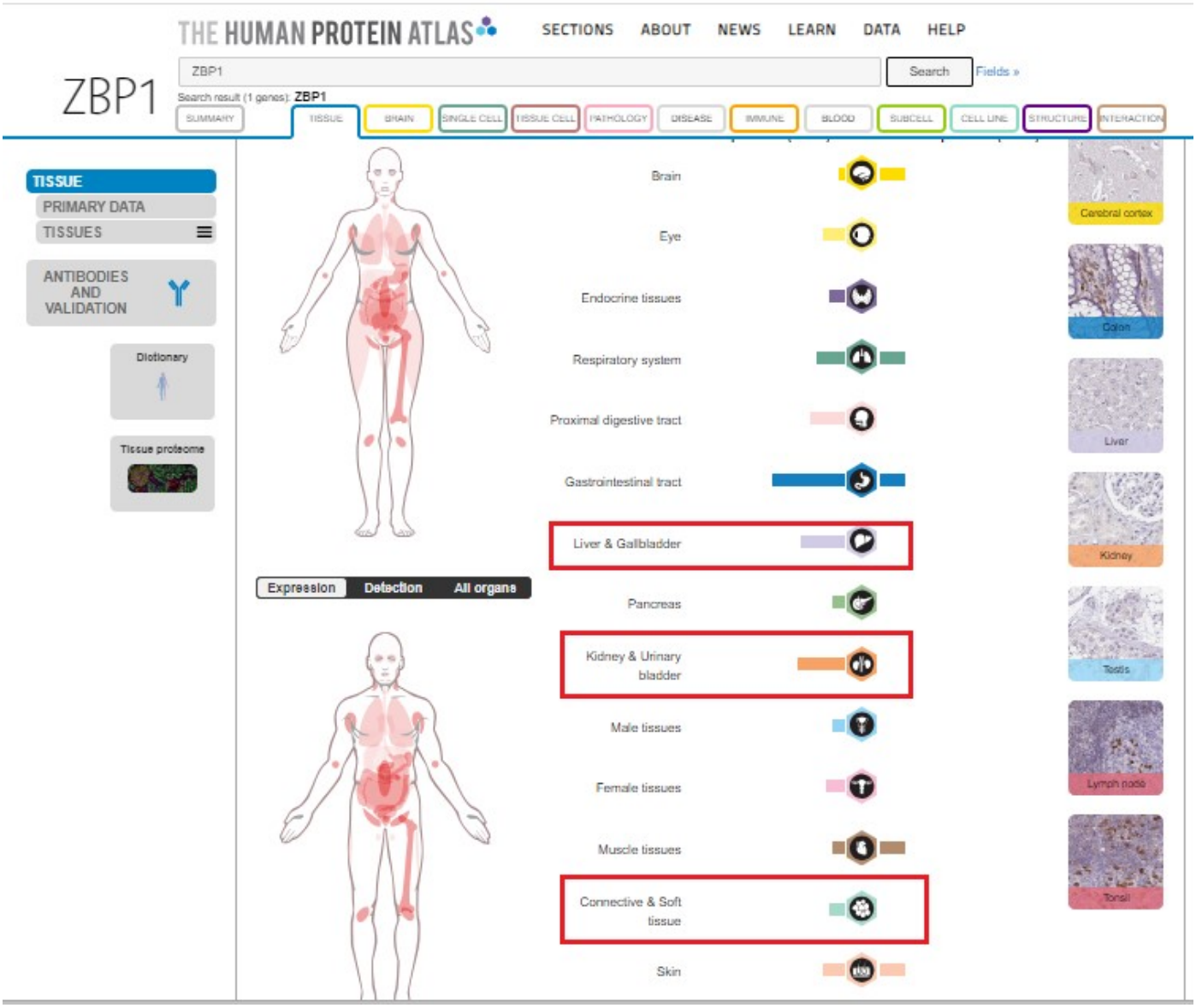
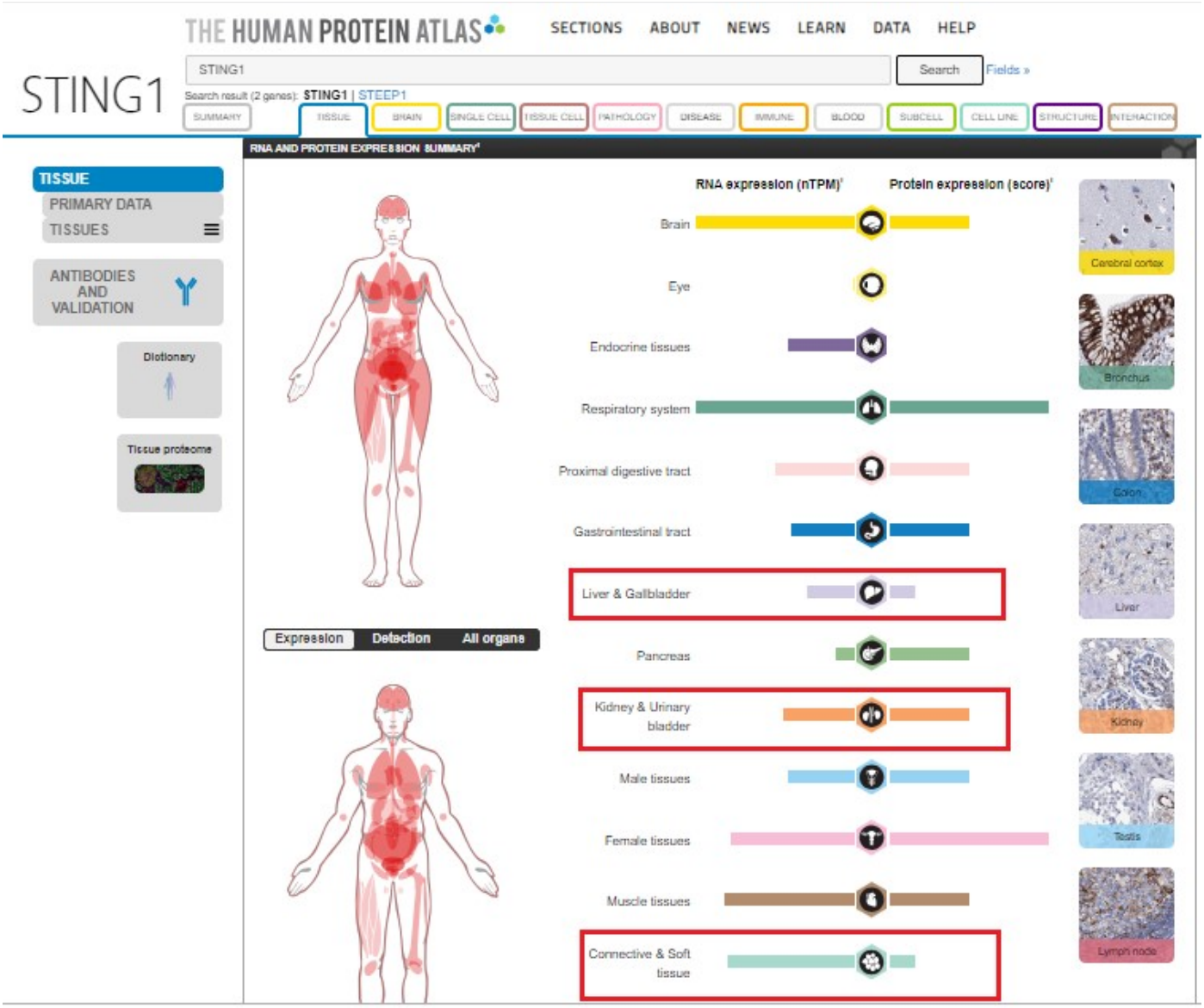
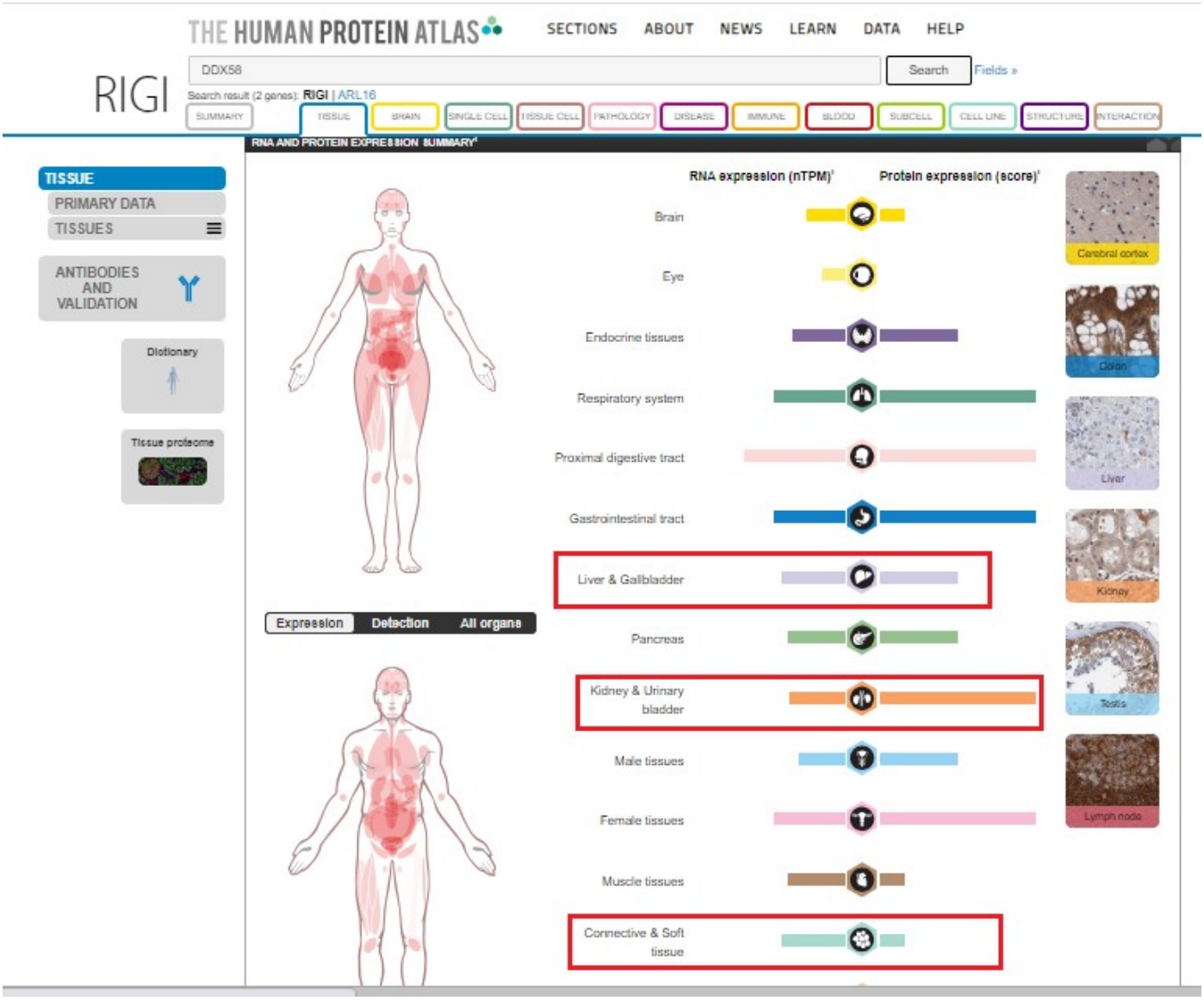
# Supplementary information:

