Gene network of hepatocellular carcinoma under mechanical stress of the cell

P. M. Revva, P. S. Demenkov, V. A. Ivanisenko
Novosibirsk State University, Institute of Cytology and Genetics

Purpose

- Reconstruction of the gene network of hepatocellular carcinoma under mechanical stress and analysis of its relationship with the main components of the external pathway of apoptosis.

Tasks

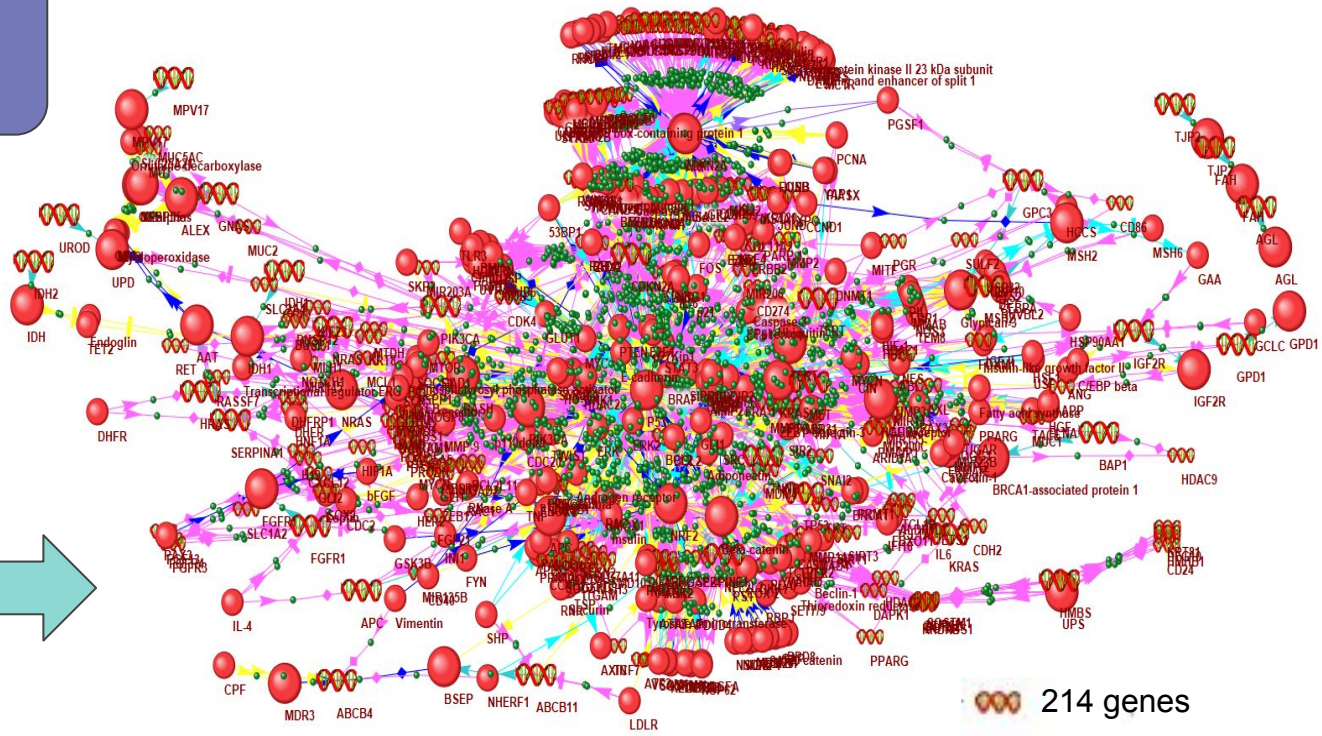
1. Reconstruct the gene network of hepatocellular carcinoma based on human SNP data and expand it through third-party interactions of network genes identified in the analysis of scientific publications using the ANDSystem computer system;
2. Reconstruct molecular genetic pathways of regulation of the external pathway of apoptosis under mechanical stress using the ANDSystem;
3. Reconstruct and analyze the structural and functional features of regulatory pathways, including components (proteins/genes) of the external pathway of apoptosis, mechanical stress, and genes associated with HCC;
4. To identify proteins that are simultaneously involved in three processes: they are components of the HCC gene network, a signaling pathway for response to mechanical stress, and are associated with markers of receptor-induced apoptosis.

