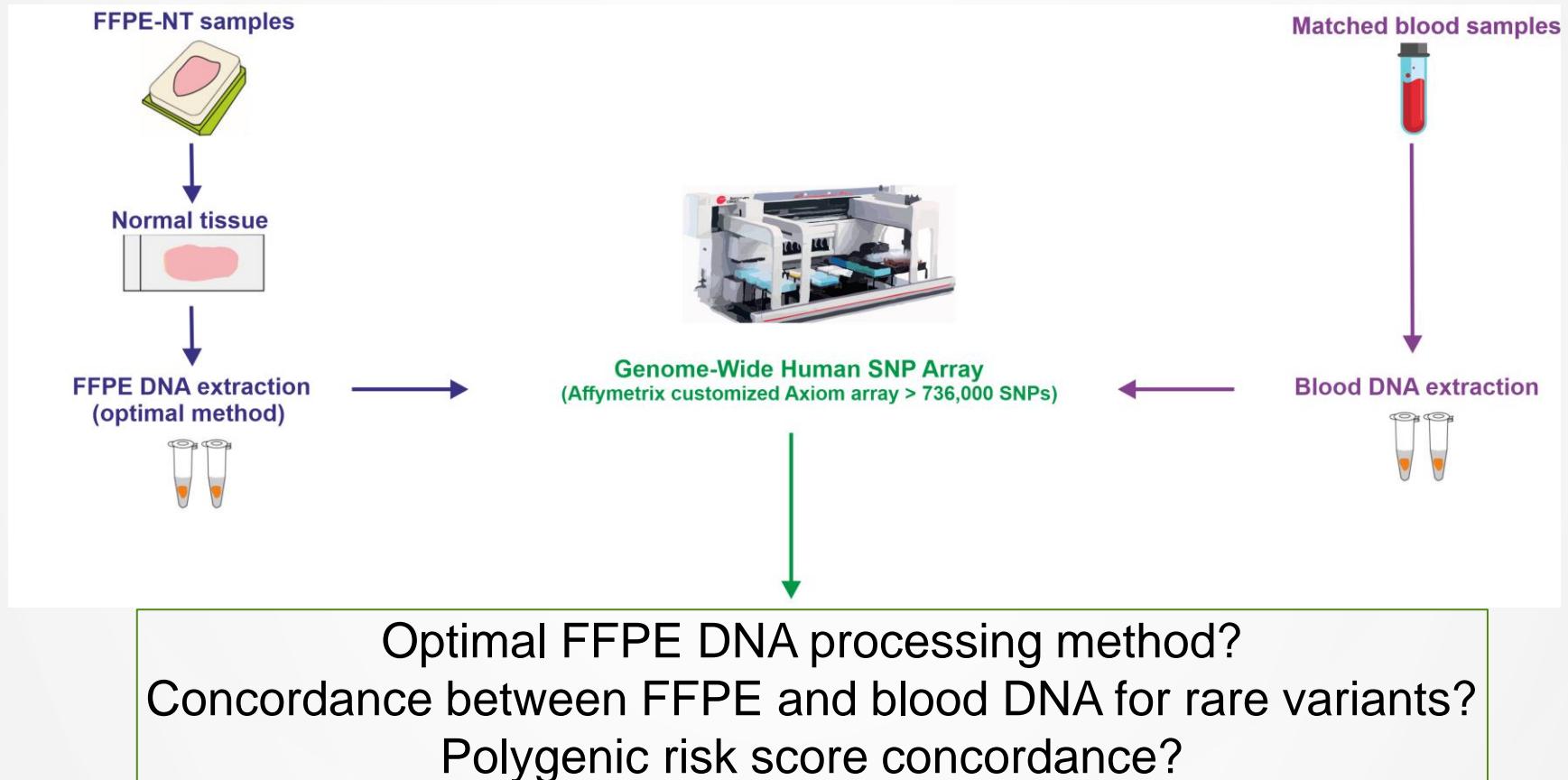
# GENOTYPING AND POLYGENIC RISK SCORE – COHORT EXPANSION WITH FFPE BIOBANK SAMPLES

## Why:

- Rare disease cohorts hard to collect
- PRS analyses require large cohorts
- Legacy FFPE samples can help in cohort expansion
- Are often associated with useful phenotypic follow-up information

