From histones to RNA: role of methylation in cancer

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Abstract
Cancer results from abnormal gene expression that transforms cellular identity. A rising consensus is that genetic mutations and epigenetic alterations act in concert to achieve tumorigenesis. On one hand, cancer cells harbor classic genetic mutations that activate oncogenes and inhibit tumor suppressors. On the other hand, they also display broad alterations of their epigenomes, as defined by modifications of DNA, histones and coding/noncoding RNAs. In particular, methylation is a ubiquitous modification that affects several residues/sites in these molecules. In this review, I will discuss the central role of this modification in the regulation of gene expression, its alterations in cancer as well as its possible targeting for cancer therapies.

Keywords: chromatin; histone; RNA; methylation; cancer

INTRODUCTION
Although all somatic cells have the same genetic information contained within the sequence of their DNA, only a portion of this information is utilized in each cell, and a large fraction of cellular transactions is dedicated to regulating its expression at four main levels: transcriptional, co-/post-transcriptional, translational and post-translational. These regulatory processes rely heavily on the use of modifications that target the three biopolymer mediators of genetic information, DNA, RNA and proteins. Interestingly, all three of them can be chemically modified by methylation, which consists of the addition of a methyl group (−CH3) to different acceptor sites. This modification is usually catalyzed by methyltransferase enzymes that use S-adenosylmethionine (SAM) as a methyl group donor. In many cases, methylation can also be reversed through the action of demethylases. In general, methylation does not change the sequence of these polymers, but modifies their biochemical properties and interaction partners. Consequently, methylation is often considered as an epigenetic modification. Although methylations of DNA and histones have been a major research focus since the 1980s and 1990s, respectively, the study of RNA methylations has lagged mainly due to technical challenges for its detection. However, recent technical advances and the discovery of novel RNA methylases and demethylases have announced the birth of a new field, termed RNA epigenetics [1]. In this review, I will give a brief description of the different types of known sites of methylation on chromatin and RNA and will focus on the ones that have either been already implicated in cancer or that could be of potential interest in anticancer therapies.

CHROMATIN METHYLATION
Both the DNA and the histone components of chromatin are modified by methylation. DNA is methylated on the carbon 5 of the pyrimidine ring of cytosines and this constitutes a bona fide epigenetic modification, i.e. heritable information that is not encoded within the primary sequence of DNA. DNA methylation occurs at specific sites and is established by two de novo methyltransferases, DNMT3A and DNMT3B, and is maintained by DNMT1, whose activity is specific for hemi-methylated DNA. Global and gene-specific patterns of DNA methylation are often perturbed in cancer, and this has been an intensive area of research for
Histones are highly conserved small basic proteins, which assemble in octamers composed of two H2A/H2B dimers and one H3/H4 tetramer and associate with DNA to form nucleosomes. In addition to the core histones, there exist variant histones as well as intranucleosomal H1 histones. Until not long ago, histones were considered as a mere structural component whose only function was to package the DNA. However, a wind of change came with the discovery of histone modifications that highly correlated with the transcriptional state of genes [3]. Indeed, histones, and especially their protruding tails, are highly modified by a myriad of post-translational modifications (PTMs), either by small chemical groups, such as acetylation, methylation and phosphorylation, or peptides, such as ubiquitin and Small Ubiquitin-like MOdifier (SUMO). These modifications are laid on the lateral chains of specific residues by ‘writer’ enzymes, and in the majority of cases, they can also be reversed by ‘eraser’ enzymes. Histone PTMs act by either perturbing the interaction of histones with DNA or other chromatin factors, or by increasing the affinity of ‘binder’ proteins that specifically recognize the modification. In particular, methylation of histones occurs on lysines, arginines and histidines, however, lysine methylations are by far the best characterized, with the main sites being H3K4, H3K9, H3K27, H3K36, H3K79 and H4K20. The complexity is increased by the fact that lysines can accept up to three methylations on lysine residues have now been discovered [4–6]. Analysis of the genomic localization of histone methylations by chromatin immunoprecipitation (ChIP) using antibodies against specific methylations has led to their simplistic separation into two broad categories, ‘active’: trimethyl H3K4, H3K36 and H3K79, correlating with transcriptionally active genes and ‘inactive’: trimethyl H3K9, H3K27 and H4K20, correlating with transcriptionally inactive genes and/or heterochromatin. For more details, I refer you to several reviews on the subject and references therein [7–9].