## Supplementary Figures:

**S1 Figures:** Validation of the significant expression of the candidate mRNAs (ZBP1, STING1, and DDX58=RIG-1) in the T2DM-related tissues using THE HUMAN PROTEIN ATLAS database https://www.proteinatlas.org/, Jan 2022.




THE HUMAN PROTEIN ATLAS
SECTIONS ABOUT NEWS LEARN DATA HELP
STING1
STING1
Search
Fields »
Search result (2 genes): STING1 | STEEP1
SUMMARY TISSUE BRAIN SINGLE CELL TISSUE CELL PATHOLOGY DISEASE IMMUNE BLOOD SUBCELL CELL LINE STRUCTURE INTERACTION
TISSUE
PRIMARY DATA
TISSUES
ANTIBODIES AND VALIDATION
Dictionary
Tissue proteome
RNA AND PROTEIN EXPRESSION SUMMARY
RNA expression (nTPM)
Protein expression (score)
Brain
Eye
Endocrine tissues
Respiratory system
Proximal digestive tract
Gastrointestinal tract
Liver & Gallbladder
Pancreas
Kidney & Urinary bladder
Male tissues
Female tissues
Muscle tissues
Connective & Soft tissue
Expression
Detection
All organs
Cerebral cortex
Bronchus
Colon
Liver
Kidney
Testis
Lymph node


THE HUMAN PROTEIN ATLAS
SECTIONS
ABOUT
NEWS
LEARN
DATA
HELP
RIGI
DDX58
Search
Fields »
Search result (2 genes): RIGI | ARL16
SUMMARY
TISSUE
BRAIN
SINGLE CELL
TISSUE CELL
PATHOLOGY
DISEASE
IMMUNE
BLOOD
SUBCELL
CELL LINE
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INTERACTION
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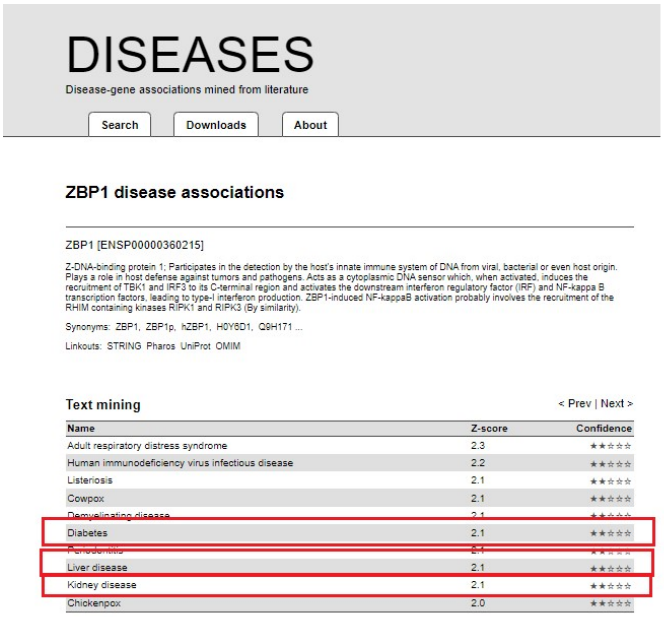
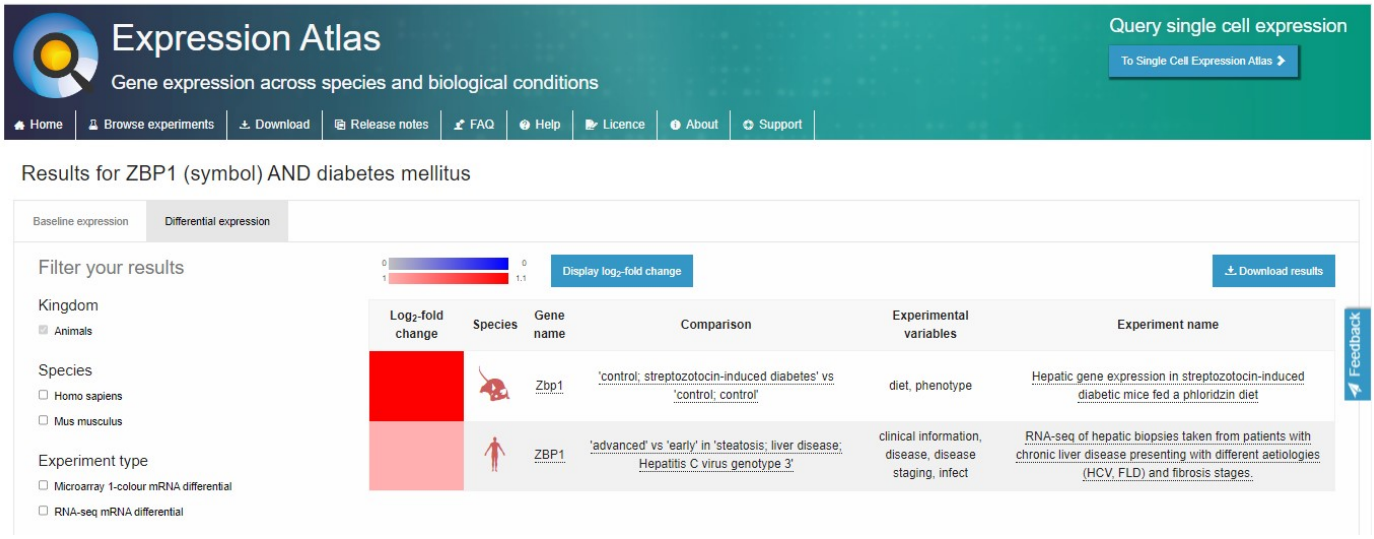
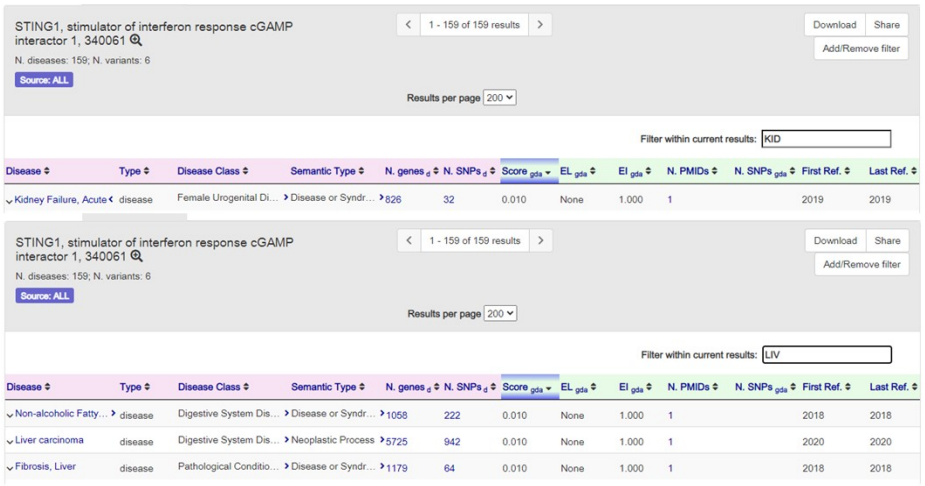
Gastrointestinal tract
Liver & Gallbladder
Pancreas
Kidney & Urinary bladder
Male tissues
Female tissues
Muscle tissues
Connective & Soft tissue
Expression
Detection
All organs
Cerebral cortex
Colon
Liver
Kidney
Testis
Lymph node

