

# Bioinformatička reanaliza ekspresijskih podataka otkriva niz prethodno neprepoznatih lncRNA uključenih u patogenezu aortne stenozе

## Bioinformatic reanalysis of gene expression microarray data reveals a number of previously unrecognized lncRNAs implicated in the pathogenesis of aortic stenosis

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**Uvod:** Duge nekodirajuće RNA (lncRNAs) molekule, odnosno nekodirajuće RNA veće od 200 nukleotida, tvore heterogenu skupinu regulatornih RNA molekula koja pored ostalog obuhvaća intergenske lncRNA, antisens lncRNA transkripte i eRNA (enhancer lncRNA) molekule. S obzirom na sposobnost moduliranja stanične miR/mRNA mreže i strukture kromatina terapijski potencijal lncRNA izrazio je velik te otvara mogućnosti za razvoj novih strategija liječenja u kardiovaskularnoj medicini. Nedavne studije pokazuju da promjene u ekspresiji i funkciji lncRNA igraju važnu ulogu u razvoju i progresiji aortne stenozе (AS) i AS-inducirane hipertrofije srca. Međutim, naše znanje o lncRNA diferencijalno izraženima u stenozom tkivu aortalnih zalistaka ili tijekom AS-inducirane srčane fibroze i remodeliranja miokarda ograničeno je tek na nekoliko primjera.<sup>1</sup>

**Metode:** Bioinformatička reanaliza dosad objavljenih ekspresijskih podataka dobivenih obradom postoperativnih uzoraka AS pacijenata te kontrolnih, patološki nepromijenjenih uzoraka aortalnih zalistaka izvršena je uporabom mrežnog programa DAVID (Database for Annotation, Visualization and Integrated Discovery) v6.8.

**Rezultati:** Osim lncRNA, MALAT1 i H19 sa već poznatom ulogom u osteogenoj transdiferencijaciji valvularnih intersticijskih stanica tijekom kalcifikacije aortalnih zalistaka, bioinformatička reanaliza otkrila je nekoliko prethodno neprepoznatih intergenskih, intronskih i antisens lncRNA molekula različito izraženih u stenotičkim zalisticima AS pacijenata u odnosu na kontrolno, patološki nepromijenjeno tkivo aortalnih zalistaka (slika 1).

**Zaključak:** Bioinformatička analiza ekspresijskih studija u kombinaciji s novim, dorađenim podacima o nukleotidnom slijedu humanog genoma predstavlja koristan alat za otkrivanje prethodno neprepoznatih lncRNA transkripta upletenih u nastanak i razvoj aortalne stenozе.

**Objective:** Long noncoding RNAs (lncRNAs), a class of noncoding RNA larger than 200 nucleotides, constitute a heterogenic class of regulatory RNAs that includes, for example, intergenic lncRNAs, antisense transcripts, and enhancer RNAs. Due to their ability to modulate miR/mRNA networks and chromatin structure their therapeutic potential is extremely vast thus opening the opportunity for the development of new treatment strategies to be used in cardiovascular medicine. Recent studies indicate that altered expression and function of lncRNAs have also an important role in the development and progression of aortic valve stenosis (AS) and AS-induced cardiac hypertrophy. However, our knowledge of lncRNAs differentially expressed in stenotic aortic valves or during AS-induced cardiac fibrosis and remodelling is still limited on a few examples and as such, requires further investigation.<sup>1</sup>

**Methods:** We performed bioinformatic reanalysis of published microarray expression studies of stenotic and control human aortic valves tissue samples. Data are analyzed using the online Database for Annotation, Visualization and Integrated Discovery (DAVID) v6.8.

**Results:** In addition to lncRNA MALAT1 and H19 with known role in the osteogenic transdifferentiation of valvular interstitial cells during the process of aortic valve calcification bioinformatic analysis revealed several previously unrecognized intergenic, intronic and antisense lncRNAs and lncRNA relate miRNA host genes that are differentially expressed in aortic valve tissue of AS patients compared to control valves (Figure 1).

**Conclusion:** Bioinformatic data mining of gene expression microarray data combined with upgraded annotation of the human genome landscape provides a useful tool for revealing many previously unrecognized lncRNA transcripts implicated in the pathogenesis of AS.

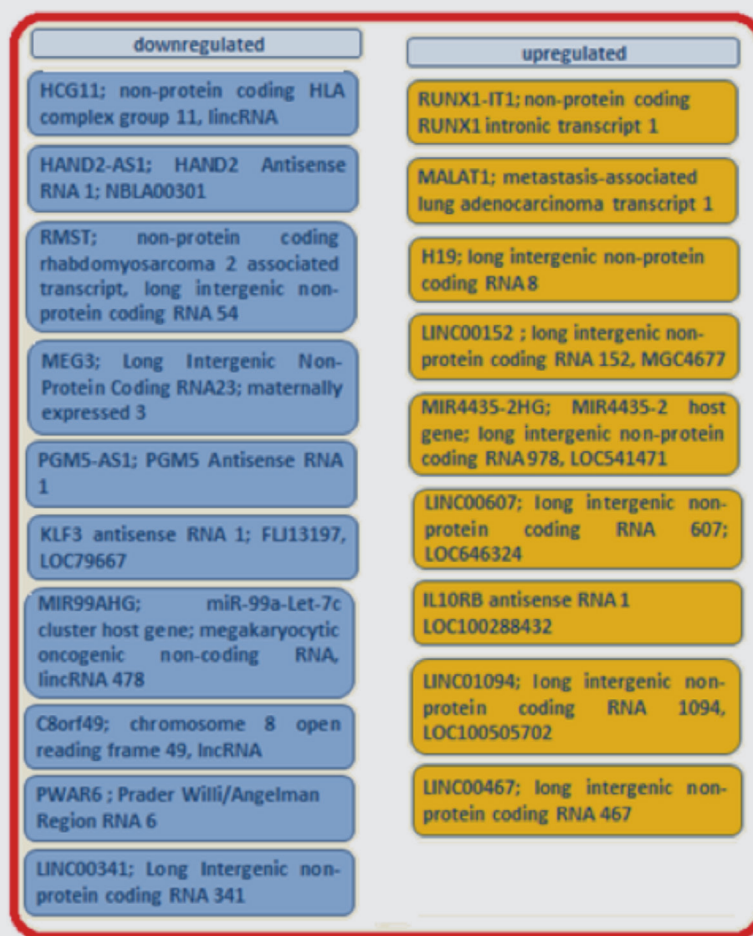


FIGURE 1. LncRNA differentially expressed in aortic stenosis tissue compared to normal aortic valve leaflets.

#### LITERATURE

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