

### Intended use

EPICUP is an epigenetic diagnostic test based on DNA methylation profile that helps identify the primary tumor in patients with cancers of unknown primary.

EPICUP is not a substitute for clinical, radiological or histopathological procedures. Its results should be taken within the context of the aforementioned procedures.

### Validation study

EPICUP has been developed and clinically validated using over 10,000 oncology patient samples, achieving overall sensitivity and specificity results of 96.7% and 99.9% respectively.<sup>1,2,3</sup>

### Understanding the results

#### Main prediction

This indicates the tumor type within the prediction area that achieved the highest similarity score.

The similarity shows the closeness of the sample analyzed to the prediction.

#### Haematoxylin and eosin staining (H&E)

This indicates the tumor sample area used to carry out the test.

#### Cannot be ruled out

This indicates the tumor types within the prediction area with lower scores than the main prediction.

#### Ruled out

This indicates the tumor types within the exclusion area ordered from the highest to the lowest score values.

For a more detailed explanation please see the other side of the report.

EPICUP was carried out by:



Cancer Epigenetics and Biology Programme

Bellvitge Biomedical Research Institute.



Certification UNE-EN-ISO13485



Ferrer Internacional S.A.

08029 Av. Diagonal, 549, 5th floor  
Barcelona, Spain

### Request information

#### Ferrer ID:

EC700461

#### Hospital ID:

694516

#### Idibell ID:

EC700461

#### FFPE block ID:

17B 13969-3

#### Date of birth:

29 Apr 1970

#### Sex:

Male

#### Date sample collected:

-

#### Date sample received:

20 Sep 2017

#### Site of biopsy:

Adenopatía yugular izquierda

#### Date report issued:

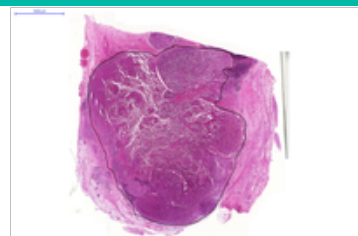
25 Oct 2017

## EPICUP RESULT

### Main Prediction

#### Renal tumour papillary

### H&E



Tumor cells' 80%

Necrosis 0%

### Cannot be ruled out

Renal tumour clear cell

### Ruled out with 99.9% specificity

Stomach carcinoma (intestinal & diffuse)  
Small-cell lung carcinoma  
Skin cutaneous melanoma  
Thyroid carcinoma (papillary & follicular)  
Acute myeloid leukaemia  
Non-small-cell lung ca. (squamous & adenoca)  
Mesothelioma  
Hepatocellular carcinoma  
Glioma  
Thymoma  
Endometrial carcinoma (serous & endometrioid)  
Neuroblastoma  
Cervical carcinoma (squamous & adenoca)  
Cutaneous lymphoma  
Adrenocortical carcinoma  
Acute lymphoblastic leukaemia  
Multiple myeloma  
Diffuse large B-cell lymphoma

Colon adenocarcinoma  
Pancreatic carcinoma  
Breast carcinoma  
Sarcoma  
Ovarian carcinoma  
Meningioma  
Retinoblastoma  
Seminoma  
Renal tumour chromophobe  
Bladder urothelial carcinoma  
Non-seminomatous germ cell tumors  
Head and neck squamous cell carcinoma  
Prostate carcinoma  
Oesophageal carcinoma (squamous & adenoca)  
Rectal adenocarcinoma  
Pheochromocytoma  
Chronic lymphocytic leukaemia  
Uveal melanoma

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Laboratory Director

## Laboratory comments

The prediction of the primary tumor of the analyzed sample is consistent with Renal tumour papillary having obtained a similarity score (SS) of 17%. In the validation study of EPICUP, the prediction of Renal tumour papillary obtained a Positive Predictive Value of 92.2%.

They can not be excluded:

Renal tumour clear cell with a SS of 16.7%

The remaining tumor types are discarded with a specificity greater than 99.9%.

## Understanding EPICUP

**The Similarity Score (SS)** shows the closeness of the sample analyzed to the prediction obtained. In the development of EPICUP, a cut-off was established to delimit two areas: i) the prediction area, including SS values greater than or equal to 12 and ii) the exclusion area, including SS values lower than 12. Thus, for the 38 tumor types included in the database, the overall sensitivity, specificity, positive predictive value and negative predictive value are 96.7%, 99.9%, 96.5% and 99.9%, respectively.<sup>1,2,3</sup>

When a sample obtains more than one result in the prediction area, the highest SS value becomes the “main prediction” while the remaining predictions are included in the “cannot be ruled out” section. Likewise, those tumor types with a SS lower than 12 are ruled out with 99.9% specificity.

**Positive predictive value** is the proportion of patients where the prediction matches the primary tumor.<sup>3</sup>

## Bibliography

1. Moran S, Vizoso M, Martínez-Cardús A, Gomez A, Matías-Guiu X, Chiavenna SM, Fernandez AG, Esteller M. Validation of DNA methylation profiling in formalin-fixed paraffin-embedded samples using the Infinium HumanMethylation450 Microarray. *Epigenetics*. 2014 Jun;9(6):829-33.
2. Moran S, Martínez-Cardús A, Sayols S, Musulén E, Balañá C, Estival-Gonzalez A, Moutinho C, Heyn H, Diaz-Lagares A, de Moura MC, Stella GM, Comoglio PM, Ruiz-Miró M, Matías-Guiu X, Pazo-Cid R, Antón A, Lopez-Lopez R, Soler G, Longo F, Guerra I, Fernandez S, Assenov Y, Plass C, Morales R, Carles J, Bowtell D, Mileskin L, Sia D, Tothill R, Tabernero J, Llovet JM, Esteller M. Epigenetic profiling to classify cancer of unknown primary: a multicentre, retrospective analysis. *Lancet Oncol*. 2016 Oct;17(10):1386-1395.
3. Data on file. EPICUP technical report (EPY-FOR-030/B)



*EPICUP is an epigenetics-based test recommended to help as a guide during the tumor-classification process. The aim is not to diagnose the origin of tumors that cannot be diagnosed using current clinical procedures, nor is it to sub-classify or alter classifications obtained via said procedures. EPICUP does not aim to predict the course of the disease, survival rate or efficacy of any treatment, nor to distinguish primary tumors from metastatic tumors. Tumor types that are not included in the database may have similar methylation profiles to the tumors that are included. Consequently, the test results cannot be used to distinguish among the tumors included in the EPICUP test and those that are not. **EPICUP is not a substitute for clinical, radiological or histopathological procedures. EPICUP results should be taken within the context of the aforementioned procedures.***