**S2 Figures:** Validation of the implication of the candidate mRNAs (ZBP1, STING1, and DDX58=RIG-1) in the development of diabetes, and kidney and liver diseases using DisGeNET database (https://www.disgenet.org/home/), the Expression Atlas database (https://www.ebi.ac.uk/gxa/home) and diseases database (https://diseases.jensenlab.org/Search), Jan 2022.





STING1, stimulator of interferon response cGAMP interactor 1, 340061

N. diseases: 159; N. variants: 6

Source: ALL

1 - 159 of 159 results

Download | Share | Add/Remove filter

Results per page 200

Filter within current results: KID

| Disease | Type | Disease Class | Semantic Type | N. genes $_d$ | N. SNPs $_d$ | Score $_{gda}$ | EL $_{gda}$ | EI $_{gda}$ | N. PMIDs | N. SNPs $_{gda}$ | First Ref. | Last Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney Failure, Acute | disease | Female Urogenital Di… | Disease or Syndr… | 826 | 32 | 0.010 | None | 1.000 | 1 | | 2019 | 2019 |



STING1, stimulator of interferon response cGAMP interactor 1, 340061

N. diseases: 159; N. variants: 6

Source: ALL

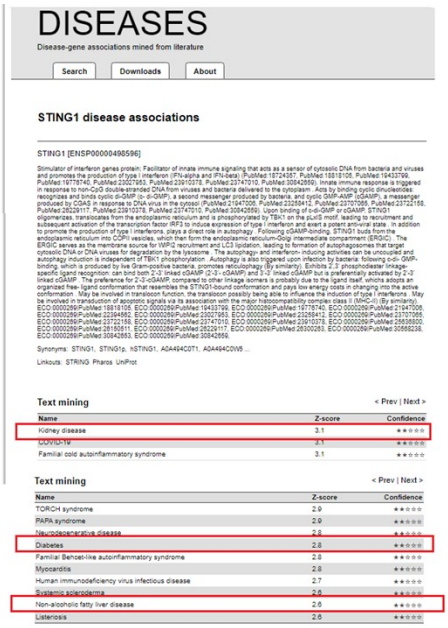
1 - 159 of 159 results

Download | Share | Add/Remove filter

Results per page 200

Filter within current results: LIV

| Disease | Type | Disease Class | Semantic Type | N. genes $_d$ | N. SNPs $_d$ | Score $_{gda}$ | EL $_{gda}$ | EI $_{gda}$ | N. PMIDs | N. SNPs $_{gda}$ | First Ref. | Last Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Non-alcoholic Fatty… | disease | Digestive System Dis… | Disease or Syndr… | 1058 | 222 | 0.010 | None | 1.000 | 1 | | 2018 | 2018 |
| Liver carcinoma | disease | Digestive System Dis… | Neoplastic Process | 5725 | 942 | 0.010 | None | 1.000 | 1 | | 2020 | 2020 |
| Fibrosis, Liver | disease | Pathological Conditio… | Disease or Syndr… | 1179 | 64 | 0.010 | None | 1.000 | 1 | | 2018 | 2018 |



DISEASES

Disease-gene associations mined from literature

Search | Downloads | About

STING1 disease associations

STING1 [ENSP00000496596]

Synonyms: STING1, STING1p, hSTING1, A0A494C0T1, A0A494C0W5 ...

Linkouts: STRING Pharos UniProt

Text mining

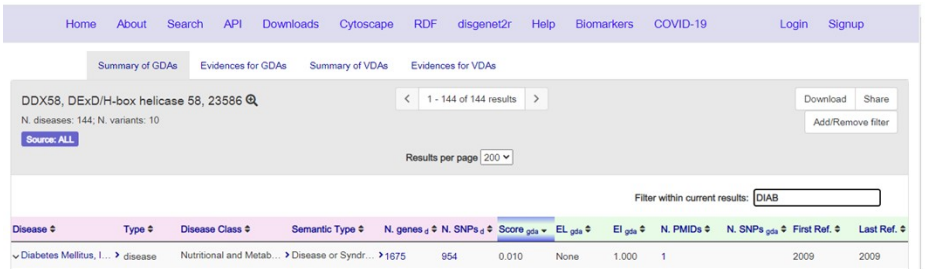
< Prev | Next >

| Name | Z-score | Confidence |
|---|---|---|
| Kidney disease | 3.1 | ★★★☆☆ |
| Lupus | 3.1 | ★★★☆☆ |
| Familial cold autoinflammatory syndrome | 3.1 | ★★★☆☆ |

Text mining

< Prev | Next >

| Name | Z-score | Confidence |
|---|---|---|
| TORCH syndrome | 2.9 | ★★☆☆☆ |
| PAPA syndrome | 2.9 | ★★☆☆☆ |
| Neurodegenerative disease | 2.8 | ★★☆☆☆ |
| Diabetes | 2.8 | ★★☆☆☆ |
| Familial Behcet-like autoinflammatory syndrome | 2.8 | ★★☆☆☆ |
| Myocarditis | 2.8 | ★★☆☆☆ |
| Human immunodeficiency virus infectious disease | 2.7 | ★★☆☆☆ |
| Systemic scleroderma | 2.6 | ★★☆☆☆ |
| Non-alcoholic fatty liver disease | 2.6 | ★★☆☆☆ |
| Listeriosis | 2.6 | ★★☆☆☆ |



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Summary of GDAs | Evidences for GDAs | Summary of VDAs | Evidences for VDAs

DDX58, DExD/H-box helicase 58, 23586

N. diseases: 144; N. variants: 10

Source: ALL

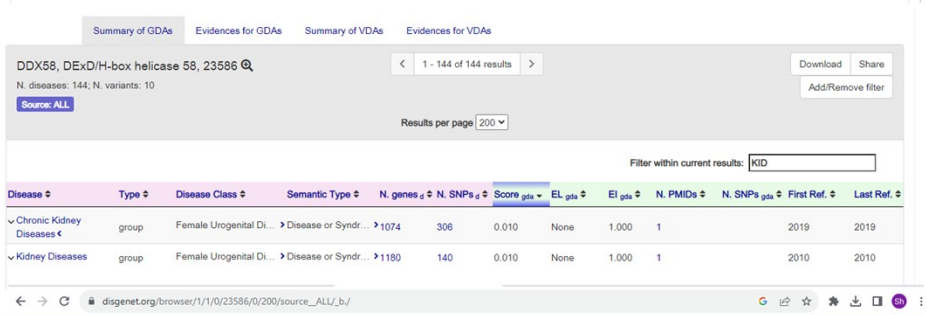
1 - 144 of 144 results

Download | Share | Add/Remove filter

Results per page 200

Filter within current results: DIAB

| Disease | Type | Disease Class | Semantic Type | N. genes $_d$ | N. SNPs $_d$ | Score $_{gda}$ | EL $_{gda}$ | EI $_{gda}$ | N. PMIDs | N. SNPs $_{gda}$ | First Ref. | Last Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Diabetes Mellitus, I… | disease | Nutritional and Metab… | Disease or Syndr… | 1675 | 954 | 0.010 | None | 1.000 | 1 | | 2009 | 2009 |



Summary of GDAs | Evidences for GDAs | Summary of VDAs | Evidences for VDAs

DDX58, DExD/H-box helicase 58, 23586

N. diseases: 144; N. variants: 10

Source: ALL

1 - 144 of 144 results

Download | Share | Add/Remove filter

Results per page 200

Filter within current results: KID

| Disease | Type | Disease Class | Semantic Type | N. genes $_d$ | N. SNPs $_d$ | Score $_{gda}$ | EL $_{gda}$ | EI $_{gda}$ | N. PMIDs | N. SNPs $_{gda}$ | First Ref. | Last Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Chronic Kidney Diseases | group | Female Urogenital Di… | Disease or Syndr… | 1074 | 306 | 0.010 | None | 1.000 | 1 | | 2019 | 2019 |
| Kidney Diseases | group | Female Urogenital Di… | Disease or Syndr… | 1180 | 140 | 0.010 | None | 1.000 | 1 | | 2010 | 2010 |

disgenet.org/browser/1/1/0/23586/0/200/source_ALL/_b/

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Summary of GDAs | Evidences for GDAs | Summary of VDAs | Evidences for VDAs

