ACL-IJCAI-SIGIR
顶级会议论文报告会
(AIS 2022)

KenMeSH: Knowledge-enhanced End-to-end Biomedical Text Labelling

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Western UNIVERSITY · CANADA

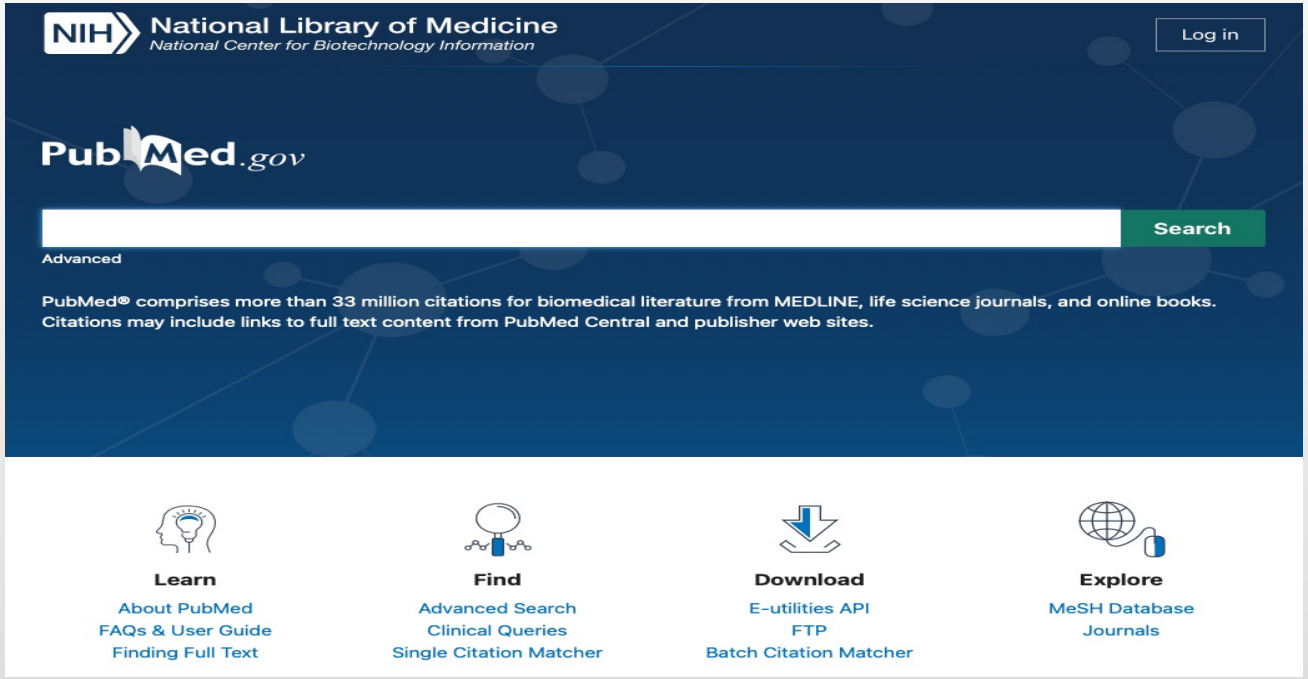
VECTOR INSTITUTE

UNIVERSITY OF TORONTO

UNITY HEALTH TORONTO

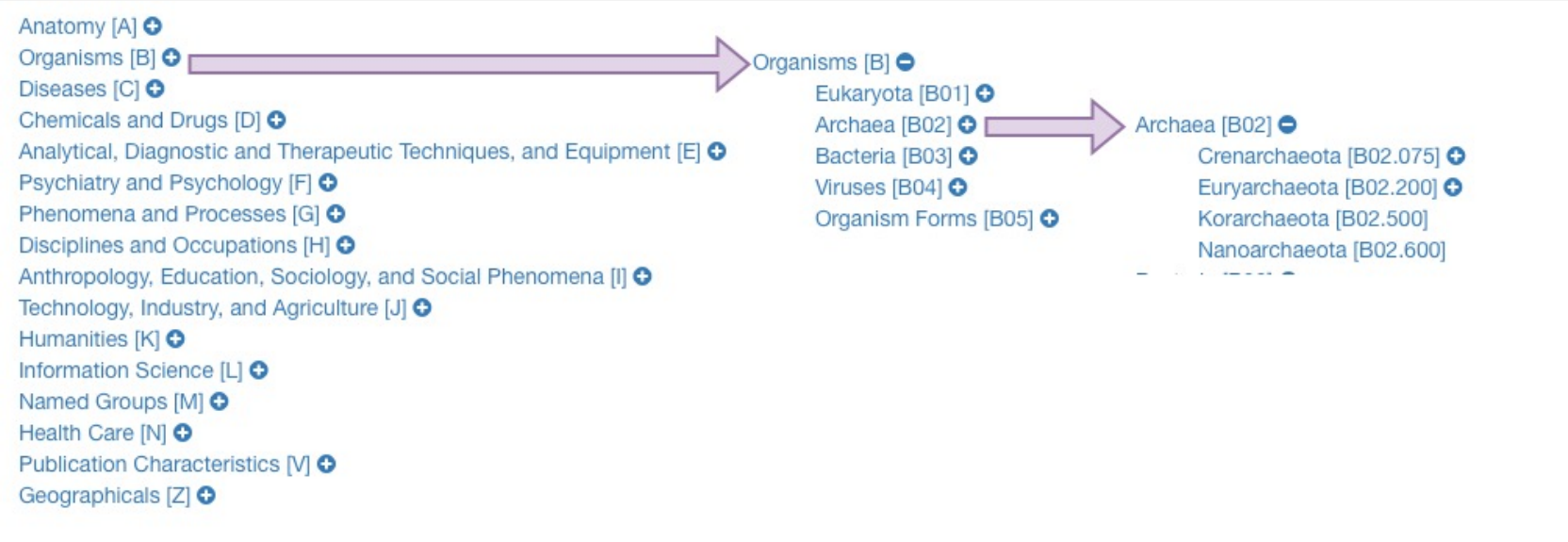
Background

- PubMed
  - Produced by the National Library of Medicine (NLM).
  - A free access search engine for abstracting and indexing biomedical citations.
  - Comprises more than 33 million citations for biomedical literature from MEDLINE (as of Apr. 2022).