With respect to cancer, two major observations have brought histone methylations into the focus of attention: the patterns of several histone methyl marks are altered in malignancies, and importantly, mutations in specific histone methyltransferases, demethylases and associated factors have been reported in many cancers, especially in hematological malignancies (Table 1) [10]. For example, comprehensive analysis of normal tissues, cancer cell lines and primary tumors has revealed a global aberrant pattern characterized by a loss of acetylation at H4K16 and trimethylation at H4K20, predominantly located at DNA repetitive sequences that also undergo DNA hypomethylation in cancer cells [11]. However, the function of H4K20 trimethylation as well as its interdependency with DNA methylation in cancer are still poorly understood.

Another example comes from the human homolog of the Drosophila trithorax gene, MLL (mixed lineage leukemia), which is a Suvar3-9, Enhancer-of-zeste, Trithorax (SET) domain containing methyltransferase that specifically methylates H3K4 [12, 13] (Table 1). The H3K4 methyl marks are generally associated with transcriptionally active regions of chromatin, with its monomethyl form being associated with gene enhancers and its di-/trimethyl form enriched at the transcription start site of active genes [14]. MLL mutations are found in transitional cell carcinoma (TCC) of the bladder [15], but most importantly, the MLL gene is a translocation hot spot, with nearly 100 proteins resulting from fusions of the N-terminal portion of MLL with the C-terminus of the translocation partner [16]. These MLL-related rearrangements occur in ~10% of adult acute myelogenous leukemia (AML) and 70% of infant leukemia, and their presence generally confers poor prognosis [16]. The MLL gene encodes a large protein of 3969 amino acids, which is cleaved into MLLN and MLLC by the aspartic protease Taspase 1 [17]. MLLN carries several interaction motifs that directly or indirectly tether MLL to chromatin, whereas MLLC carries the SET domain, which is responsible for its methyltransferase activity as well as interaction domains that facilitate this enzymatic activity or that recruit other chromatin modifier activities such as acetylation [16]. The function of MLL cleavage is subtle, because MLLN and MLLC form a stable complex after cleavage [17]. Most of MLL translocations disrupt this interaction, and interestingly, it was recently shown that MLL–AF9 leukemic cells still require the presence of an
unaltered copy of MLL to preserve their tumorigenic potential [18], suggesting that the methyltransferase activity of MLLC plays an important role in this process. Therefore, the development of MLL SET domain-specific inhibitors may be useful, especially if fine dosage can find a window of opportunity where the cancer cells carrying MLL translocations are more sensitive than normal cells, due to their loss of one of the two wild type (WT) MLL alleles during the translocation event (Figure 1). However, most of the drugs presently available have utilized other subterfuges, acting either upstream or downstream of the action of MLL fusion protein on the genes required for leukemic transformation. MI-2, an inhibitor of the Menin-Multiple endocrine neoplasia type 1 protein (MLL)N interaction, inhibits their recruitment to the target genes [19] (Figure 1), whereas other inhibitors act downstream of this recruitment. Indeed, the most common mechanism for the action of MLL fusion proteins is through the aberrant enhancement of transcriptional elongation at target genes, usually mediated by phosphorylation of Ser2 on the carboxy-terminal domain (CTD) of RNA Polymerase II through pTEFb and associated complexes [16] (Figure 1). One such downstream factor is DOT1L, which catalyzes the methylation of H3K79, a

