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DNA错配修复与癌症的发生及治疗

毕利军[1]、周亚凤[2]、张先恩*[1,2]
1 中国科学院生物物理研究所生物大分子国家重点实验室
2 中国科学院武汉病毒研究所病毒学国家重点实验室

DNA错配修复（Mismatch repair, MMR）是细胞复制后的一种修复机制，具有维持DNA复制保真度，控制基因变异的作用。DNA错配修复基因缺陷使整个基因组不稳定，最终导致肿瘤和癌症的发生。MMR系统不仅通过矫正在DNA重组和复制过程中产生的碱基错配而保持基因组的稳定，而且通过诱导DNA损伤细胞的凋亡而消除由突变细胞生长形成的癌变。错配修复介导的细胞凋亡对于肿瘤抑制是非常重要的，错配修复缺陷细胞的抗药性也引起癌症化疗方面的关注。大多数情况下错配修复健全型细胞对肿瘤化疗药物敏感，而错配修复缺陷细胞却有较高的抗性。错配修复系统通过它的修复和细胞凋亡功能维护基因组稳定性显示了错配修复途径在癌症生物学和分子医学中的重要性。

DNA Mismatch Repair and Occurrence and Therapy of Cancer

DNA mismatch repair (MMR) primarily corrects mismatched or unpaired bases incorporated by DNA polymerase, increasing the overall fidelity of DNA replication. DNA MMR system not only ensures the precision of chromosomal replication and maintains genomic stability by correcting the mismatches during the replication and recombination, but also eliminate cancer cells by promoting apoptosis of cells with severely damaged DNA. Defective mismatch repair proteins result in genomic instability, elevated mutation rate and increased incidence of various cancers. It has been found almost universally that while cells that are proficient in MMR are sensitive to chemical agents, cells that are deficient in MMR are more resistant to killing by these agents. While MMR-mediated apoptosis is important for tumor suppression, the drug resistance property of MMR-deficient cells raises concerns for cancer chemotherapy. The genomic maintenance capability of MMR by both its repair and apoptotic functions underscores the importance of the MMR pathway in cancer biology and molecular medicine.

关键词