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Tumor tracking and evolution analysis of hepatocellular carcinoma progression by ultra-deep sequencing of the entire mitochondrial genome

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Hepatocellular carcinoma (HCC) is the third most lethal cancer due to its late detection, high recurrence and limited therapeutic option. Since mitochondrial (mt) genome is highly susceptible to DNA alterations due to the lack of protective histones and limited repair system, the mt-mutation pattern can be targeted as a novel tool of tumor evolution analysis. Herein, we aimed to characterize intratumor clonal structure by ultra-deep sequencing of entire mt-genome for better understanding how HCC originate, develop and progress. In total, 48 HCC nodules and corresponding peri-tumor areas were analyzed. Primer sets spanning the whole mt-DNA were designed and multiplex-PCR setup was established. Target enriched libraries of mt-DNA was sequenced by MiSeq-platform and NGS data was interpreted by the CLC Software. Notably, 100% of reads mapped to the mt-target regions indicating efficient mt-primer design and a good run performance. Whole mt-genome screening revealed a wide spectrum of mt-alterations, typically distributed in the D-Loop region and the respiratory chain complex genes. Particularly in HCC nodules of non-cirrhotic origin mt-mutations were higher than cirrhosis-related HCC. However, high mt-mutation rate was also observed in the peri-tumor areas suggesting that mt-genome is susceptible at earliest stage of hepatocarcinogenesis. Furthermore, most HCC nodules of individual sample have identical mt-mutations indicating the monoclonal HCC origin. Interestingly, the increasing numbers and frequency of particular panel of mt-hot-spot mutations refer to the progression of HCC dedifferentiation. In conclusion, our mt-genome screening based approach representing rapid and sensitive molecular tool and provide novel insights in cancer diagnostics and therapeutic strategies.

Biography

Wafa Amer is a Physician who was awarded MBBCh in 2010 from Misurata University, Libya. She has migrated to Germany to learn state-of-the-art techniques and did her Master thesis at the Institute for Pathology at the University Hospital of Cologne, Germany.

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