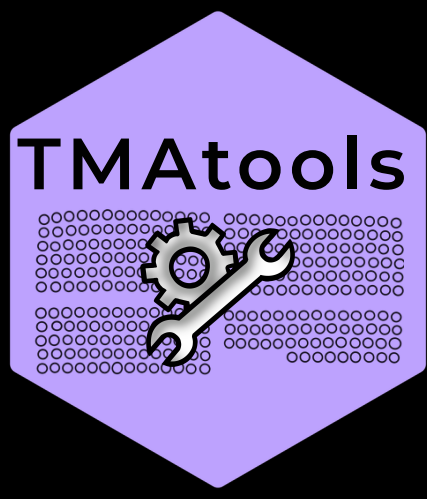


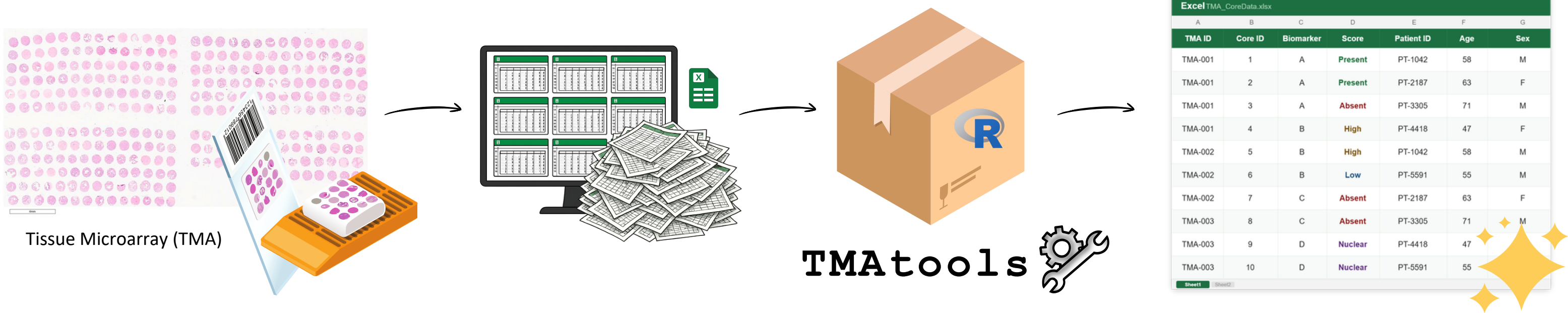


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BACKGROUND

Tissue Microarrays (TMAs) enable high-throughput analysis of hundreds of patient samples simultaneously. Yet, data processing remains hindered by **lack of standardization**, laborious **manual steps**, and tools that fail to provide end-to-end processing or comply with FAIR principles.