DDX58, DExD/H-box helicase 58, 23586

N. diseases: 144; N. variants: 10

Source: ALL

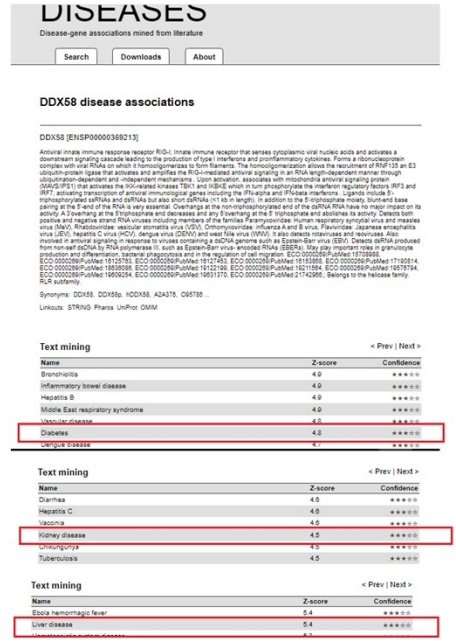
1 - 144 of 144 results

Download | Share | Add/Remove filter

Results per page 200

Filter within current results: LIV

| Disease | Type | Disease Class | Semantic Type | N. genes $_d$ | N. SNPs $_d$ | Score $_{gda}$ | EL $_{gda}$ | EI $_{gda}$ | N. PMIDs | N. SNPs $_{gda}$ | First Ref. | Last Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Liver carcinoma | disease | Digestive System Dis… | Neoplastic Process | 5725 | 942 | 0.020 | None | 1.000 | 2 | | 2014 | 2016 |
| Steatohepatitis | disease | Digestive System Dis… | Disease or Syndr… | 1143 | 75 | 0.010 | None | 1.000 | 1 | | 2013 | 2013 |



DISEASES

Disease-gene associations mined from literature

Search | Downloads | About

DDX58 disease associations

DDX58 [ENSP00000369213]

Synonyms: DDX58, DDX58p, hDDX58, A2A376, O95786 ...

Linkouts: STRING Pharos UniProt OMIM

Text mining

< Prev | Next >

| Name | Z-score | Confidence |
|---|---|---|
| Bronchiolitis | 4.9 | ★★★★☆ |
| Inflammatory bowel disease | 4.9 | ★★★★☆ |
| Hepatitis B | 4.9 | ★★★★☆ |
| Middle East respiratory syndrome | 4.9 | ★★★★☆ |
| Vascular disease | 4.8 | ★★★★☆ |
| Diabetes | 4.8 | ★★★★☆ |
| Dengue disease | 4.7 | ★★★★☆ |

Text mining

< Prev | Next >

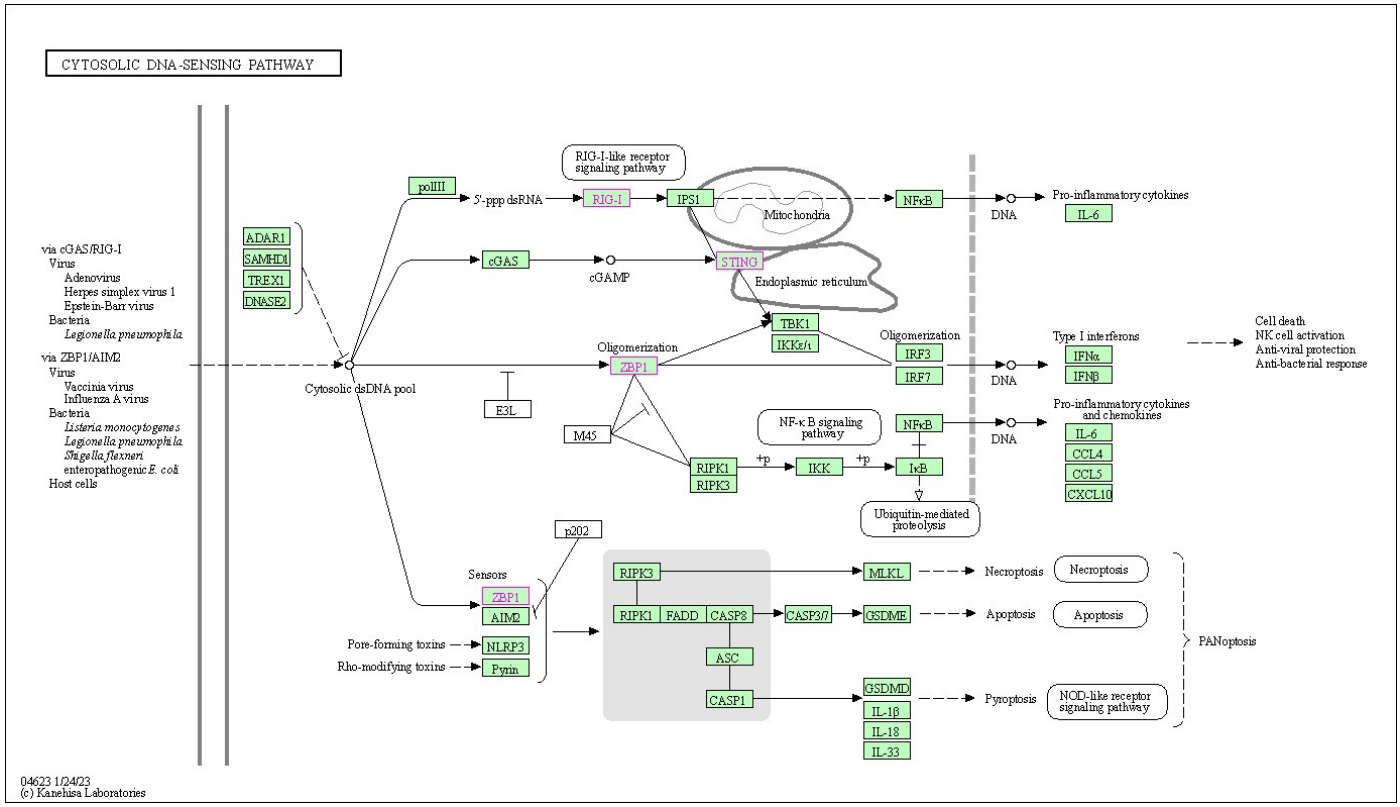
| Name | Z-score | Confidence |
|---|---|---|
| Diarrhea | 4.6 | ★★★★☆ |
| Hepatitis C | 4.6 | ★★★★☆ |
| Vasculitis | 4.6 | ★★★★☆ |
| Kidney disease | 4.5 | ★★★★☆ |
| Chikungunya | 4.5 | ★★★★☆ |
| Tuberculosis | 4.5 | ★★★★☆ |