### Table 1: List of histone methyltransferases and demethylases mutated or aberrantly expressed in cancer

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Activity</th>
<th>Biochemical/biological properties</th>
<th>Perturbations</th>
<th>Tumors</th>
<th>Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLL1 (KMT2A)</td>
<td>H3K4 KMT</td>
<td>Active transcription</td>
<td>T PTD M</td>
<td>AML, ALL, bladder TCC</td>
<td>Mi-2 (MLL-Menin inhibitor)</td>
</tr>
<tr>
<td>MLL2 (KMT2B)</td>
<td>H3K4 KMT</td>
<td>Active transcription</td>
<td>N F M</td>
<td>Medulloblastoma, renal, DLBCL, FL</td>
<td></td>
</tr>
<tr>
<td>MLL3 (KMT2C)</td>
<td>H3K4 KMT</td>
<td>Active transcription</td>
<td>N</td>
<td>Medulloblastoma, TCC, breast</td>
<td></td>
</tr>
<tr>
<td>EZH2 (KMT6)</td>
<td>H3K27 KMT</td>
<td>Polycist silencing/ X-chromosome inactivation</td>
<td>AE M</td>
<td>Prostate, breast, bladder, gastric, lung, liver, DLBCL, MPD, MDS, T-ALL</td>
<td>GSK126</td>
</tr>
<tr>
<td>G9A (KMT1C)</td>
<td>H3K9 KMT</td>
<td>Heterochromatin formation/silencing</td>
<td>AE</td>
<td>HCC</td>
<td></td>
</tr>
<tr>
<td>HYPB/SETD2</td>
<td>H3K36 KMT</td>
<td>Transcriptional elongation/splicing</td>
<td>N F S M D</td>
<td>Breast, renal, ETP-ALL</td>
<td></td>
</tr>
<tr>
<td>NSD1</td>
<td>H3K36 KMT</td>
<td>Transcriptional elongation/splicing</td>
<td>T</td>
<td>AML</td>
<td></td>
</tr>
<tr>
<td>NSD2/WHSCI/MMSF</td>
<td>H3K36 KMT</td>
<td>Transcriptional elongation/splicing</td>
<td>T AE</td>
<td>Multiple myeloma, various cancers</td>
<td></td>
</tr>
<tr>
<td>NSD3</td>
<td>H3K36 KMT</td>
<td>Transcriptional elongation/splicing</td>
<td>T</td>
<td>AML</td>
<td></td>
</tr>
<tr>
<td>PRMT1</td>
<td>H4R3me2As</td>
<td>Transcriptional co-activator</td>
<td>AE</td>
<td>Breast</td>
<td></td>
</tr>
<tr>
<td>PRMT5</td>
<td>H2A/H4R3me2S</td>
<td>Transcriptional repression</td>
<td>AE</td>
<td>MPN, testis, gastric</td>
<td></td>
</tr>
<tr>
<td>UTX (KDM6A)</td>
<td>H3K27 KDM</td>
<td>Transcriptional activation</td>
<td>D N F S</td>
<td>Multiple myeloma, AML, TCC</td>
<td></td>
</tr>
<tr>
<td>JARIDIA/RBP2</td>
<td>H3K4 KDM</td>
<td>Transcriptional repression</td>
<td>T</td>
<td>AML</td>
<td></td>
</tr>
<tr>
<td>JARIDIC/SMCX</td>
<td>H3K4 KDM</td>
<td>Transcriptional repression</td>
<td>N F S</td>
<td>Renal</td>
<td></td>
</tr>
</tbody>
</table>

Notes: KMT, lysine methyltransferase; PRMT, protein arginine methyltransferase; KDM, lysine demethylase; PTD, partial tandem duplication; AE, aberrant expression; ALL, acute lymphoid leukemia; DLBCL, diffuse large B-cell lymphoma; ETP-ALL, early T-cell precursor acute lymphoblastic leukemia; FL, follicular lymphoma; HCC, hepatocellular carcinoma; MPD, myeloproliferative diseases; MPN, myeloproliferative neoplasms; MPS, myeloproliferative syndromes; T-ALL, T-cell ALL; TCC, transitional cell carcinoma; D, deletion; F, frameshift; M, missense; N, nonsense; S, splice site mutation; T, translocation.
chromatin modification associated with transcriptional elongation [20] (Figure 1). DOT1L is the only lysine methyltransferase without a SET domain, and this was recently exploited to make EPZ004777, an inhibitor that specifically inhibits the methyltransferase activity of DOT1L by mimicking and thus preventing its binding to the methyl group donor SAM [21] (Figure 1). EPZ004777 potently inhibits H3K79 methylation and blocks MLL fusion target gene expression, resulting in selective killing of cells bearing the MLL translocation in culture as well as antitumor activity in \emph{in vivo} models of MLL. Another MLL downstream factor is BRD4, whose inhibition by BRD inhibitors JQ1 and GSK525762 has also shown great potential and thus created a lot of excitement in the field [22] (Figure 1). For more details on these inhibitors, their effects and potential mode of action, I refer you to the excellent review by Barbieri and Dawson in this special edition.