INPUTS EXCEL FILES FAMILIAR TO PATHOLOGY WORKFLOWS

TMA Map

Score sheets

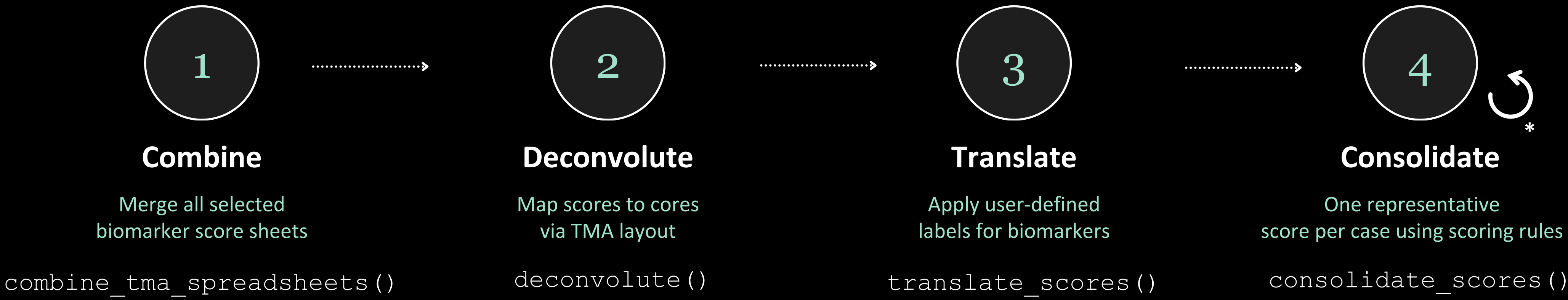
Score system

Metadata

| biomarker | original_score | translated_score |
|-----------|----------------|------------------|
| ER        | 0              | negative         |
| ER        | 1              | focal (1-50%)    |
| ER        | 2              | diffuse (>50%)   |
| ER        | 9              | Unk              |
| ER        | x              | Unk              |
| ER        | Unk            | Unk              |
| PD-L1     | x              | Unk              |
| PD-L1     | quantitative   |                  |

To address this gap, we aimed to develop TMAtools: a FAIR software package designed to integrate, deconvolute, translate, consolidate, and quality-control large-scale TMA datasets with multiple biomarkers and heterogeneous templates.

