EXPEL: A Novel Non-Destructive Method for Mining Soluble Tumor Biomarkers

**Brunella Costanza1**, Arnaud Blomme1, Akeila Bellhacene1, Olivier Peulen1, Eugene Mutijima2, Philippe Delvenne2, Edwin De Pauw3, Olivier Detry4, Carla Coimbra4 , Vincent Castronovo\*1, Andrei Turtoi\*1

1Metastasis Research Laboratory, Giga Cancer, University of Liege, Belgium; 2Department of Pathology, University Hospital Liege, Belgium. 3Laboratory of Mass Spectrometry, Dept. of Chemistry, University of Liege, Belgium. 4Department of Abdominal Surgery, University Hospital Liege, Belgium

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. Here we present an innovative procedure that we have named EXPEL, which entirely overcomes these limitations. It makes any tissue, regardless of its size, available for both omics research and histological investigation.  Our original device and approach extracts soluble tumor biomarkers and small metabolites within few minutes and without altering the tissue morphology. For this purpose a small tissue biopsy is incubated in a slightly hypertonic extraction buffer while subjected to alternating pressure. Upon extraction the tissue is fixed in formalin and can be used for histological analysis. The soluble extract is further prepared for proteomic and metabolomic analysis. In a proof of concept study we have extracted and analyzed soluble biomarkers from human colorectal carcinoma liver metastases (N=10) as well as primary colorectal tumors (N=10). Pathology validation demonstrates that EXPEL procedure does not alter tissue morphology or subsequent molecular and clinical tests. The comparison of proteins and metabolites identified in tumor lesions with those found in adjacent normal tissues revealed a promising group of novel and differentially expressed targets. Their potential usefulness as diagnostic or predictive markers is currently being explored.

brunellacostanza@gmail.com