Text mining

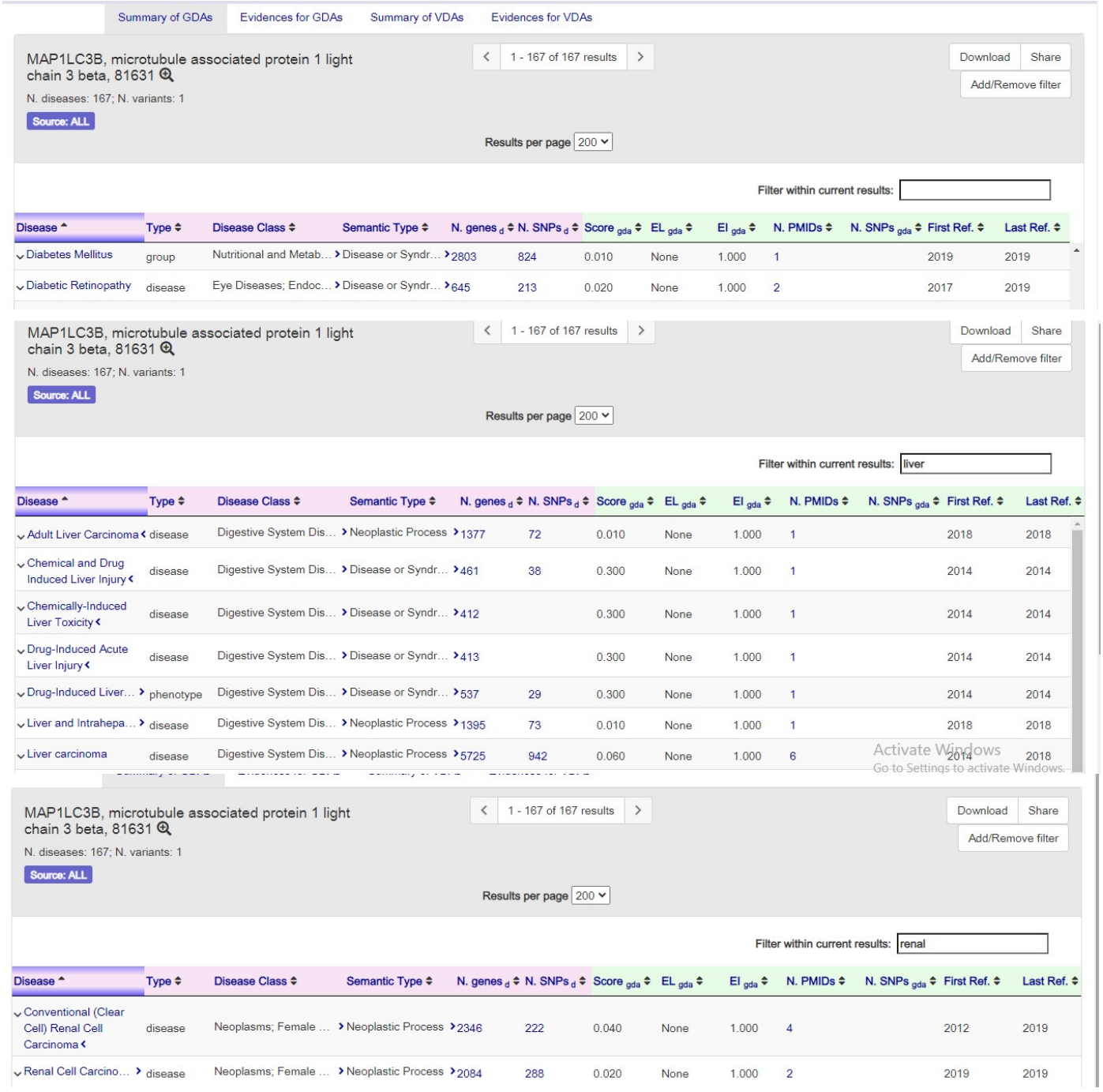
< Prev | Next >

| Name | Z-score | Confidence |
|---|---|---|
| Ebola hemorrhagic fever | 5.4 | ★★★★☆ |
| Liver disease | 5.4 | ★★★★☆ |

**S3 Figure:** The visualization of the candidate mRNAs (ZBP1, STING1, and DDX58=RIG-1) in the cGAS-STING pathway through KEGG pathway database (https://www.genome.jp/kegg/, Jan 2022)



**S4 Figures:** Validation of the implication of the selected biochemical effectors proteins (LC3B=MAP1LC3B, and TNF) in the development of diabetes, and kidney and liver diseases using DisGeNET database (https://www.disgenet.org/home/), Jan 2022.



Summary of GDAs | Evidences for GDAs | Summary of VDAs | Evidences for VDAs

MAP1LC3B, microtubule associated protein 1 light chain 3 beta, 81631

N. diseases: 167; N. variants: 1

Source: ALL

1 - 167 of 167 results

Download | Share | Add/Remove filter

Results per page 200

Filter within current results:

| Disease | Type | Disease Class | Semantic Type | N. genes $_d$ | N. SNPs $_d$ | Score $_{gda}$ | EL $_{gda}$ | EI $_{gda}$ | N. PMIDs | N. SNPs $_{gda}$ | First Ref. | Last Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Diabetes Mellitus | group | Nutritional and Metab… | Disease or Syndr… | 2803 | 824 | 0.010 | None | 1.000 | 1 | | 2019 | 2019 |
| Diabetic Retinopathy | disease | Eye Diseases; Endoc… | Disease or Syndr… | 645 | 213 | 0.020 | None | 1.000 | 2 | | 2017 | 2019 |

MAP1LC3B, microtubule associated protein 1 light chain 3 beta, 81631

N. diseases: 167; N. variants: 1

Source: ALL

1 - 167 of 167 results

Download | Share | Add/Remove filter

Results per page 200

Filter within current results: liver

| Disease | Type | Disease Class | Semantic Type | N. genes $_d$ | N. SNPs $_d$ | Score $_{gda}$ | EL $_{gda}$ | EI $_{gda}$ | N. PMIDs | N. SNPs $_{gda}$ | First Ref. | Last Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adult Liver Carcinoma | disease | Digestive System Dis… | Neoplastic Process | 1377 | 72 | 0.010 | None | 1.000 | 1 | | 2018 | 2018 |
| Chemical and Drug Induced Liver Injury | disease | Digestive System Dis… | Disease or Syndr… | 461 | 38 | 0.300 | None | 1.000 | 1 | | 2014 | 2014 |
| Chemically-Induced Liver Toxicity | disease | Digestive System Dis… | Disease or Syndr… | 412 | | 0.300 | None | 1.000 | 1 | | 2014 | 2014 |
| Drug-Induced Acute Liver Injury | disease | Digestive System Dis… | Disease or Syndr… | 413 | | 0.300 | None | 1.000 | 1 | | 2014 | 2014 |
| Drug-Induced Liver… | phenotype | Digestive System Dis… | Disease or Syndr… | 537 | 29 | 0.300 | None | 1.000 | 1 | | 2014 | 2014 |
| Liver and Intrahepa… | disease | Digestive System Dis… | Neoplastic Process | 1395 | 73 | 0.010 | None | 1.000 | 1 | | 2018 | 2018 |
| Liver carcinoma | disease | Digestive System Dis… | Neoplastic Process | 5725 | 942 | 0.060 | None | 1.000 | 6 | | 2014 | 2018 |



MAP1LC3B, microtubule associated protein 1 light chain 3 beta, 81631

N. diseases: 167; N. variants: 1

Source: ALL

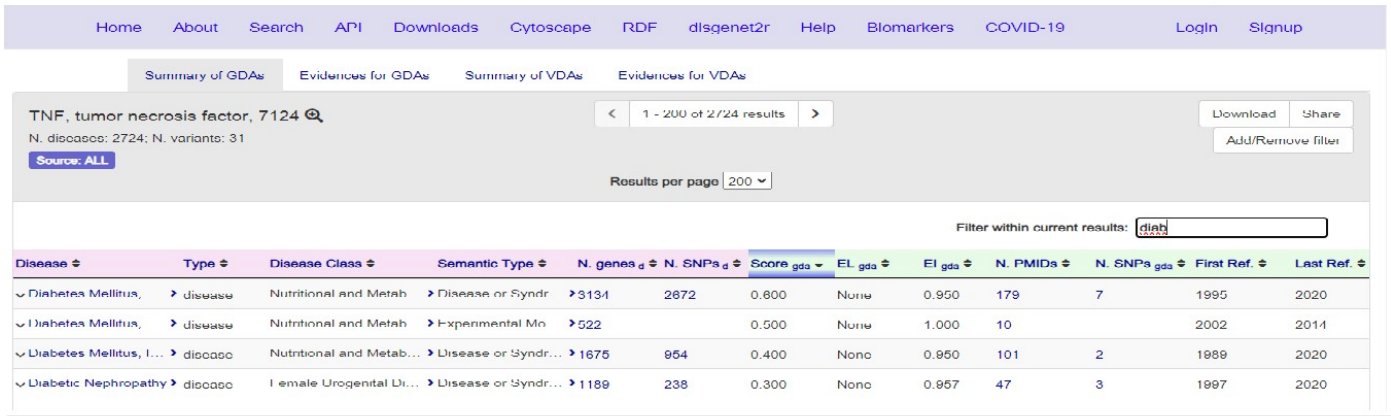
1 - 167 of 167 results

Download | Share | Add/Remove filter

Results per page 200

Filter within current results: renal

| Disease | Type | Disease Class | Semantic Type | N. genes $_d$ | N. SNPs $_d$ | Score $_{gda}$ | EL $_{gda}$ | EI $_{gda}$ | N. PMIDs | N. SNPs $_{gda}$ | First Ref. | Last Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Conventional (Clear Cell) Renal Cell Carcinoma | disease | Neoplasms; Female … | Neoplastic Process | 2346 | 222 | 0.040 | None | 1.000 | 4 | | 2012 | 2019 |
| Renal Cell Carcino… | disease | Neoplasms; Female … | Neoplastic Process | 2084 | 288 | 0.020 | None | 1.000 | 2 | | 2019 | 2019 |



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Summary of GDAs | Evidences for GDAs | Summary of VDAs | Evidences for VDAs