TMATOOLS PIPELINE – STEP BY STEP

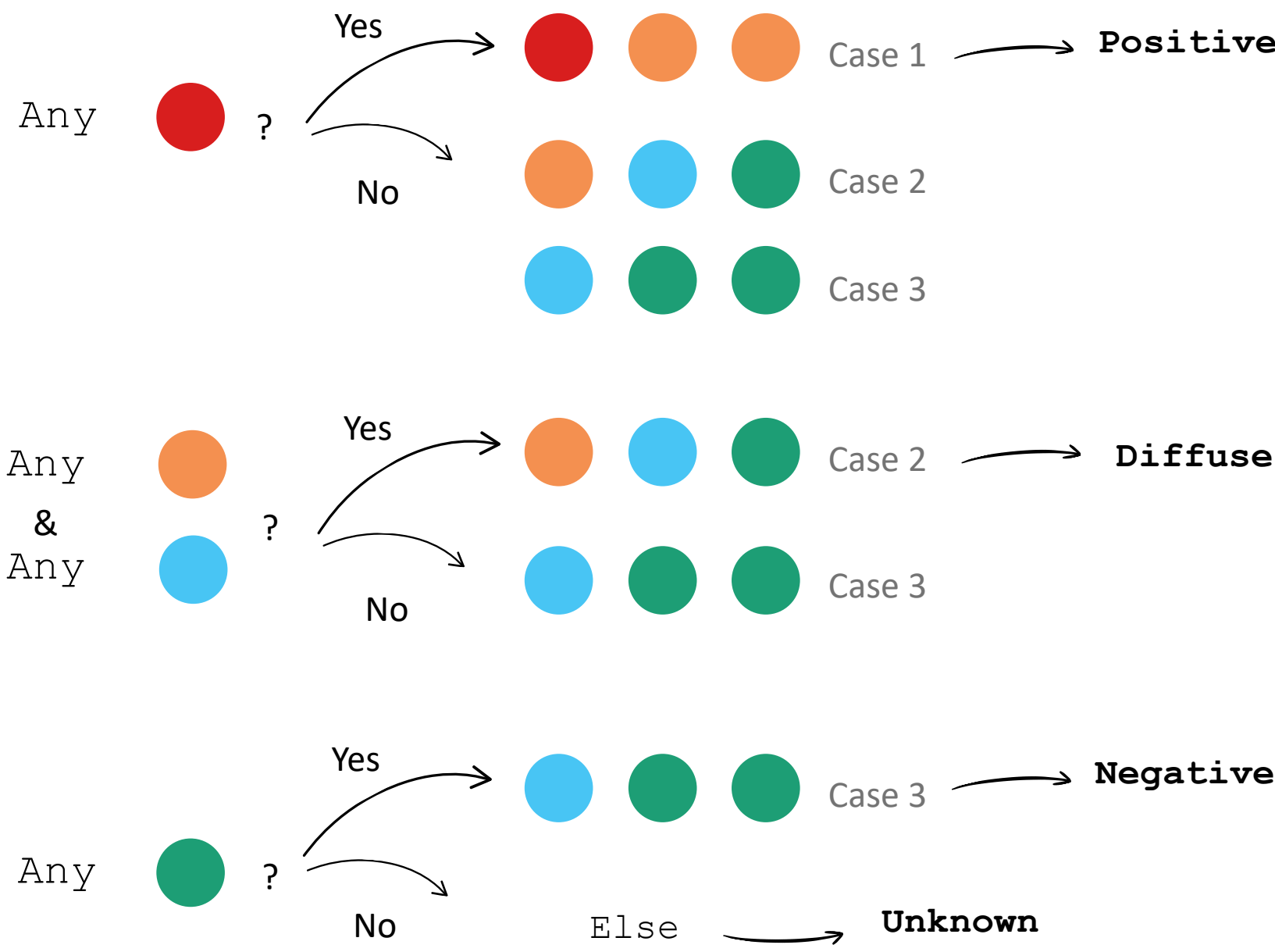


SINGLE COMMAND EXECUTION

```
tmtools(  
  # path to folder containing TMA scores  
  tma_dirs = "C:/Users/JaneDoe/Documents/TMA_data",  
  # customizable template  
  biomarker_rules_file = "C:/Users/JaneDoe/Documents/Biomarker_Rules.xlsx",  
  # output folder for results  
  output_dir = "C:/Users/JaneDoe/Documents/TMAtools_output"  
)
```

**\* Re-consolidation**  
Datasets with scores replicated cases across TMAs are automatically reconsolidated, preventing duplication.

CUSTOMIZABLE SCORING SYSTEM



| biomarker | rule_type | rule_value | consolidated_value |
|-----------|-----------|------------|--------------------|
| A         | any       |            | Positive           |
| A         | any; any  |            | Diffuse            |
| A         | any       |            | Negative           |
| A         | else      |            | Unknown            |
| B         | mean      |            |                    |

Scoring systems support **qualitative** and **quantitative** score systems

SCORING SYSTEM AVAILABLE · BIOMARKER PANEL · 22 TARGETS

MISMATCH REPAIR (MMR)