Construction of the HCC gene network

ClinVar
Clinically relevant variation

29 genes

ANDVisio



214 genes

279 proteins

2002 connections

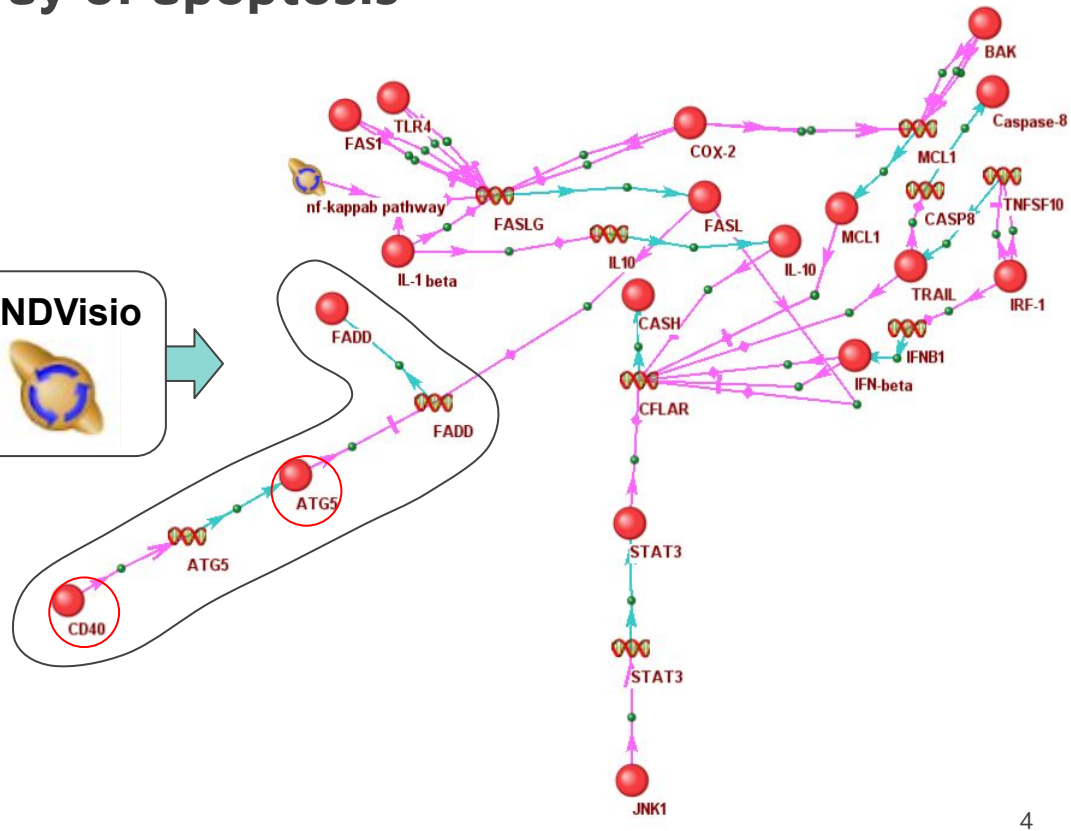
Reconstruction and analysis of gene networks combining molecular genetic pathways of regulation by mechanical stress of the external pathway of apoptosis