TNF, tumor necrosis factor, 7124

N. diseases: 2724; N. variants: 31

Source: ALL

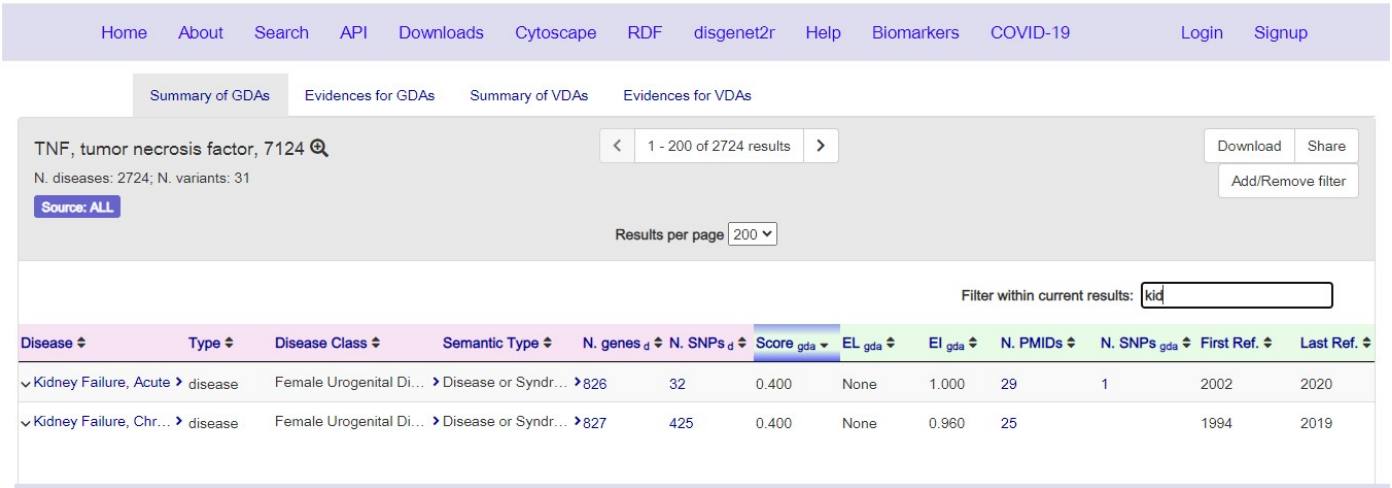
1 - 200 of 2724 results

Download | Share | Add/Remove filter

Results per page 200

Filter within current results: diab

| Disease | Type | Disease Class | Semantic Type | N. genes d | N. SNPs d | Score gda | EL gda | EI gda | N. PMIDs | N. SNPs gda | First Ref. | Last Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Diabetes Mellitus, | disease | Nutritional and Metab | Disease or Syndr | 3134 | 2672 | 0.600 | None | 0.950 | 179 | 7 | 1995 | 2020 |
| Diabetes Mellitus, | disease | Nutritional and Metab | Experimental Mo | 522 | | 0.500 | None | 1.000 | 10 | | 2002 | 2014 |
| Diabetes Mellitus, I... | disease | Nutritional and Metab... | Disease or Syndr... | 1675 | 954 | 0.400 | None | 0.950 | 101 | 2 | 1989 | 2020 |
| Diabetic Nephropathy | disease | Female Urogenital Di... | Disease or Syndr... | 1189 | 238 | 0.300 | None | 0.957 | 47 | 3 | 1997 | 2020 |



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Summary of GDAs | Evidences for GDAs | Summary of VDAs | Evidences for VDAs

TNF, tumor necrosis factor, 7124

N. diseases: 2724; N. variants: 31

Source: ALL

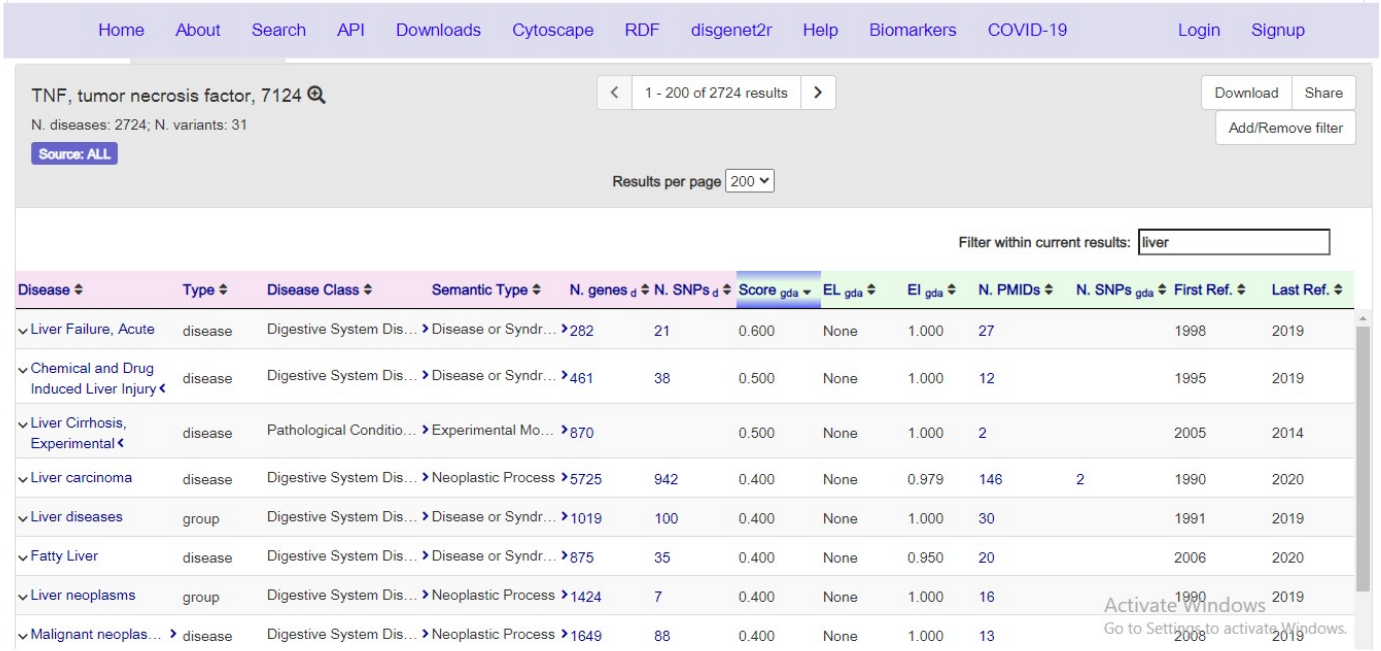
1 - 200 of 2724 results

Download | Share | Add/Remove filter

Results per page 200

Filter within current results: kid

| Disease | Type | Disease Class | Semantic Type | N. genes d | N. SNPs d | Score gda | EL gda | EI gda | N. PMIDs | N. SNPs gda | First Ref. | Last Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney Failure, Acute | disease | Female Urogenital Di... | Disease or Syndr... | 826 | 32 | 0.400 | None | 1.000 | 29 | 1 | 2002 | 2020 |
| Kidney Failure, Chr... | disease | Female Urogenital Di... | Disease or Syndr... | 827 | 425 | 0.400 | None | 0.960 | 25 | | 1994 | 2019 |



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TNF, tumor necrosis factor, 7124