A further example linking histone PTMs to human malignancies is the methylation of H3K27 (Table 1). H3K27 trimethylation is considered an ‘inactive’ mark involved in the silencing of lineage-specific genes with important roles during development and cellular differentiation [23]. H3K27 methylation is catalyzed by the Polycomb Repressive Complex 2 (PRC2), which comprises four core components: EZH1/2 (the methyltransferase subunits), SUZ12, EED and RbAp46/48 as well as other more recently discovered interacting proteins: AEBP2, PCLs and JARID2 [24]. In addition, this methylation can be reversed by the action of demethylases, so far comprising UTX and JMJD3 [25]. Altered expression or mutations of factors involved in H3K27 methylation have been observed in many cancers, and these perturbations are seemingly contradictory. Indeed, on one hand, EZH2 overexpression is observed in prostate, breast, bladder, gastric, lung cancers and hepatocellular carcinoma ([26] and references therein). Going in the same direction, heterozygous missense mutations at Y641 and A677 within the SET domain of EZH2 showing enhanced catalytic activity were found in lymphomas [27, 28], whereas UTX mutations were found in multiple cancer types, with the highest prevalence.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Figure_1.png}
\caption{Model illustrating how MLL fusions may enhance transcriptional elongation of leukemic driver genes. WT and fusion MLL proteins interact with their target genes through MENIN and LEDGF and probably through other interaction domains found in MLLN. The methyltransferase activity of WT copy of MLL, not affected by the translocation, may be required for optimal trimethylation of H3K4 at the promoter of target genes. The MLL fusion partners enhance the recruitment of factors involved in transcriptional elongation, such as (i) pTEFb, which phosphorylates Ser2 in the CTD of RNA Polymerase II; (ii) SEC, the super elongation complex; (iii) PAFc, polymerase-associated factor complex; (iv) BRD4, a bromodomain containing protein that binds to acetylated H4 and also interacts with SEC and PAFc; (v) DOTIL which dimethylates H3K79, etc. The blunt arrows indicate (i) the 7SK noncoding RNA that inhibits pTEFb activity and is itself stabilized by the methyltransferase MePCE/BCDIN3; (ii) chemical inhibitors, either potential, indicated by a question mark, or already existing, indicated by their name/code. The gray scale bars indicate the typical enrichment of the indicated modifications as determined by ChIP or ChIPseq.}
\end{figure}
in multiple myeloma [29]. Importantly, GSK126, a specific inhibitor of the activating mutations of EZH2, was shown to exhibit antiproliferative effects both in vitro and in mice xenografts of diffuse large B-cell lymphoma cell lines [30]. These observations would categorize increased H3K27 trimethylation as having an oncogenic activity. However, loss of function mutations of EZH2 has been associated with poor prognosis in myeloid neoplasms and T-ALL, and loss of function mutations has also been observed in the EZH2–interacting partners SUZ12, EED and Jarid2 ([26] and references therein). In addition, it was recently shown that the recurrent mutations of ASXL1 in myeloid malignancies may function through loss of PRC2-mediated gene repression [31]. These later observations would rather classify H3K27 trimethylation as having a tumor suppressive activity. The simplest explanation would be that depending on the cellular origin and context of various cancers, the repressive activity of PRC2 may be required to inactivate tumor suppressors or it may be attenuated to allow the activation of oncogenes. In addition, these complexes may also regulate targets other than H3K27. Altogether, these examples linking H3K27 methylation to cancer demonstrate the complexity of chromatin-based interactions in tumorigenesis and highlight the necessity for systematic characterization of mutations in cancer patients and the development of ‘personalized’ epigenetic inhibitors that take into account the molecular fingerprint of each cancer.

**RNA METHYLAITION**

RNA is the intermediate molecule between DNA and proteins in the chain that links genetic information contained in genes to its expression in functional proteins, by either carrying this information in the form of messenger RNA (mRNA) or participating in mRNA expression, splicing, stability and translation in the form of noncoding RNAs. The last decade has added new players in the growing list of noncoding RNAs, which is likely to be even further extended by the improvement of RNA detection and sequencing technologies. Methylation, once again, is involved in many steps of RNA biology, with it counting for more than two-thirds of the >100 chemically distinct known RNA modifications [32]. However, despite the abundance of RNA methylations, little is known about the function of most of these modifications and their alterations in cancer.