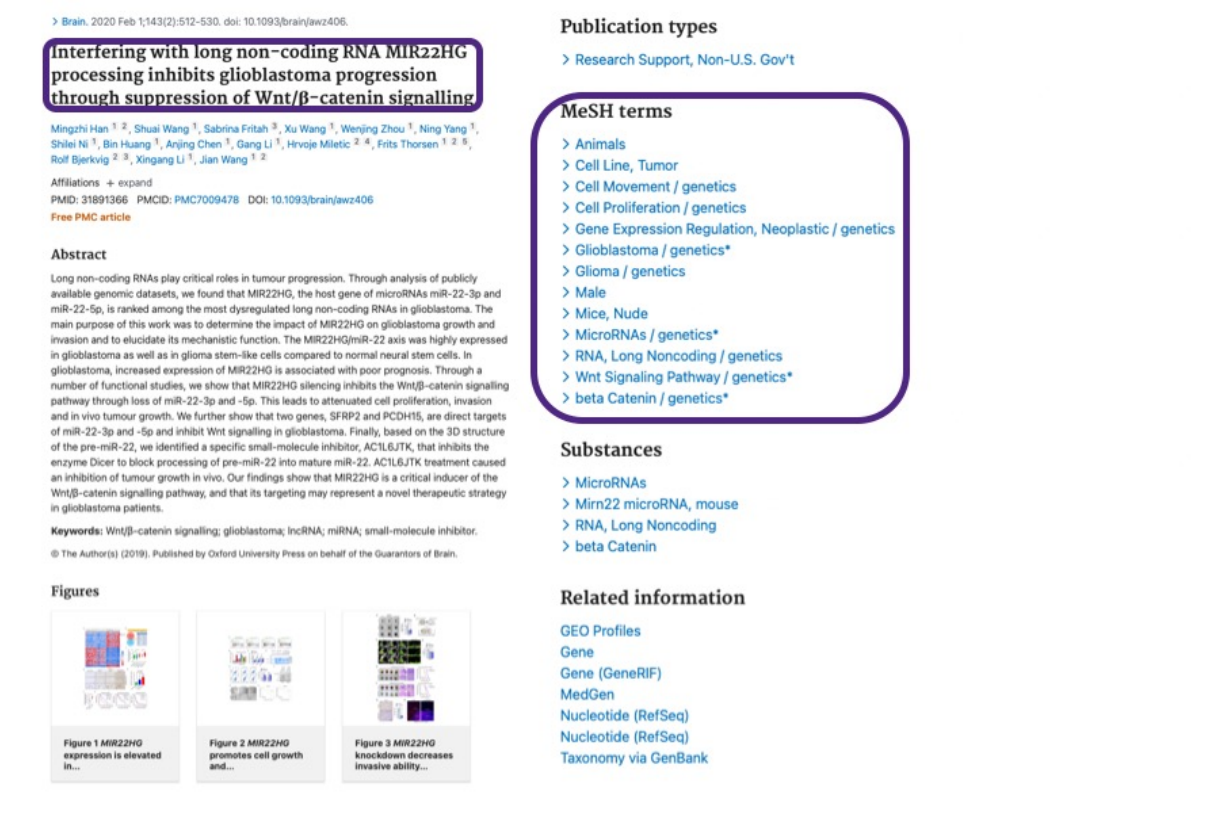
Background

- Medical Subject Headings (MeSH Terms)
  - Uses to index articles in the MEDLINE database
  - Controlled by National Library of Medicine (NLM)
  - Represents concepts in the biomedical literature
  - Organized hierarchically
  - 29, 369 main MeSH terms (as of 2021), and revised annually



Automatic MeSH Indexing Task

- An extreme multi-label text classification problem
  - Each MEDLINE citation is assigned to a set of MeSH terms
- Challenges:
  - Number of MeSH terms is large, and they have varying occurrence frequencies.
  - The number of MeSH terms assigned to each citation varies



> Brain. 2020 Feb 1;143(2):512–530. doi: 10.1093/brain/awz406.

Interfering with long non-coding RNA MIR22HG processing inhibits glioblastoma progression through suppression of Wnt/β-catenin signalling

Mingzhi Han [1 2], Shuai Wang [1], Sabrina Fritah [3], Xu Wang [1], Wenjing Zhou [1], Ning Yang [1], Shilei Ni [1], Bin Huang [1], Anjing Chen [1], Gang Li [1], Hrvoje Miletic [2 4], Frits Thorsen [1 2 5], Rolf Bjerkvig [2 3], Xingang Li [1], Jian Wang [1 2]

Affiliations + expand

PMID: 31891366 PMCID: PMC7009478 DOI: 10.1093/brain/awz406

Free PMC article

Abstract

Long non-coding RNAs play critical roles in tumour progression. Through analysis of publicly available genomic datasets, we found that MIR22HG, the host gene of microRNAs miR-22-3p and miR-22-5p, is ranked among the most dysregulated long