A COST-EFFECTIVE MULTIPLEXED TEST FOR CHROMOSOMAL TRANSLOCATION DETECTION IN TUMORS

CALYM offers a new molecular biology method which allows the detection of hundreds of different fusion transcripts from a tumor sample.

■ BACKGROUND

Recruent genomic rearrangements leading to fusion genes occur in approximately 20% of all neoplasms. Most encode hybrid proteins, often transcription factors or tyrosine kinases, directly involved in the transformation process. They are specifically associated with unique tumor subsets and can be used to establish an exact diagnosis. Some of the proteins they code can also be targeted by pharmacological agents, such as Imatinib and Crizotinib which have revolutionized the management of chronic myeloid leukemia and pulmonary carcinomas. Due to their importance at diagnosis and in treatment decision making, some frequent fusion genes are almost systematically tested in leukaemia, sarcomas, and in some carcinomas, either by cytogenetics or RT-PCR. Yet, due to the limitations of these methods, only few among the dozens of known rearrangements are systematically tested. Many abnormalities which could provide important clinical information remain ignored, mainly due to the impossibility of performing a cost effective multiplexed screening.

■ DESCRIPTION

The CALYM U918 team has developed two prototypes diagnostic kits allowing the detection of hundreds of fusion transcripts from a tumor sample: more than 400 fusion transcripts detected in leukaemia with the first kit, and hundreds in sarcomas, lymphomas and carcinomas with the second one. The capacity of the first assay to identify the most frequent fusions was validated on a cohort of 430 leukaemia samples. 96.8% of fusions were identified whereas cytogenetics and RT-PCR conventional methods only detected 54.1% and 71.3% of fusions respectively. The second assay can also detect different fusions in sarcomas (EWS1-FLI1, SYT-SSX, PAX-FKHR...) and lymphomas (NPM-ALK, ATIC-ALK...), even starting from paraffin embedded tissues. The test was validated in an independent laboratory on a cohort of 858 patients with a success rate of 96%.

■ ADVANTAGES

- New robust and time-saving method allowing the detection of dozens of genomic rearrangements which are almost never tested in daily practice.
- Up to 40 patients tested routinely in parallel.
- Results obtained in less than one day.
- Cost-effective method suitable for a daily practice, requiring only a PCR module, a pyrosequencer and basic molecular biology reagents.
- Validated diagnostic assay superior over conventional methods.

This method could provide many important diagnosis and prognosis information, and enable the stratification of patients in prospective clinical trials.

■ KEYWORDS

Multiplex, Transcripts, Genomic Rearrangement

PARTNERSHIP
Collaboration to finalize the development of the method
Licensing

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