ribosome, on which life relies. Indeed, it appeared that loss of 2'O-methylation at a few numbers of rRNA sites in yeast is critical for ribosome functions and induces cell death (4-5). However, more recent findings indicate that in yeast, loss of rRNA 2'O-methylation at other sites have only little or no effect.

Indeed, it emerges from the last decade that rRNA 2'O-methylation is an additional layer of gene expression regulation, highlighting the ribosome as a novel actor of translation control. This new layer of gene expression regulation recently uncovered, joins the numerous descriptions of chemical modifications of both coding and non-coding RNAs that regulates post-transcriptional processes, a field known as epitranscriptomics (5-6).

To date, this major finding lies on evidences coming mainly, if not exclusively, from cellular models most of them representing either cancer cell lines or experimentally-modified *in vitro* models, the latter being established using genetic or molecular biology approaches for trying to mimic pre-cancerous stage, tumoral initiation or tumour progression (3, 5). Moreover, since the currently available technics used to be site-specific approaches, having a comprehensive overview of the variability of rRNA 2'O-methylation at all the positions in cellular models was difficult to obtain. Thus, at present, it is unclear whether rRNA 2'O-methylation varies in humans.

Although genetics, genomics, epigenetics, transcriptomics and proteomics revealed the heterogeneity of tumors at the molecular level, identification of novel molecular layers are required to fully capture all the inter-patient variability, essential for developing clinical applications. Indeed, all if not all these approaches concentrated their attention on transcription regulation. However, in several physio-pathological conditions including cancer, transcriptome is clearly different from the translatome, indicating that translational regulation plays a yet underestimated role in shaping cellular phenotype. Among these transcription-centered approaches, epigenetics appears as promising additional molecular fingerprints to improve diagnosis (i.e., patient classification), prognosis or treatment. Epigenetic mainly corresponds to base methylation of the cytosine nucleotide in DNA that can be added by different methyltransferases in a sequence-specific manner thanks to the cooperation with transcription factors, and that can be interpretated by additional proteins to regulate transcription. Due to the accessibility of -omic approaches dedicated to both transcriptomic and epigenetic, numerous studies demonstrated the importance of these two molecular mechanisms in shaping cellular phenotype. However, it also fails to illustrate all the heterogeneity of cancer phenotype by focusing only on transcription regulation.

In the molecular portraits of cancers, RNA epitranscriptomics and in particular rRNA 2'O-methylation, has never been investigated.

Summary

In one aspect, the present disclosure relates to a method for identifying potentially relevant markers in cancer diagnosis, prognosis and/or estimation of treatment benefit and/or therapy comprising: a) measuring the 2'O-ribose methylation level of the 2'O-ribose methylation positions

of ribosomal RNAs (rRNAs) in biological samples from a representative population of patients suffering from a cancer, b) assessing the individual methylation status for each 2'O-ribose methylation positions by determining the variability of the 2'O-ribose methylation level thus measured for each 2'O-ribose methylation position between each sample of patients from the representative population, c) selecting the set of 2'O-ribose methylation positions for which the individual methylation status is a "variable status".

In another aspect, the present disclosure relates to a method for determining the prognostic of a patient suffering from cancer irrespective of the treatment, comprising: a) measuring the 2'O-ribose methylation level of the 2'O-ribose methylation positions of ribosomal RNAs (rRNAs) in a sample from a patient suffering from a cancer of whom the prognostic is to be determined, called "tested patient", b) comparing of the 2'O-ribose methylation level of the 2'O-ribose methylation positions of ribosomal RNAs (rRNAs) measured with that of a representative population of patients suffering from the same cancer than the "tested patient" and for whom the clinical outcome is known, c) determining the prognostic of the "tested patient" by identifying the one corresponding to the group of patients from the representative population which has the 2'O-ribose methylation level measures closer to that of the "tested patient".

In another aspect, the present disclosure relates to a method for estimating the benefit of a treatment in a patient suffering from cancer, comprising: a) measuring the 2'O-ribose methylation level of the 2'O-ribose methylation positions of ribosomal RNAs (rRNAs) in a sample from a patient suffering from a cancer for whom the benefit of a specific treatment is to be determined, called "tested patient", b) comparing of the 2'O-ribose methylation level of the 2'O-ribose methylation positions of ribosomal RNAs (rRNAs) measured with that of a representative population of patients suffering from the same cancer than the "tested patient" and for whom the benefit of one or more specific treatments is known, c) determining the expected benefit of the specific treatment for the "tested patient" by selecting the one corresponding to the group of patients from the representative population which has the 2'O-ribose methylation level measures closer to that of the "tested patient".

In another aspect, the present disclosure relates to a method for selecting one or more therapeutic drug(s) targeting ribosomes, useful for treating cancers, comprising: - determining the target region(s) on the ribosome corresponding to ribosomal region(s) which comprise one or more 2'O-ribose methylation positions, the 2'O-ribose methylation level of which being known to be associated with cancer, and - identifying one or more ribosome-targeting drugs, including antibiotics, directed to said target region(s).

Detailed description of the invention

Thanks to the recent resolution of technological issues, including the development of RNA-seq based approaches dedicated to the profiling of rRNA 2'O-methylation (3, 7-9), the inventors had achieved rRNA 2'O-methylation profiling in human samples to determine whether it can provide