N. diseases: 2724; N. variants: 31

Source: ALL

1 - 200 of 2724 results

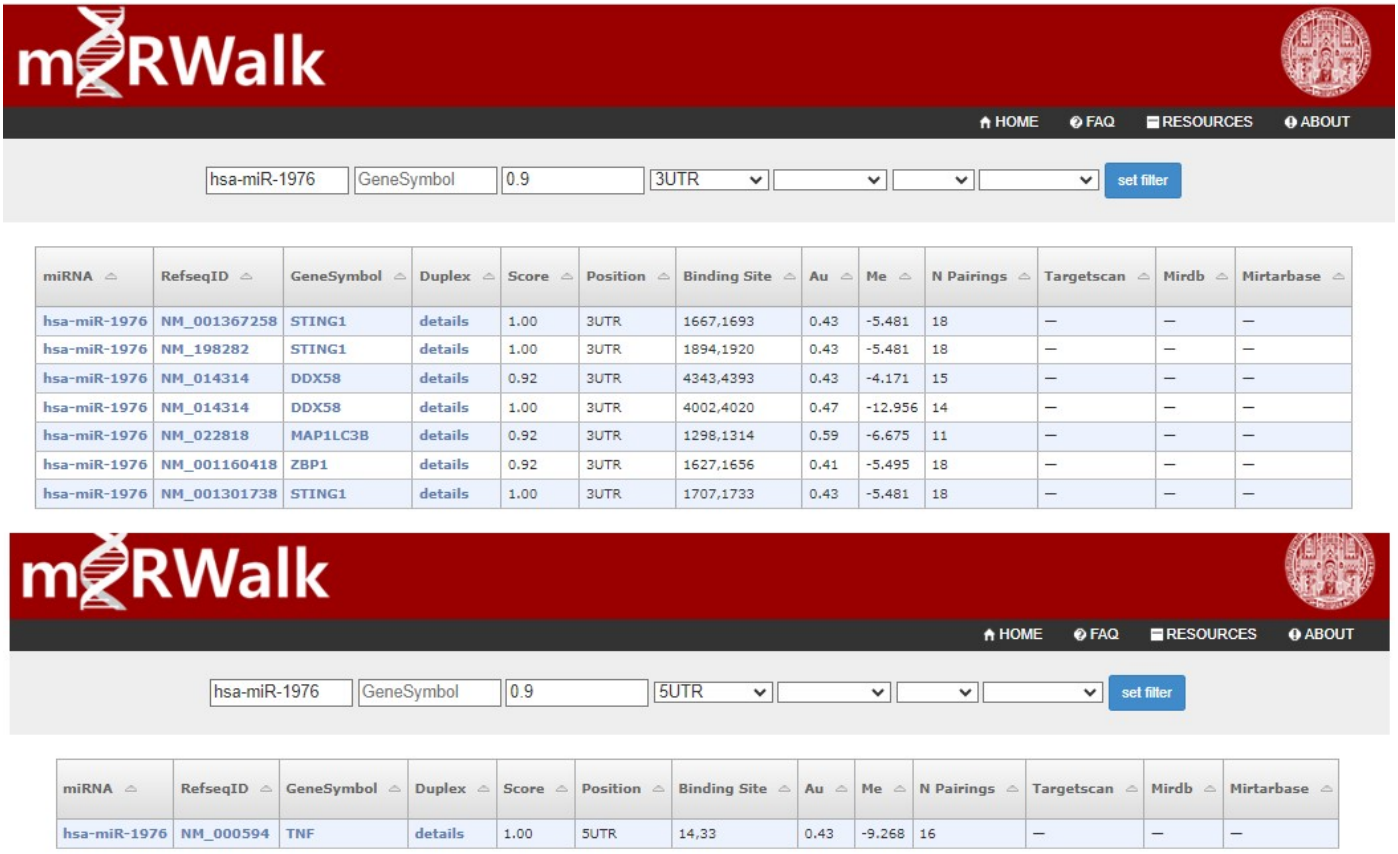
Download | Share | Add/Remove filter

Results per page 200

Filter within current results: liver

| Disease | Type | Disease Class | Semantic Type | N. genes d | N. SNPs d | Score gda | EL gda | EI gda | N. PMIDs | N. SNPs gda | First Ref. | Last Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Liver Failure, Acute | disease | Digestive System Dis... | Disease or Syndr... | 282 | 21 | 0.600 | None | 1.000 | 27 | | 1998 | 2019 |
| Chemical and Drug Induced Liver Injury | disease | Digestive System Dis... | Disease or Syndr... | 461 | 38 | 0.500 | None | 1.000 | 12 | | 1995 | 2019 |
| Liver Cirrhosis, Experimental | disease | Pathological Conditio... | Experimental Mo... | 870 | | 0.500 | None | 1.000 | 2 | | 2005 | 2014 |
| Liver carcinoma | disease | Digestive System Dis... | Neoplastic Process | 5725 | 942 | 0.400 | None | 0.979 | 146 | 2 | 1990 | 2020 |
| Liver diseases | group | Digestive System Dis... | Disease or Syndr... | 1019 | 100 | 0.400 | None | 1.000 | 30 | | 1991 | 2019 |
| Fatty Liver | disease | Digestive System Dis... | Disease or Syndr... | 875 | 35 | 0.400 | None | 0.950 | 20 | | 2006 | 2020 |
| Liver neoplasms | group | Digestive System Dis... | Neoplastic Process | 1424 | 7 | 0.400 | None | 1.000 | 16 | | 1990 | 2019 |
| Malignant neoplas... | disease | Digestive System Dis... | Neoplastic Process | 1649 | 88 | 0.400 | None | 1.000 | 13 | | 2008 | 2019 |

**S5 Figure:** Validation of the interaction between the three key mRNAs and two effector proteins with the retrieved miR-1976 from mirwalk3 (http://mirwalk.umm.uni-heidelberg.de/, Jan 2022)




| miRNA | RefseqID | GeneSymbol | Duplex | Score | Position | Binding Site | Au | Me | N Pairings | Targetscan | Mirdb | Mirtarbase |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| hsa-miR-1976 | NM_001367258 | STING1 | details | 1.00 | 3UTR | 1667,1693 | 0.43 | -5.481 | 18 | – | – | – |
| hsa-miR-1976 | NM_198282 | STING1 | details | 1.00 | 3UTR | 1894,1920 | 0.43 | -5.481 | 18 | – | – | – |
| hsa-miR-1976 | NM_014314 | DDX58 | details | 0.92 | 3UTR | 4343,4393 | 0.43 | -4.171 | 15 | – | – | – |
| hsa-miR-1976 | NM_014314 | DDX58 | details | 1.00 | 3UTR | 4002,4020 | 0.47 | -12.956 | 14 | – | – | – |
| hsa-miR-1976 | NM_022818 | MAP1LC3B | details | 0.92 | 3UTR | 1298,1314 | 0.59 | -6.675 | 11 | – | – | – |
| hsa-miR-1976 | NM_001160418 | ZBP1 | details | 0.92 | 3UTR | 1627,1656 | 0.41 | -5.495 | 18 | – | – | – |
| hsa-miR-1976 | NM_001301738 | STING1 | details | 1.00 | 3UTR | 1707,1733 | 0.43 | -5.481 | 18 | – | – | – |




| miRNA | RefseqID | GeneSymbol | Duplex | Score | Position | Binding Site | Au | Me | N Pairings | Targetscan | Mirdb | Mirtarbase |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| hsa-miR-1976 | NM_000594 | TNF | details | 1.00 | 5UTR | 14,33 | 0.43 | -9.268 | 16 | – | – | – |

**S6 Figure:** The association of miR-1976 with cGAS-STING-related pathways through DIANA tools mirPath 3 (http://www.microrna.gr/miRPathv3, Jan 2022)