Therefore, this part of the review will be more ‘forward thinking’ on the aspects of RNA methylations that may be of interest in future studies of tumorigenesis.

RNA methylations are generally catalyzed post transcriptionally and can be divided into two major groups depending on their localization on the RNA polymer: they either decorate the RNA extremities: 5’- and 3’-ends or occur on specific residues on the bases or 2’-hydroxyls of the RNA nucleotides.

Methylation occurring on the 5’-ends of RNAs are dependent on how the RNAs are generated [33]. mRNAs, long noncoding RNAs and other RNAs generated by RNA polymerase II are 7-methylguanosine (7-mG) capped through three enzymatic activities, triphosphatase, guanylytransferase and (guanine-N7) methyltransferase. These activities are essential for viability, probably due to the essential role of the 7-mG cap in protecting mRNAs against degradation by 5’ exonucleases and in promoting transcription, splicing, polyadenylation, nuclear export and translation of mRNAs [33, 34]. Some noncoding RNAs are also hypermodified on their 5’-ends by 2,2,7-trimethylguanosine (TMG) caps through the TMG synthase, which adds two methyl groups on the N2 atom of the 7-mG cap. TMG caps are characteristic of the spliceosomal snRNAs U1, U2, U4 and U5 and also of the RNA subunit of telomerase [35]. As telomerase is reactivated in many cancers [36], it would be interesting to determine the effect of TMG synthase inhibitors on tumor growth. Other noncoding RNAs are simply modified on their 5’-ends by the addition of a methyl group on the γ-phosphate of their primary transcript. One such RNA is 7SK, a noncoding RNA, synthesized by RNA polymerase III and methylated by the methyl phosphate capping enzyme MePCE, also known as BCDIN3 [37, 38]. 7SK associates with the CDK9 kinase subunit of pTEFb to inhibit its activity on Ser2 on the CTD of RNA Polymerase II, which in turn inhibits transcriptional elongation (Figure 1). Knockdown of MePCE in human cells leads to a significant decrease in the cellular amounts of 7SK, probably due to a protective effect of the cap against 5’ exo-nucleolytic degradation [37]. Given the link between pTEFb and cancer, it is tempting to speculate that MePCE could be a interesting target for anticancer therapies [39]. I also recently identified BCDIN3D, a paralog of MePCE, as an RNA methyltransferase whose enzymatic activity consists of the methylation of
the two available oxygen moieties of a 5′ monophosphate, resulting in a complete loss of its negative charge [40] (Figure 2). Specifically, I showed that BCDIN3D methylates the precursor of specific microRNAs (miRNAs) to perturb their interaction with Dicer, and thus inhibits their processing into mature miRNAs [40] (Figure 2). It will also be interesting to determine if this enzyme can methylate other RNAs that result from endonucleolytic processing that leave 5′ monophosphate termini. Given that knockdown of BCDIN3D in MDA-MB-231 triple-negative breast cancer cells greatly reduces their invasive potential, in a similar manner to the overexpression of its miRNA targets, this enzyme could also be of interest as a cancer therapy target [40].

The methylations that occur on the RNA nucleotides are by far the most diverse. Their target sites include the majority of nitrogens on the four major ribonucleotides, in addition to inosine and pseudouridine as well as the oxygen at position 2 of the ribose and a few carbon atoms in the bases [41]. In most cases, the function and biological consequences of these methylations remain elusive. However, the field of RNA nucleotide modifications is re-emerging, thanks to the development of new analysis tools. A good example of this revival is provided by the recent advances in the study of the N6-methyladenosine (m6A) modification, which occurs not only on noncoding RNAs [32] but also constitutes the dominant methylation of bases in miRNAs [42]. This methylation has been known since the 1970s, but has only recently regained widespread interest, thanks to the discovery that the fat- and obesity-associated protein FTO is a m6A demethylase [43]. The development of profiling
methods, which make use of antibodies that specifically recognize this modification coupled to next generation sequencing, has allowed to map this modification transcriptome-wide [44, 45]. These analyses revealed m^6A to be widespread and enriched near stop codons and in the 3'-UTRs of mRNAs. The molecular function of the uncovered methylation sites remains unknown; however, the enzymes involved in the m^6A modification have interesting phenotypes. Knockdown of one of the m^6A methyltransferases METTL3 in human cells leads to apoptosis [44], whereas activating mutations of the m^6A demethylase FTO are tightly linked to human obesity [46]. Altogether, these observations point to an important role of this modification in cellular metabolism and call for this pathway to be further studied from both the metabolism and cancer angles. In addition, the discovery of the FTO demethylase suggests that RNA nucleotide methylations may also be reversible and opens the way for the discovery of novel enzymes that affect RNA metabolism [47].