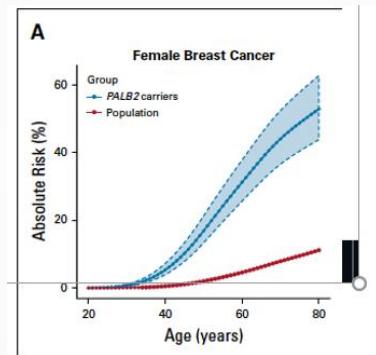
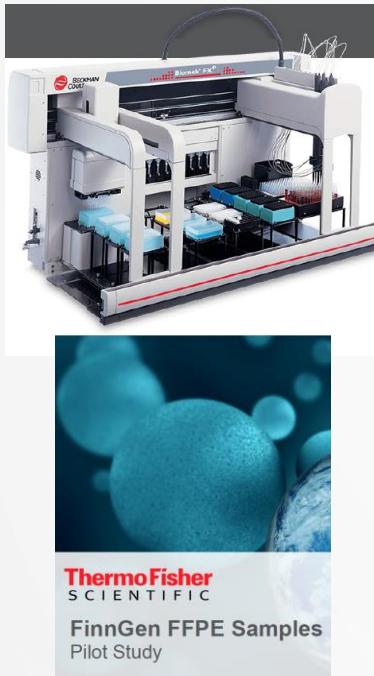


# CAN FFPE-DERIVED DNA BE USED FOR LARGE SCALE GENOTYPING?

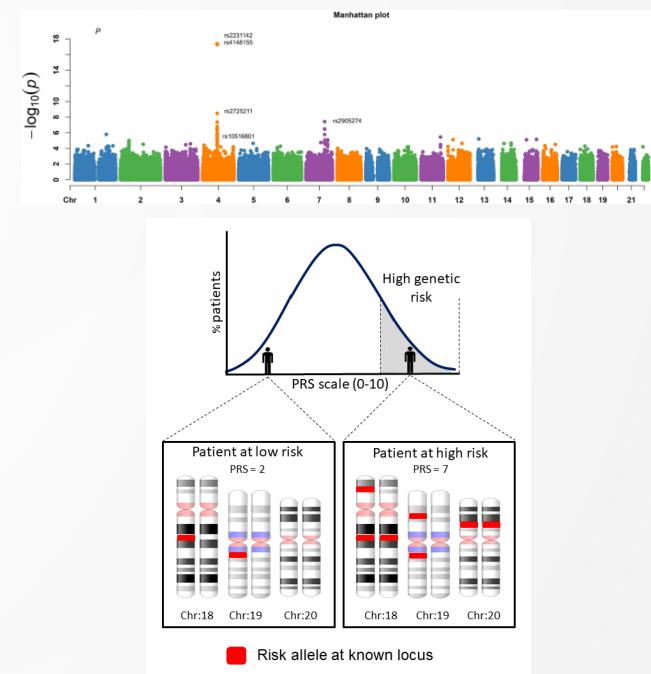


# Project main phases

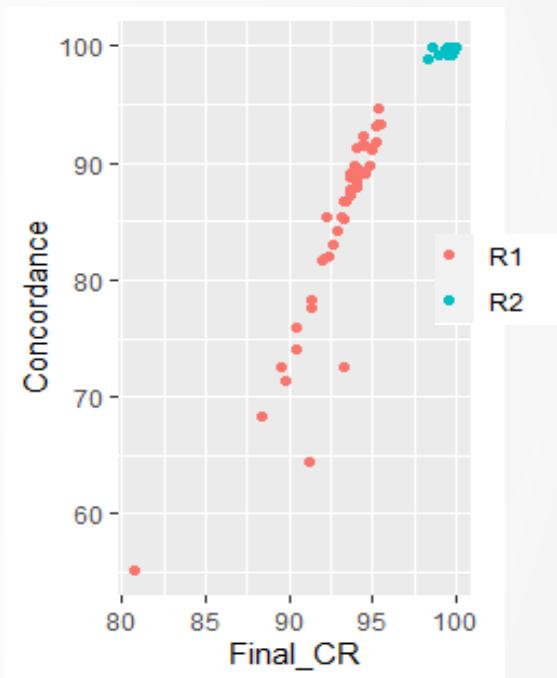
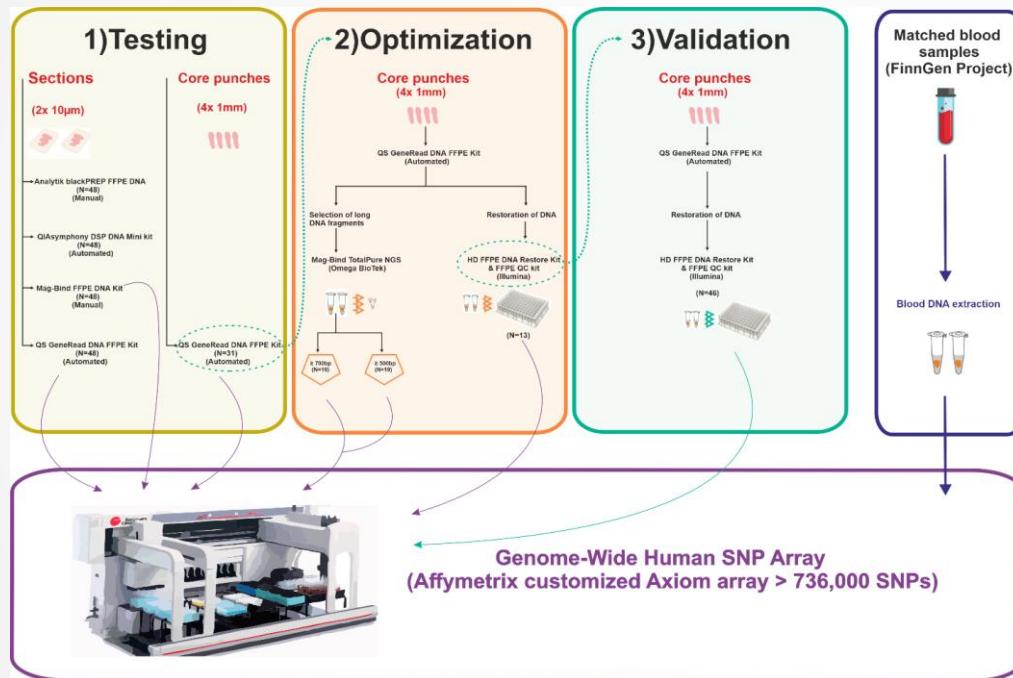
1. Protocol establishment
2. *PALB2* variant detection
3. Polygenic risk score