non-coding RNAs in glioblastoma. The main purpose of this work was to determine the impact of MIR22HG on glioblastoma growth and invasion and to elucidate its mechanistic function. The MIR22HG/miR-22 axis was highly expressed in glioblastoma as well as in glioma stem-like cells compared to normal neural stem cells. In glioblastoma, increased expression of MIR22HG is associated with poor prognosis. Through a number of functional studies, we show that MIR22HG silencing inhibits the Wnt/β-catenin signalling pathway through loss of miR-22-3p and -5p. This leads to attenuated cell proliferation, invasion and in vivo tumour growth. We further show that two genes, SFRP2 and PCDH15, are direct targets of miR-22-3p and -5p and inhibit Wnt signalling in glioblastoma. Finally, based on the 3D structure of the pre-miR-22, we identified a specific small-molecule inhibitor, AC1L6JTK, that inhibits the enzyme Dicer to block processing of pre-miR-22 into mature miR-22. AC1L6JTK treatment caused an inhibition of tumour growth in vivo. Our findings show that MIR22HG is a critical inducer of the Wnt/β-catenin signalling pathway, and that its targeting may represent a novel therapeutic strategy in glioblastoma patients.

Keywords: Wnt/β-catenin signalling; glioblastoma; lncRNA; miRNA; small-molecule inhibitor.

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Figures

Figure 1 *MIR22HG* expression is elevated in...

Figure 2 *MIR22HG* promotes cell growth and...

