The search for biomarkers able to detect and evaluate disease such as cancer at an early stage, or to predict resistance and response to therapies, has been and remains a major challenge. Despite very important progresses in all fields of omics technologies, the success of discovery of clinically valuable biomarkers is surprisingly disappointing. Difficult mining of secreted proteins in biological fluids poses the first major hurdle, mainly because the concentration of interesting proteins in serum or urine is generally very low. The second key limitation in the field is the inaccessibility of tissue specimens from early lesions. Those are routinely required in their integrity for the complete histological evaluation in the clinical routine, leaving no residual material for research.

**Material and methods** We have developed a simple and original proximal tissue fluid mining method we named EXPEL. It enables efficient extraction of soluble biomarkers while conserving the tissue intact for subsequent pathological analysis. Importantly, the EXPEL method will not only allow the researchers to access human tissues that are very difficult to obtain, but for the first time, scientists and clinicians can share the same material for both experimental research and routine clinical analysis.

**Results and discussions** We hypothesised that subjecting tissue biopsies to cycles of low-pressure pulses under mild hypertonic conditions would allow a rapid extrusion of interstitial fluid containing the biomarkers of interest, while preserving the morphology and antigenicity of the sample for subsequent pathological investigation.

To test the value of the EXPEL method we have applied our procedure to a series of primary colorectal tumours (CRC) and liver metastasis samples (CRC-LM). This proof-of-principle study demonstrates the validity of EXPEL-extruded fluid as unique starting material for the most advanced OMICs methodologies such as proteomic, genomic, metabolic, while showing no disadvantage for routine clinical and pathological investigations.

**Conclusion** Our method enables, for the first time, both clinicians and scientists to explore identical clinical material regardless of its origin and size, which has a major positive impact on translation to the clinic.