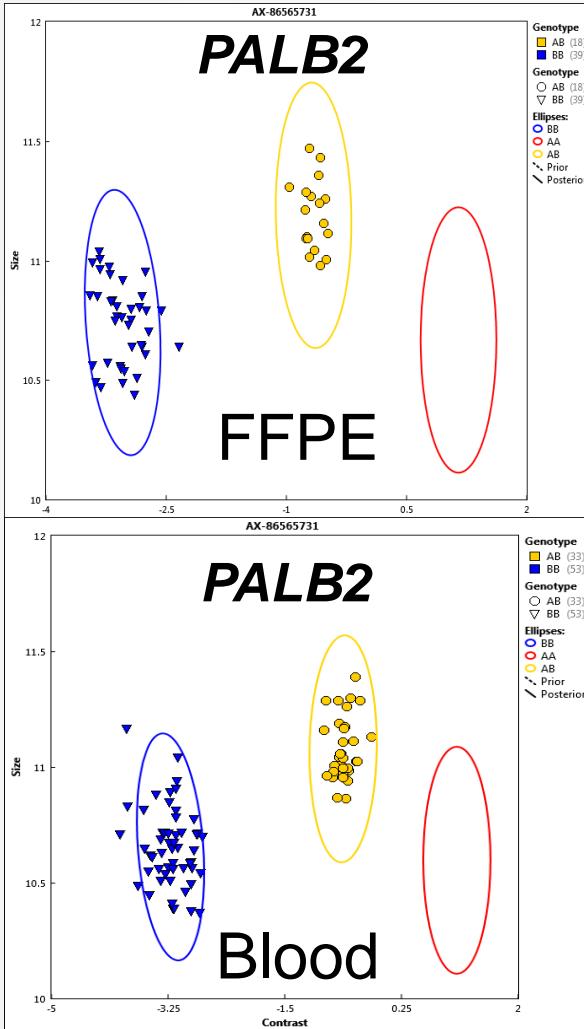
Mars et al. *Nat. Comm.* 2020



# Protocol development & establishment



Core punch -> QS GeneRead DNA FFPE kit -> HD FFPE DNA restore kit



### Phenotype

FFPE-PRS  
concordance  
with blood-PRS  
( $r$  pearson  
correlation)

FFPE-PRS  
concordance with  
blood-PRS  
( $p$  value)

Breast cancer

0.99

$p < 2.2e-16$

Prostate  
cancer

0.98

$p < 2.2e-16$

Colorectal  
cancer

0.98

$p < 2.2e-16$

BMI

0.99

$p < 2.2e-16$

Smoking/day

0.99

$p < 2.2e-16$

Drinks/week

0.99

$p < 2.2e-16$

Perfect match in rare variant analysis (left) and very high PRS concordance between FFPE and blood DNA (right)

# SUMMARY:

Novel technologies have markedly increased the value of pathology FFPE specimens

Tissue specimens collected and processed in routine care can be utilised for multiple R&D applications to improve cancer diagnostics and care

Quality standards and careful documentation are crucial and should be implemented in every pathology laboratory

Multiple national and international quality control proposals are being developed for digital pathology and sample-related activities



*Thank you!*