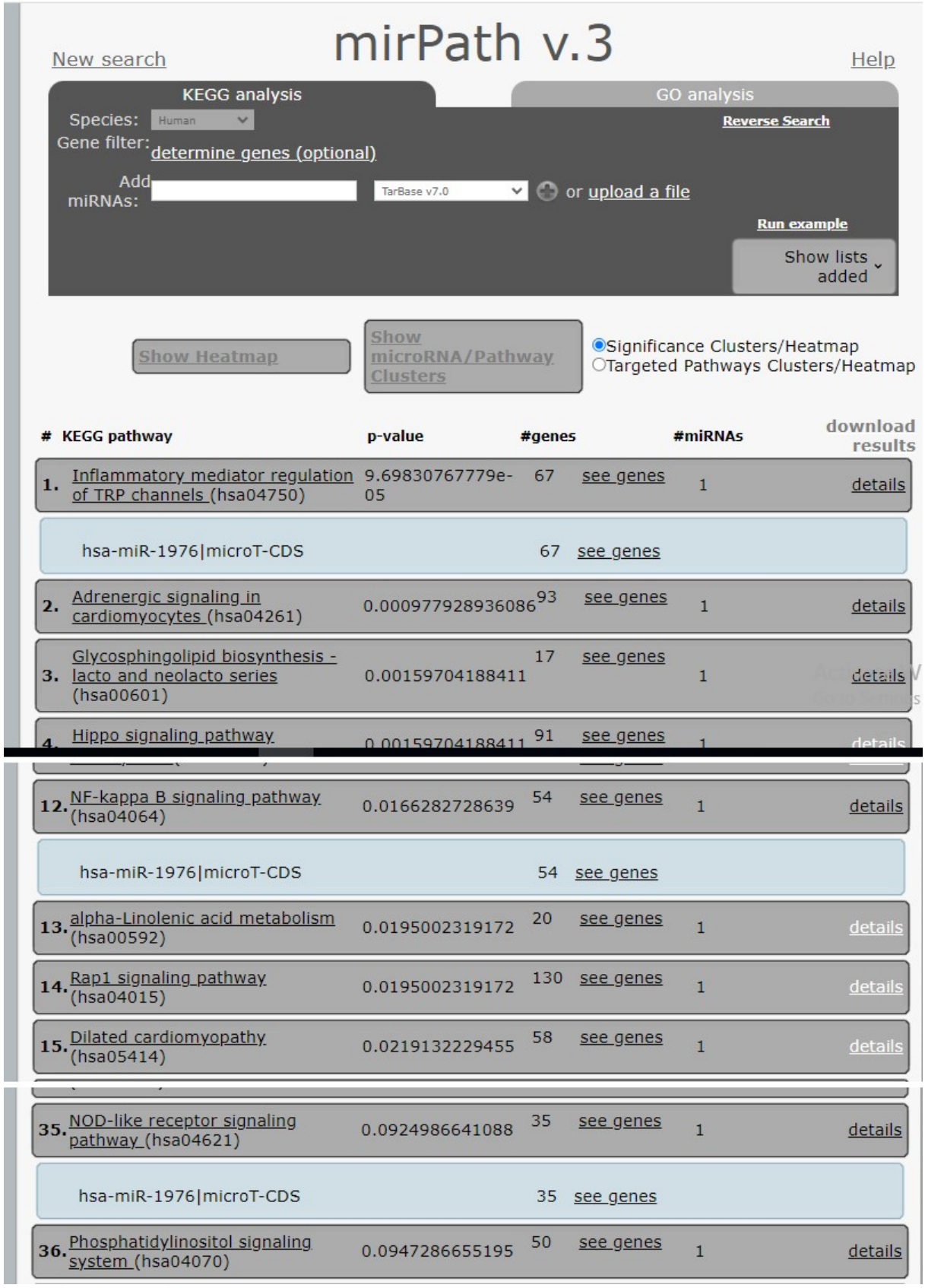


**Figure S7:** Retrieval of AC074117.2 lncRNA from DIANA Tools database (https://diana.e-ce.uth.gr/lncbasev3, Jan 2022)

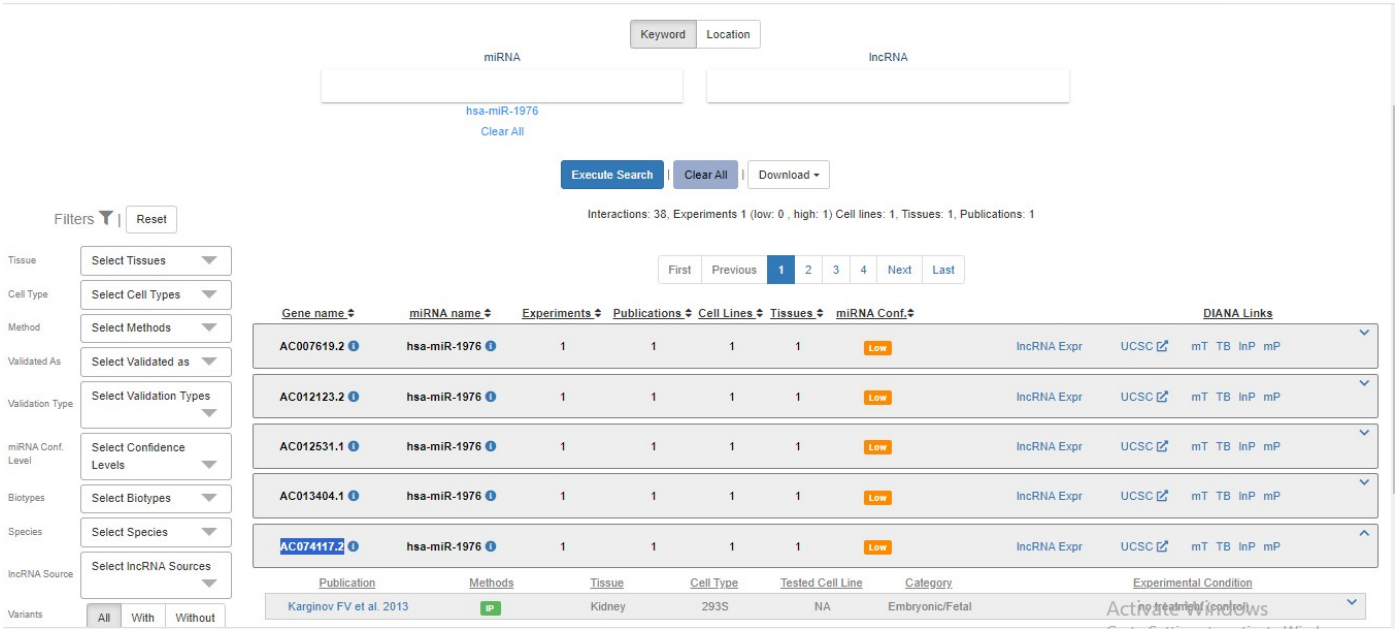
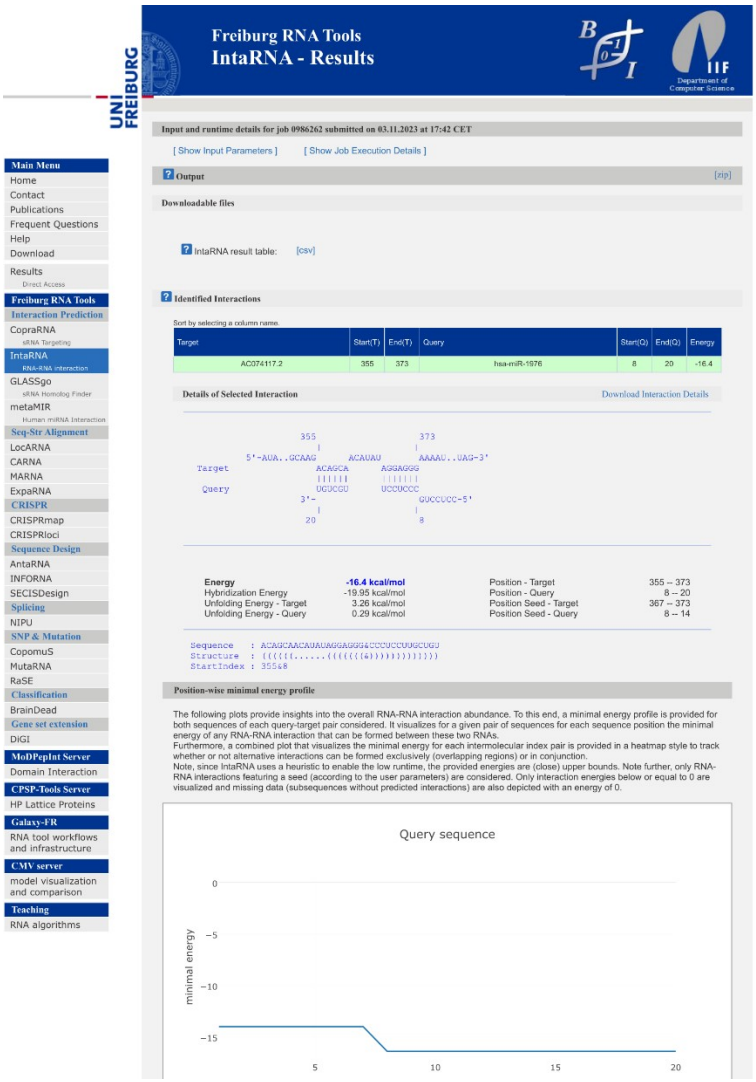
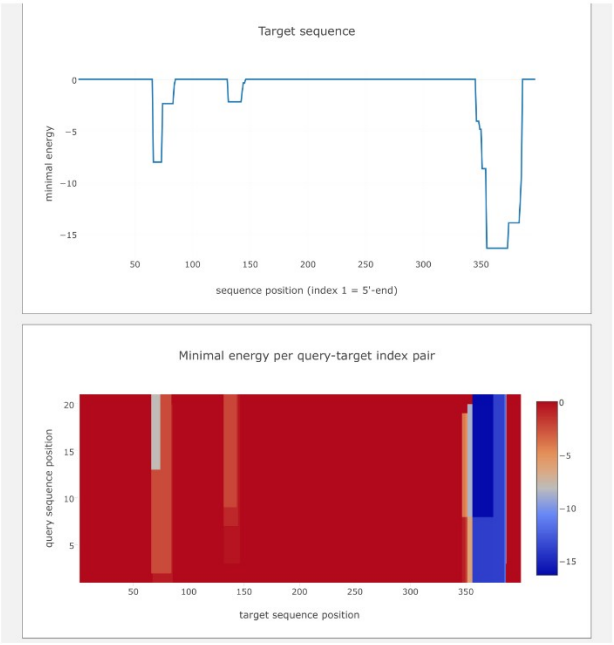


**Figure S8:** lncRNA AC074117.2 / miR-1976 interaction using IntaRNA 2.0 tool.



## Supplementary Tables:

**Table S4:** Primers used for qPCR.

| Primer name | Gene ID | Cat.no. | Tm | Product size |
|---|---|---|---|---|
| ***TMEM173 (STING1)*** | NM_198282 | 249900<br>**Gene Globe ID:**<br>QT00055440 | 70 °C | 125 bp |
| ***ZBP1*** | NM_001160418 | 249900<br>**Gene Globe ID:**<br>QT00029631 | 70 °C | 83 bp |
| ***DDX58*** | NM_014314 | 249900<br>**Gene Globe ID:**<br>QT00040509 | 70 °C | 114 bp |
| ***GAPDH*** | NM_002046 | 249900<br>**Gene Globe ID:**<br>QT00079247 | 70°C | 95 bp |
| ***miR_1976*** | MIMAT0009451 | 339350<br>**Gene Globe ID:**<br>ZP00000388 | 75 °C | 85 bp |
| ***AC074117.2*** | ENST00000417130 | **Gene Globe ID:**<br>UPFH0284997 | 58.8 °C | 82 bp |