MLH1, MSH2, MSH6, PMS2

TUMOR SUPPRESSORS

PTEN, p53, RB1, ARID1A, p16

HORMONE RECEPTORS

ER, PR

DIFFERENTIAL DIAGNOSIS

WT1, PAX2, GATA3, CDX2, CTNNB1, Napsin A, TTF1

IMMUNE

CD8, PD-L1

STRESS AND PROGRESSION

ATF4, p-S6RP

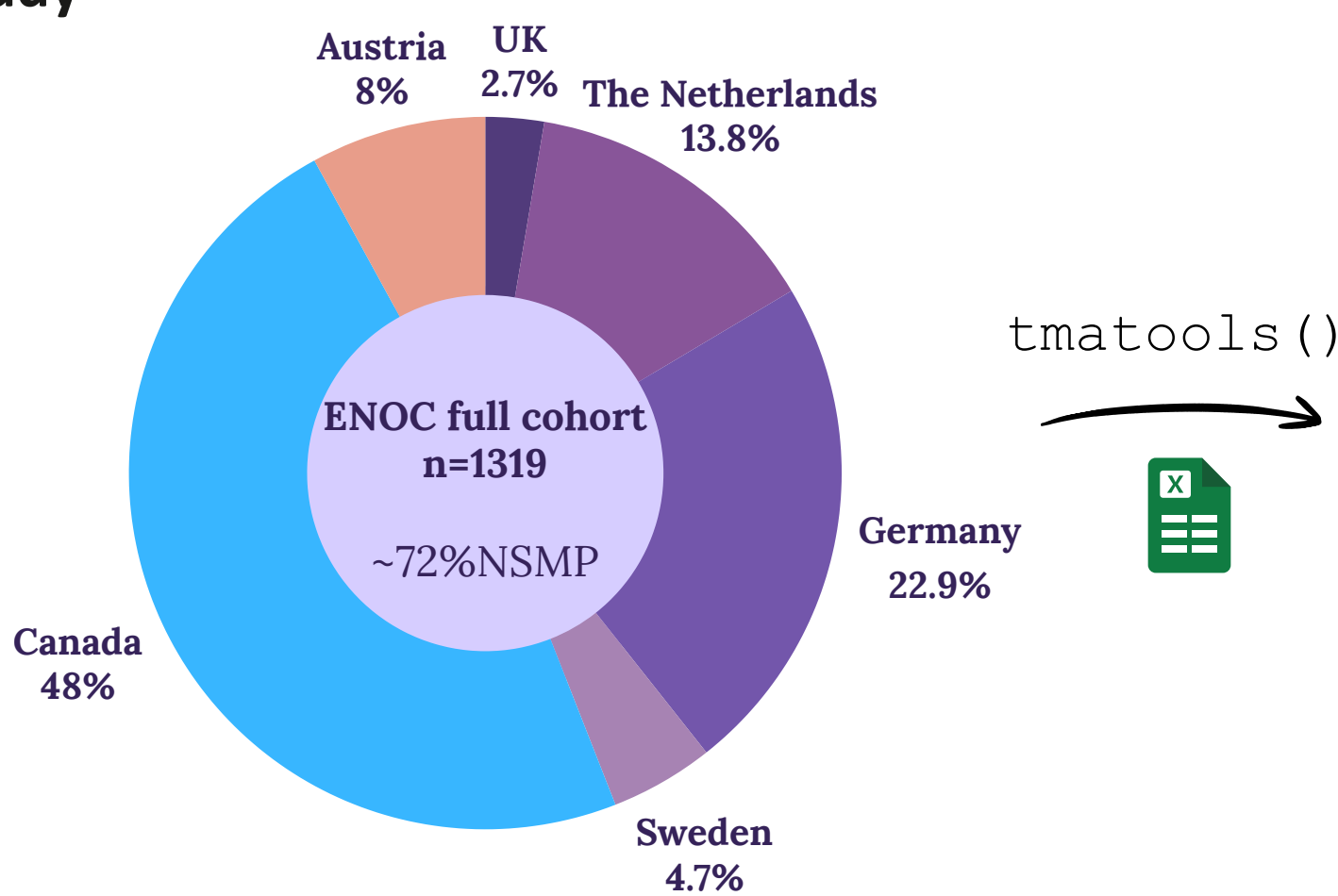
VALIDATION & APPLICATIONS

Multinational Endometrioid Ovarian Carcinoma (ENOC) cohort study

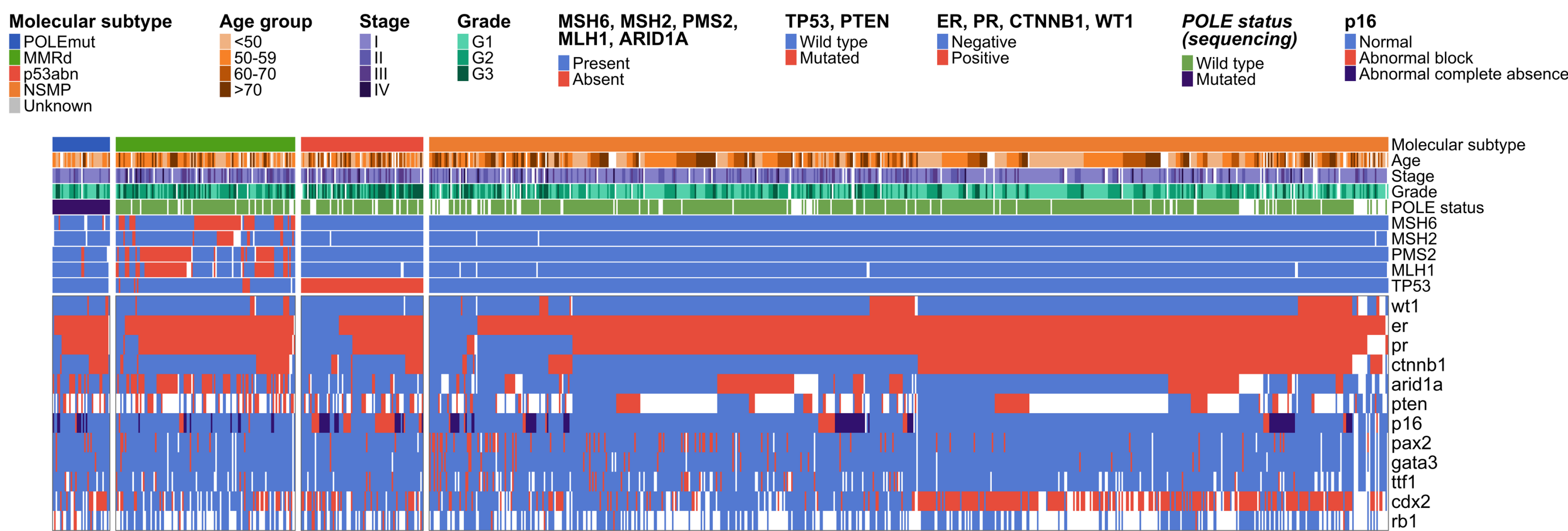
1,319  
patients across 32 centres, 6 countries