tRNAs are heavily decorated by various combinations of methylations and other chemical modifications. In particular, during the 1970s, many research groups reported distinctive tRNA species specifically found in tumor cells relative to normal tissue. These differences were inferred from altered elution profiles of purified tRNAs. It was later shown that the observed differences were actually due to differential post-transcriptional modifications. For example, Kuchino and colleagues showed that tRNA-Phe purified from hepatoma contained two supernumerary methylations, 1-methylguanine (m^1G) and 5-methylcytosine (m^5C), not found in tRNA-Phe purified from nontumor cells [48]. Despite this interesting observation, our understanding of the function of these methylations and their involvement in tumorigenesis remains underdeveloped. However, in the case of m^5C, more insights into its function have been recently gained. Dnmt2 and Nsun2 are the only known m^5C tRNA methyltransferases in higher eukaryotes [49]. Double-knockout

**Figure 3:** Simplified model of how the Dnmt2 and Nsun2 m^5C RNA methyltransferases affect protein synthesis. The Dnmt2 and Nsun2 RNA methyltransferases methylate the carbon 5 of cytosines, a modification analogous to that of DNA methylation. They target specific residues located on or around the anticodon and/or the variable loop of specific tRNAs. These methylations may protect the tRNAs from degradation. As optimal tRNA pools are required for efficient translation, Dnmt2 and Nsun2 inhibition may have an indirect negative effect on the efficiency of translation. An alternative, albeit not exclusive, hypothesis is that m^5C of these tRNAs is directly involved during the translation process. The blunt arrow indicates the possible negative effect of 5-Azacytidine on Dnmt2 activity.
suggesting that m5C of tRNA has an important role in the levels of specific mRNAs or ribosomal RNAs, reduced protein synthesis without any major changes addition, the gested by a recent work in Drosophila [51]. In addition, the Dmmt2−/−; Nsun2−/− MEFs displayed reduced protein synthesis within any major changes in the levels of specific mRNAs or ribosomal RNAs, suggesting that m5C of tRNA has an important role in translation efficiency (Figure 3). Interestingly, a recent study that mapped m5C transcriptome-wide [52] revealed that NSUN2 may also be involved in methylating mRNAs. Because NSUN2 is a c-Myc regulated target and is either amplified or overexpressed in many cancers [53–55], it will be important to determine the role of m5C in both tRNA and mRNA metabolism. Finally, it was recently shown that the DNA methylation inhibitor Azacytidine, an FDA-approved drug used in the treatment of myelodysplastic syndrome, also inhibits DNMT2-mediated tRNA methylation [56] (Figure 3). As efficient translation sustains tumor proliferation, these findings raise the possibility that targeting m5C tRNA methylation might be an effective way to target cancer cells.

CONCLUSION
As highlighted throughout this review, methylation of DNA, histones and RNAs regulates many aspects of gene expression, from RNA synthesis to translation. The enzymes that are involved in writing and erasing these marks are often either mutated/deregulated in cancer or are required to maintain cancer hallmarks such as proliferation and invasion. The fact that small molecules can be made to modulate their activity makes them ideal targets for anticancer drug therapies. Until now, comprehensive molecular characterization of tumors has focused on determining the steady-state levels of mRNAs. However, it is becoming increasingly clear that it will be important to also characterize the noncoding RNAs involved in the regulation of translation. This is already the case for miRNAs, which are now being used to successfully classify cancers [57]. Additionally, new tools will be needed to be adapted or developed to reveal the complexity of RNA modifications in cancer cells in a manner similar to the analysis of DNA and histone modifications. This will be crucial to have a more comprehensive molecular view of cancer cells and will very likely provide us with novel anticancer targets.

Key Points
- Methylation is a ubiquitous chemical modification of DNA, RNA and proteins.
- Writers, erasers and binders of specific histone methylations are frequently mutated in cancer and are possible targets for cancer therapies.
- RNA methylation is an emerging field of research with potential implications in cancer.

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References


