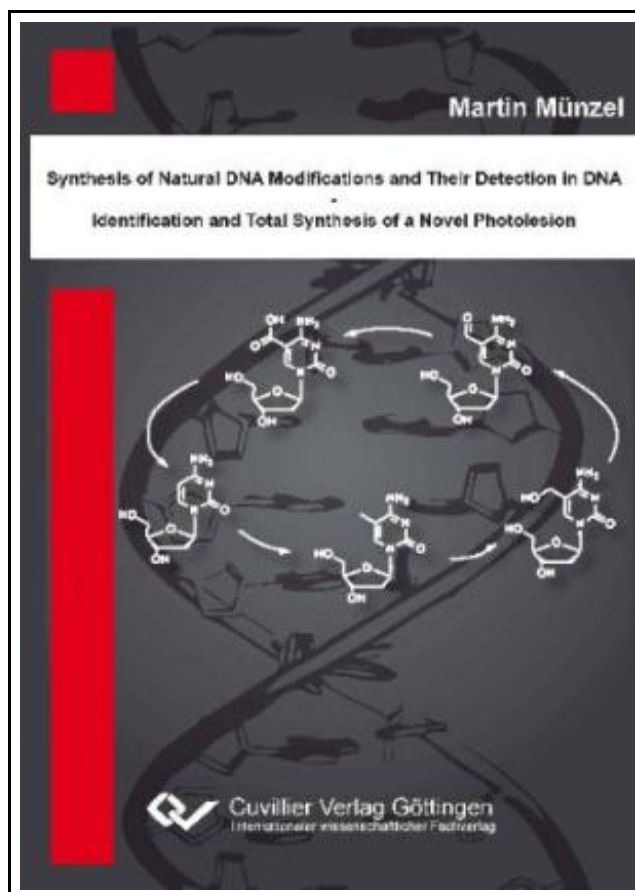


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Cuvillier Verlag Sep 2011, 2011. Buch. Book Condition: Neu. 213x147x14 mm. Neuware - In the human body almost all cells contain the same genetic material; however, individual cells can perform vastly different functions. This is only possible, if different genes are active in different cell types. Furthermore, every cell stems from the same zygote; Hence the genetic information in cells needs to undergo reprogramming during differentiation. These processes require precise time dependent and robust control of gene expression, i.e. both stable and dynamic gene activation and silencing. The 'ATCG' DNA base sequence alone cannot control these processes. To enable the regulation of gene activity, cytosine bases in DNA can be further modified. The presence of methylated cytosines is long known to silence genes and aberrant methylation is the reason for many diseases including cancer. Thus, DNA modification is one of the most fundamental events in epigenetics. To be able to detect methylated cytosines a methodology was developed that allows the efficient discrimination of cytosine and methylcytosine in DNA. The technique relies on different reaction products of the nucleosides with O-Allylhydroxylamine. These products exhibit different base pairing properties which can be readily detected by pyrosequencing. As a further DNA modification, methylcytosine can be oxidized to hydroxymethylcytosine. By using a stable isotope dilution LC-MS approach the exact distribution of hydroxymethylcytosine in the mammalian body was determined for the first time. Especially high amounts of the nucleoside are present in the central nervous system. The hydroxymethylcytosine levels increase during brain development and are strongly reduced in cancerous tissue. It was furthermore investigated, if hydroxymethylcytosine was subject to further oxidation to formylcytosine and carboxylcytosine which - after final decarboxylation or excision by a glycosylase - would be an attractive mechanism for active DNA demethylation. This study ultimately led to the identification of formylcytosine and carboxylcytosine as...



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