19×17  
TMAs × Biomarkers in panel

70k+  
individual cores processed

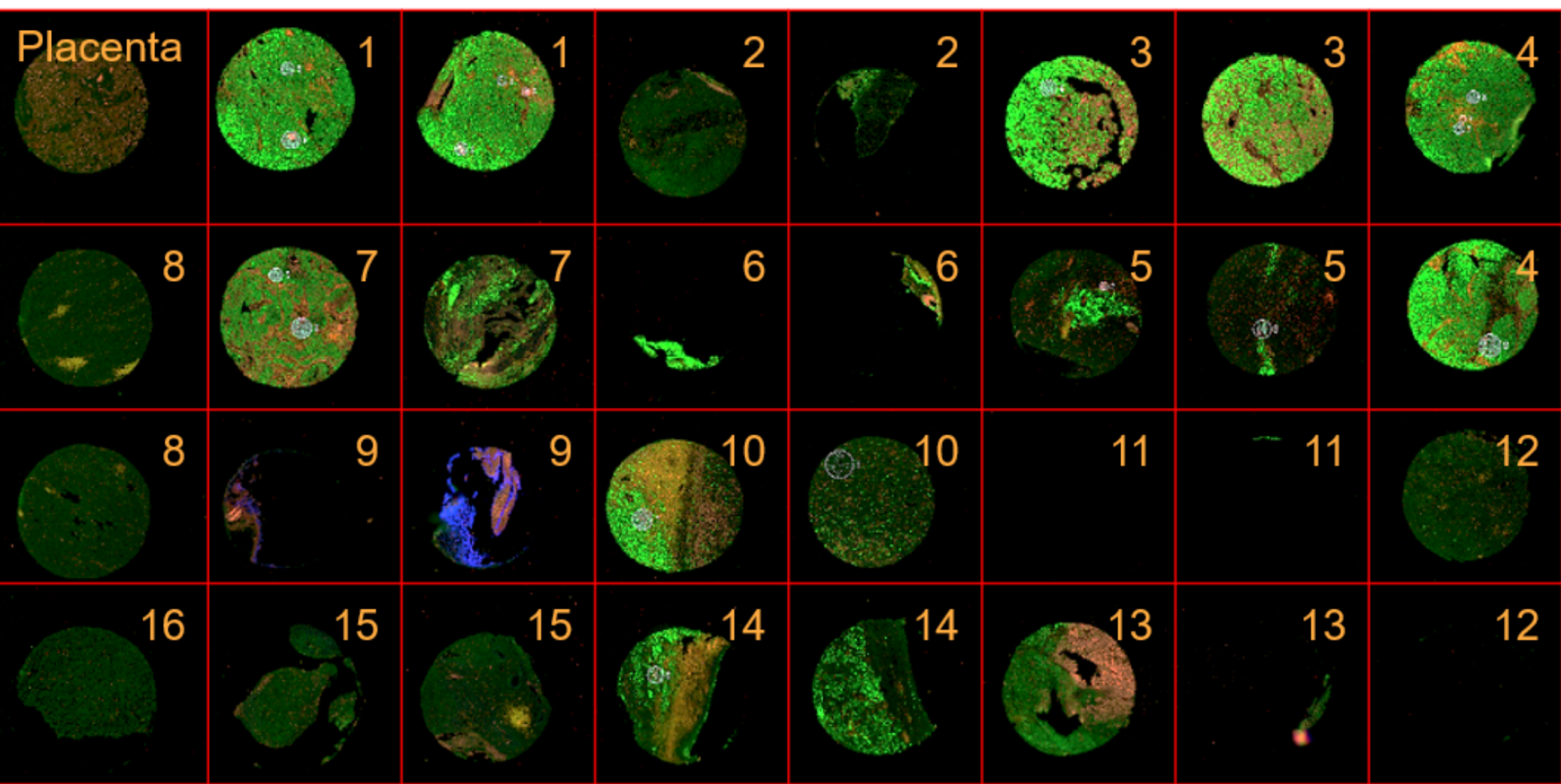


tmtools()

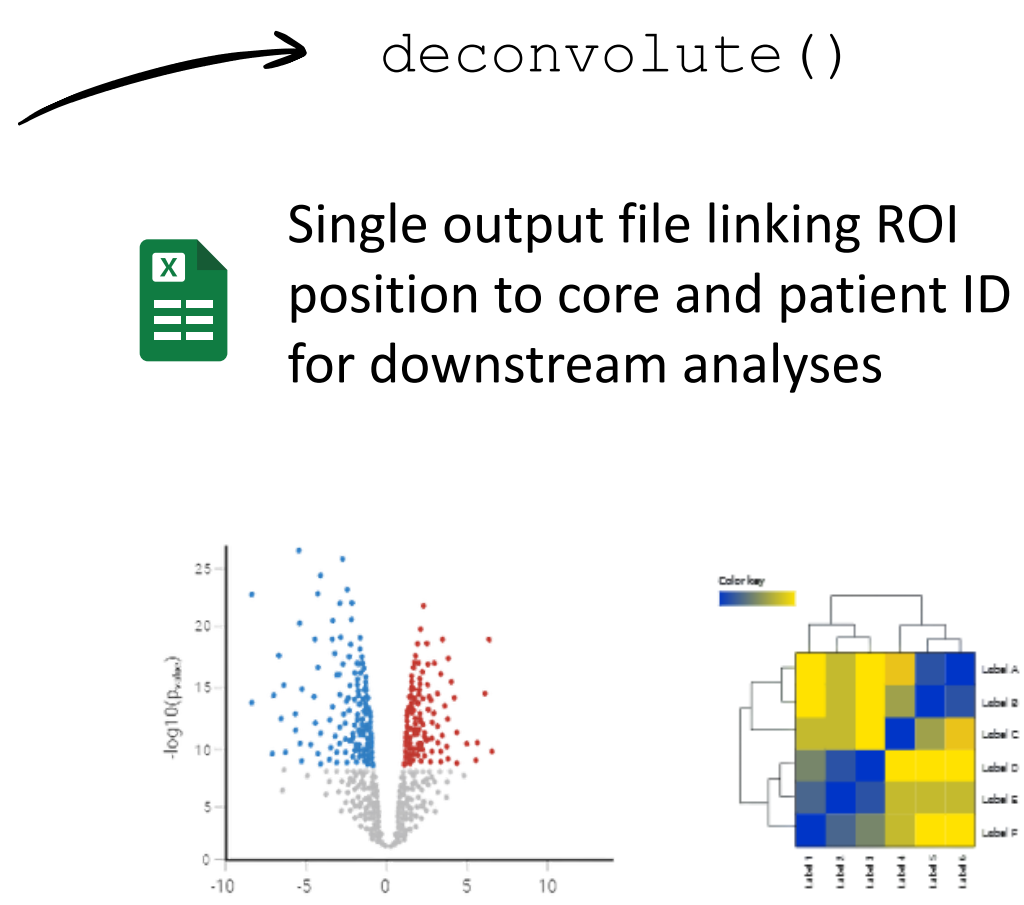


Heatmap includes consolidated scores of 17 IHC biomarkers linked to patient cohort metadata and ENOC Molecular Subtypes. Consolidated scores were obtained from over 70,000 individual TMA cores using TMAtools.

