Supplementary material

Probes identification

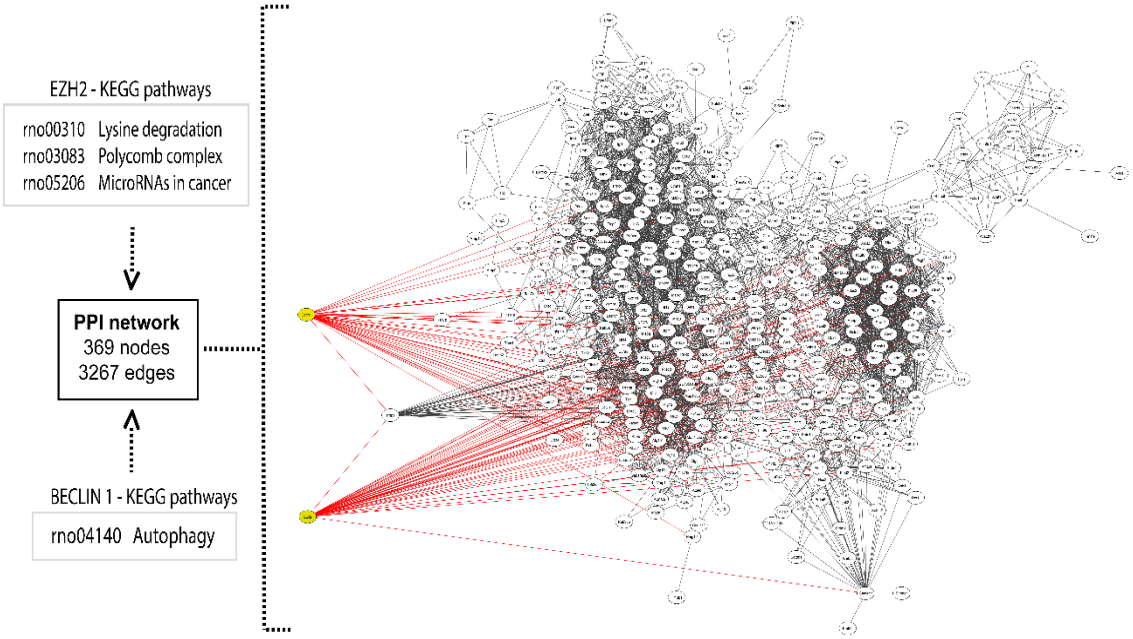
Supplementary Table 1 describes the identification of TaqMan probes that were used to evaluate the gene expression of hepatic inflammation in the liver and circulating microRNAs.

Supplementary Table 1 Probes identification

Assay name	**Assay ID**	**RefSeq**
Liver inflammatory markers		
Aldob	Rn01768292_m1	NM_012496.2
Tuba1c	Rn01761876_g1	NM_001011995.1
Afp	Rn00560661_m1	NM_012493.2
Mmp2	Rn01538170_m1	NM_031054.2
Mmp9	Rn00579162_m1	NM_031055.1
Map1lc3b	Rn02132764_s1	NM_022867.2
p62/Sqstm1	Rn00709977_m1	NM_175843.4
Becn1	Rn00586976_m1	NM_001034117.1
Ezh2	Rn01500693_m1	NM_001134979
Carm1	Rn00491422_m1	NM_001030041.3
Actb	Rn01640049_m1	NM_198130.1
microRNAs		**Mature miRNA Sequence**
rno-miR-122-5p	002245	UGGAGUGUGACAAUGGUGUUUG
hsa-miR-34a-5p	000426	UGGCAGUGUCUUAGCUGGUUGU
hsa-miR-26b-5p	000407	UUCAAGUAAUUCAGGAUAGGU
rno-miR-224-5p	464298_mat	CAAGUCACUAGUGGUUCCGUUU
hsa-mir-33a	002135	GUGCAUUGUAGUUGCAUUGCA
mmu-miR-143-5p	463509_mat	GGUGCAGUGCUGCAUCUCUGG
hsa-miR-155-5p	000479	UUAAUGCUAAUCGUGAUAGGGG
hsa-miR-375-3p	000564	UUUGUUCGUUCGGCUCGCGUGA
hsa-miR-21-5p	000397	UAGCUUAUCAGACUGAUGUUGA
cel-miR-39-3p	000200	UCACCGGGUGUAAAUCAGCUUG

Results

All signaling pathways associated with enhancer of zeste homolog-2 (EZH2) were thoroughly examined, along with the autophagy pathway in which beclin-1 (BECN1) plays a role. For to it, Input data for predicting a protein-protein interaction (PPI) network representative of EZH2 pathways (rno00310; rno03083; and rno05206), as well as the autophagy pathway (rno04140), were derived from a curated network map sourced from KEGG[1]. A network was obtained Using STRING 12. 0[2], all prediction methods were enabled, except for text-mining option, the medium degree of confidence ($P \geq 0.400$); and a network depth equal to 1. Subsequently, the Pesca 3.8.0 plugin within cytoscape was utilized to identify all the shortest paths between the EZH2 and BECN1 nodes[3]. Based on this strategy, our objective was to determine whether a direct modulation exists between EZH2 and BECN1. Notably, only the transcription bactor Dp-1 (TFDP1) protein exhibited a connection with both BECN1 and EZH2 within the network (bulk data obtained from the Pesca plugin is available in an XLS archive). In addition, the correlation between these genes or proteins suggests co-expression, as indicated by the network's score of 0.4, implying simultaneous transcription under specific cellular conditions. Based on the collective evidence presented, BECN1 is not target of the EZH2-H3K27 reaction axis. Information shown in Supplementary Figure 1.



Supplementary Figure 1 Protein-protein interaction network representing autophagy and enhancer of zeste homolog-2 cell signaling epigenetic modulation.

References

1 **Kanehisa M**, Goto S. KEGG: kyoto encyclopedia of genes and genomes. *Nucleic Acids Res* 2000; **28**: 27-30 [PMID: 10592173 DOI: 10.1093/nar/28.1.27]

2 **Szklarczyk D**, Kirsch R, Koutrouli M, Nastou K, Mehryary F, Hachilif R, Gable AL, Fang T, Doncheva NT, Pyysalo S, Bork P, Jensen LJ, von Mering C. The STRING database in 2023: protein-protein association networks and functional enrichment analyses for any sequenced genome of interest. *Nucleic Acids Res* 2023; **51**: D638-D646 [PMID: 36370105 DOI: 10.1093/nar/gkac1000]

3 **Scardoni G**, Tosadori G, Pratap S, Spoto F, Laudanna C. Finding the shortest path with PesCa: a tool for network reconstruction. *F1000Res* 2015; **4**: 484 [PMID: 27781081 DOI: 10.12688/f1000research.6769.1]