عنوان مقاله:

Lynch syndrome current screening criteria and how to improve it

محل انتشار:

سومین سمپوزیوم بین المللی سرطان نسترن (سال: 1396)

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خلاصه مقاله:

Lynch syndrome (LS), formerly called hereditary non polyposis colorectal cancer (HNPCC) was first described by Warthin in 1913 in a large family manifesting colorectal cancers (CRC) without polyposis,alongside cases of gastric and uterine cancers. Epidemiological studies have identified LS as the most common hereditary CRC, accounting for almost 3% of all CRC cases. The molecular pathogenesis ofLS is based on defective mismatch repair (MMR) system, because of mutations in its responsible genes. These mutations were described to cause replication error leading to molecular change known asmicrosatellite instability (MSI), which is detectable by polymerase chain reaction (PCR). MSI was found to be present in LS tumours, which motivated scientists to design a guideline for CRC patients whoneeded MSI testing, this guideline was named Bethesda criteria. At present, direct sequencing of all patients' MMR genes is not possible. Thus for current screening purposes, clinical features of LS incombination with MSI-high (MSI-H) results (Bethesda criteria) is used to suggest germline mutation testing as the diagnostic test for the patients. On the other hand, it has been reported that only around25% of MSI-H tumours are related to underlying MMR gene mutation. Hence, it can be said that MSI is sensitive but not specific for LS. As a result, some laboratories has suggested immunohistochemistry(IHC) assay as a complementary test for MSI testing. However, IHC has its own drawbacks, such as missing around 5% of LS cases which have full length but not functional MMR proteins and need of anexperienced pathologist to confirm the test result.MSI analysis, as well as being used for screening for Lynch syndrome, is also important for the prognosis of all CRC as these patients are resistant to thetreatment with 5-flurouracil chemotherapy regimen. Hence, its accurate detection is important. At present, multiplex PCR suffices for MSI analysis with good efficiency. But with progressing development, in a few years NGS will replace PCR for MSI analysis.A modified computational algorithm can be used for MSI analysis using NGS. The FASTQ file obtained after sequencing is not aligned to the reference human genome. Instead, the adaptor sequences used for enrichment of the MSI loci are used as a reference to group the reads into the respective locus. This reduces the burden of computational analysis to a massive extent and excludes the need for a highly trained bioinformatician.The cost of ... sequencing using an NGS platform has been reducing and this will confer a monetary benefit. Moreover

کلمات کلیدی:

Colorectal Cancer, Cancer Diagnosis, Gene and Cancer, Cell and Cancer, Cancer Treatment and Management