Spatial transcriptomics profiling of Neuroblastoma (NanoString GeoMx)



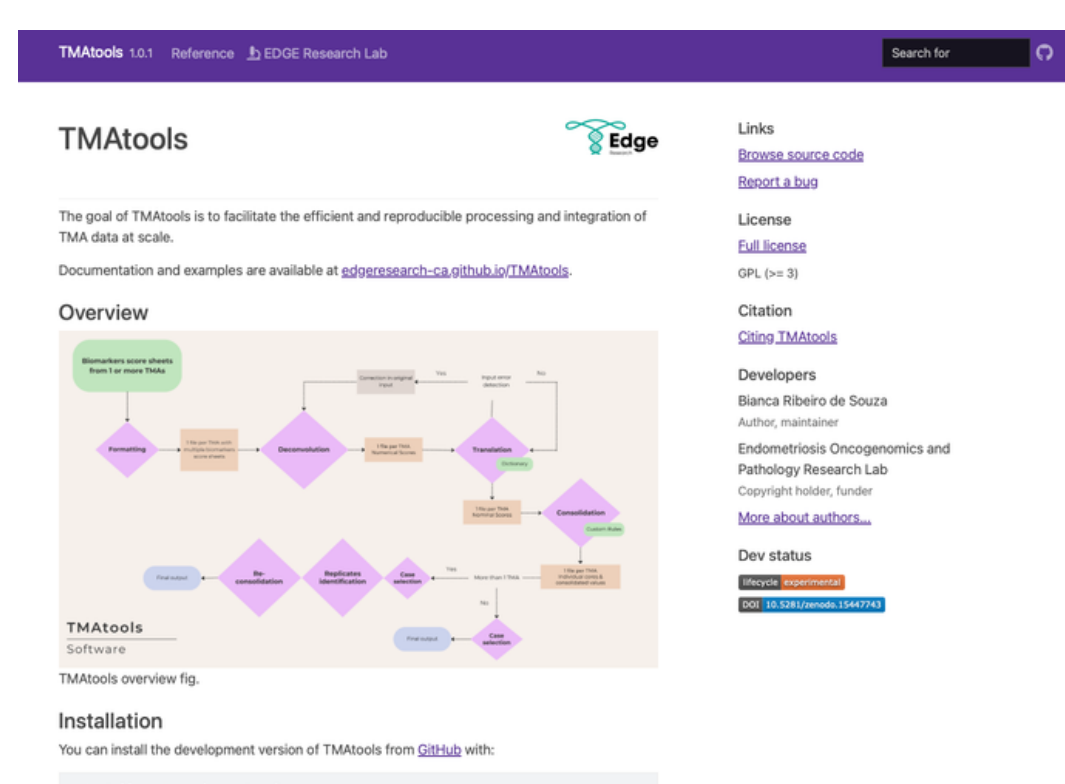
Single module used independently to map regions of interest (ROIs) in each core from TMA-based spatial transcriptomics



ONLINE AVAILABILITY & FAIR PRINCIPLES

R package & tutorials freely available at

[edgeresearch-ca.github.io/TMAtools](https://edgeresearch-ca.github.io/TMAtools)



F

FINDABLE

Open package & documented tutorials

A

ACCESSIBLE

Single-command interface, no coding needed

I

INTER OPERABLE

Excel inputs, modular implementation

R

REUSABLE

Fully reproducible with traceable outputs

CONCLUSION

TMAtools is a FAIR tool that enables **efficient**, **reproducible**, and **traceable** processing of TMA data, integrating seamlessly into pathology research workflows. By allowing diverse applications and customization, TMAtools is a valuable resource for biomarker discovery in TMA-based large-scale cancer studies.

