mediated amplification (TMA™) technology to determine a PCA3 score from male urine. TMA is an isothermal nucleic acid-based method that can amplify RNA or DNA targets a billion-fold in less than 1 h. PCA3 is the first long ncRNA to be used in clinical diagnostic assays, but with the recent developments in the ncRNA world, many more will most likely follow soon.

3.7 Epigenetic Factors

The term "epigenetic" defines all heritable changes in gene expression and chromatin structure that are not coded in the DNA sequence itself. With minor exceptions (T- and B-cells of the immune system), all differentiation processes are triggered and maintained through epigenetic mechanisms. Epigenetic inheritance includes DNA methylation, histone modifications, and RNA-mediated silencing, all of which are essential mechanisms that allow the stable propagation of gene activity states from one generation of cells to the next. Several of these major epigenetic aberrations have been developed into biomarkers. Epigenetic biomarkers can be detected in tissue and in blood as circulating DNA (Greenberg et al. 2012). The exploration of epigenetic biomarkers in cancer for clinical use is a relatively new but rapidly developing field. Applications include screening, diagnosis, classification, surveillance, and targeted therapies. If epigenetic factors are to be effective biomarkers in clinical practice, they must be detectable by noninvasive means and outperform the current gold standard, as is true for all new emerging biomarkers. One of the most exciting cases for the use of epigenetic biomarkers outside oncology was the recent finding that DNA methylation status can predict response to therapy with either methotrexate or blockers of tumor necrosis factor alpha in patients with rheumatoid arthritis (Plant et al. 2014).

3.8 Protein Biomarker

While early work has been strongly focused on nucleic acid-based biomarkers (DNA, SNPs and mRNA expression profiles), recent experience suggests that the utility of these markers as clinically applicable decision tools may generally be limited. Protein biomarkers, which offer a significantly greater degree of differentiated information content, are likely to close this gap. Two types of protein assay platforms are currently applied to discover protein biomarkers and to measure them quantitatively and qualitatively (i.e., to determine the isoform state of a protein such as phosphorylation). It is instructive to point out here that an antibody use is a "fit-for-purpose" approach. For example, the requirement for an ELISA is substantially different from that of immunohistochemistry (IHC) or diagnostic assay versus laboratory assay (Qoronfleh and Lindpaintner (2010), www.ddw-online.com).