

PP8.1. MULTI-OMICS METODE U RAZVOJU BIOMARKERA ZA MASLD – GENOMIKA I TRANSKRIPTOMIKA

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Multifaktorska priroda masne bolesti jetre udružene sa metaboličkom disfunkcijom (*metabolic dysfunction-associated steatotic liver disease*, MASLD) obuhvata interakciju genetičke predispozicije, epigenetičke regulacije i uticaja faktora sredine. Genetički i epigenetički biomarkeri su stoga dragoceni alati za rano dijagnostikovanje, procenu rizika i praćenje progresije od steatoze do naprednijih stadijuma bolesti.

Nekoliko genetičkih varijanti je značajno povezano sa MASLD-om. Među njima su najviše proučavani polimorfizmi gena PNPLA3 (*patatin-like phospholipase domain-containing 3*), TM6SF2 (*transmembrane 6 superfamily member 2*) i MBOAT7 (*membrane-bound O-acyltransferase domain-containing 7*). Ove varijante utiču na metabolizam lipida u jetri, akumulaciju triglicerida i inflamaciju.

Epigenetički mehanizmi, a naročito mikroribonukleinske kiseline (miRNA, miR), igraju ključnu ulogu u posttranskripcionoj regulaciji ekspresije gena i progresiji bolesti. Među njima miR-122 najviše je zastupljena u jetri. Njena ekspresija je povišena u ranoj fazi steatoze, ali opada tokom progresije ka steatohepatitisu i fibrozi, što ukazuje na regulatornu funkciju zavisnu od stadijuma bolesti. Zajedno sa miR-21, miR-34a stimuliše akumulaciju triglicerida u hepatocitima tokom ranih faza bolesti i doprinosi aktivaciji inflamatornih i fibrotičkih puteva kako MASLD napreduje. Inhibicija miR-192, negativnog regulatora metabolizma lipida u jetri, povećava ekspresiju enzima uključenih u sintezu mononezasićenih masnih kiselina, čime se stimuliše deponovanje triglicerida. miR-155 aktivira signalne puteve koji stimulišu sintezu holesterolu i triglicerida u jetri, dok miR-375 podstiče ekspresiju gena povezanih sa sintezom triglicerida i formiranjem masnih kapi.

Biomarkeri genomike i transkriptomike predstavljaju važne činioce patoloških procesa u MASLD-u. Njihova kombinovana analiza predstavlja obećavajuću neinvazivnu alternativu biopsiji jetre u dijagnostici, određivanju stadijuma i dugoročnom praćenju bolesti.

PP8.1. MULTI-OMICS METHODS IN DEVELOPING BIOMARKERS OF MASLD - GENOMICS AND TRANSCRIPTOMICS

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The multifactorial nature of metabolic dysfunction-associated steatotic liver disease (MASLD) reflects the interplay of genetic susceptibility, epigenetic regulation, and environmental influences. Genetic and epigenetic biomarkers are therefore valuable for early diagnosis, risk stratification, and monitoring progression from steatosis to more advanced disease stages.

Several genetic variants have been significantly associated with MASLD. Among these, polymorphisms in the patatin-like phospholipase domain-containing 3 (PNPLA3), transmembrane 6 superfamily member 2 (TM6SF2), and membrane-bound O-acyltransferase domain-containing 7 (MBOAT7) genes are the most extensively studied. These variants influence hepatic lipid metabolism, triglyceride accumulation, and inflammatory responses.

Epigenetic mechanisms, particularly microribonucleic acids (miRNA, miR), play a critical role in post-transcriptional gene regulation and disease progression. Among these, miR-122 is the most abundant liver-specific miRNA. It is upregulated in early steatosis but declines during the transition to steatohepatitis and fibrosis, suggesting a stage-dependent regulatory function. Along with miR-21, miR-34a promotes triglyceride accumulation in hepatocytes during early disease stages and contributes to the activation of inflammatory and fibrotic pathways as MASLD advances. Inhibition of miR-192, a negative regulator of hepatic lipid metabolism, increases the expression of enzymes involved in monounsaturated fatty acid synthesis, thereby promoting triglyceride accumulation. miR-155 activates signalling pathways that enhance hepatic cholesterol and triglyceride synthesis, while miR-375 upregulates genes associated with triglyceride synthesis and lipid droplet formation.

Genomic and transcriptomic biomarkers represent important factors in the pathogenic processes of MASLD. Their combined assessment offers promise as a non-invasive alternative to liver biopsy for disease diagnosis, staging, and longitudinal monitoring.