Abstract

Histone modifications affect many cellular processes including DNA damage repair. This thesis focusses on the methylation of lysine 36 of histone 3 (H3K36). The role of this modification in the localization of DNA double-stranded breaks in germinal cells is described in the first part of this thesis. Double-stranded breaks initiate meiotic recombination, which is essential for successful meiosis. This thesis also describes three histone methyltransferases. The first is PRDM9, an enzyme expressed only in oocytes and spermatocytes during meiotic prophase and responsible for the localization of recombination hotspots in most mammals. The second part of this thesis deals with the role of H3K36 methylation in DNA damage repair in somatic cells using homologous recombination (HR) and nonhomologous DNA ending joining (NHEJ). The proteins SETD2 and SETMAR are described in the second part. SETD2 trimethylates H3K36, and H3K36me3 is recognized by the LEDGF protein. Through LEDGF, other components necessary for HR are recruited to DNA. SETMAR dimethylates H3K36 and together with this histone modification promote DNA break repair with NHEJ. The research of H3K36 methylation is important for a better understanding of each DNA repair mechanisms. The correct repair of DNA breaks is necessary for maintaining genome integrity and suppression of cancer. Many human tumours are therefore affected by the incorrect regulation of H3K36 methylation.