GENEONTOLOGY
Unifying Biology

70 proteins associated with cell response to mechanical stress

ANDVisio

Apoptosis protein:
FADD, cFLIP, caspase-8



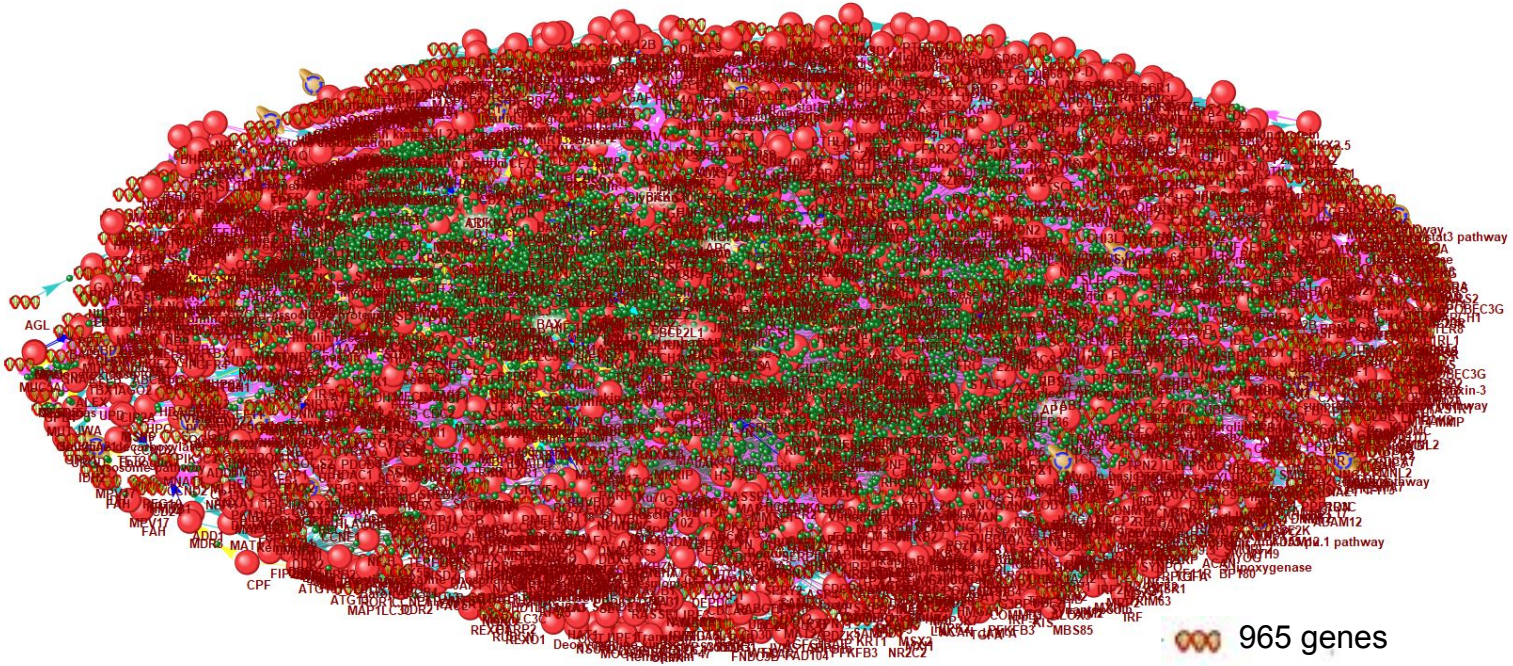
Building a union of all regulatory molecular genetic pathways and a gene network

Centrality according to the degree of vertices:

- p53
- TNF
- STAT3
- APP
- HUR

Centrality through mediation:

- p53
- TNF
- STAT3
- APP
- HUR



965 genes

1273 proteins

8369 connections

Conclusions

1. We reconstructed the HCC gene network using ANDSystem based on a two-stage approach, including building the core of the gene network according to SNP data associated with HCC, and further expanding the network by adding genes associated through interactions with core genes. The resulting gene network included 214 genes and 279 proteins interconnected by 2002 interactions;

2. We identified potential pathways describing the regulation of the extrinsic pathway of apoptosis in response to mechanical stress. Among the response proteins to mechanical stress were JNK1, CD40, among the mediator proteins: STAT3, ATG5, E-cadherin, TNF, MCL1, p21;

3. We identified potential pathways through which the influence of HCC on the function of the external apoptosis pathway is possible. Among the proteins of the HCC gene network, p53, PIK3CA, IL-1, ARF, APC, IDH1 were isolated, and among the proteins regulated by them, JNK1, CD40, STAT3, ATG5, E-cadherin, TNF, MCL1, p21 were selected.

4. An analysis of the topological properties of the resulting gene network showed that the p53, STAT3, TNF, APP, and HUR proteins have the highest mediation centrality, while the p53, STAT3, TNF, APP, and HUR proteins have degree centrality. Among proteins of regulatory molecular genetic pathways, APP and HUR had the highest centrality.