Figure 3 *MIR22HG* knockdown decreases invasive ability...

Publication types

> Research Support, Non-U.S. Gov't

MeSH terms

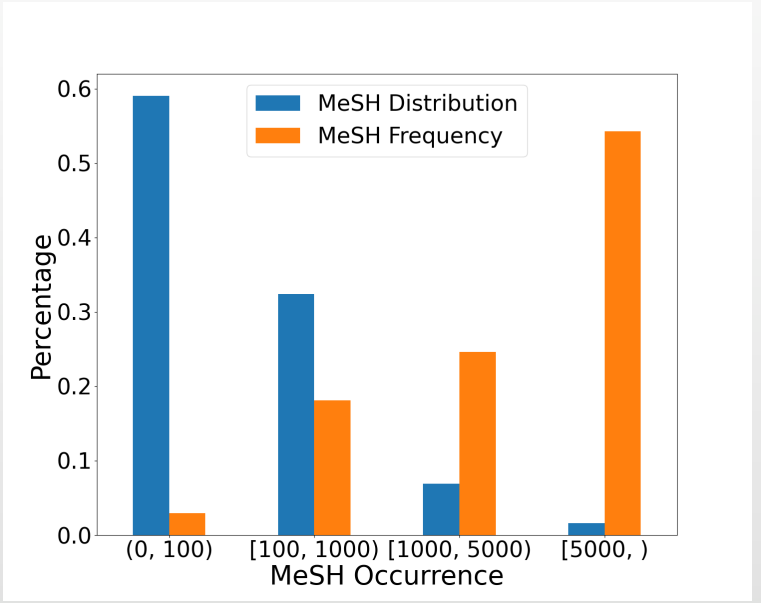
> Animals
> Cell Line, Tumor
> Cell Movement / genetics
> Cell Proliferation / genetics
> Gene Expression Regulation, Neoplastic / genetics
> Glioblastoma / genetics*
> Glioma / genetics
> Male
> Mice, Nude
> MicroRNAs / genetics*
> RNA, Long Noncoding / genetics
> Wnt Signaling Pathway / genetics*
> beta Catenin / genetics*

Substances

> MicroRNAs
> Mirn22 microRNA, mouse
> RNA, Long Noncoding
> beta Catenin

Related information

GEO Profiles
Gene
Gene (GeneRIF)
MedGen
Nucleotide (RefSeq)
Nucleotide (RefSeq)
Taxonomy via GenBank



Motivations

Eukaryota [B01]
Animals [B01.050]
Chordata [B01.050.150]
Vertebrates [B01.050.150.900]
Mammals [B01.050.150.900.649]
Eutheria [B01.050.150.900.649.313]
Rodentia [B01.050.150.900.649.313.992]
Muridae [B01.050.150.900.649.313.992.635]
Murinae [B01.050.150.900.649.313.992.635.505]
Mice [B01.050.150.900.649.313.992.635.505.500]
Mice, Congenic [B01.050.150.900.649.313.992.635.505.500.150]
Mice, Inbred Strains [B01.050.150.900.649.313.992.635.505.500.400]
Mice, Mutant Strains [B01.050.150.900.649.313.992.635.505.500.550]
Mice, Transgenic [B01.050.150.900.649.313.992.635.505.500.800]
Rats [B01.050.150.900.649.313.992.635.505.700]

VENUE (METADATA)

Brain. 2020 Feb 1;143(2):512-530. doi: 10.1093/brain/awz406.

TITLE (TEXT)

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Figures

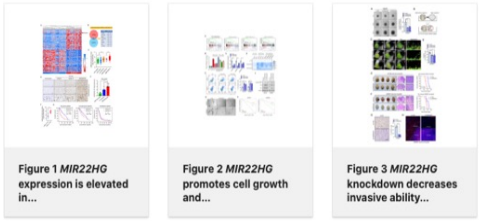

Figure 1 *MIR22HG* expression is elevated in...

Figure 2 *MIR22HG* promotes cell growth and...

Figure 3 *MIR22HG* knockdown decreases invasive ability...

Figure 4 *MIR22HG* activates the Wnt/β-catenin pathway...

Figure 5 miR-22-3p and miR-22-5p mediate *MIR22HG*...

Figure 6 *SFRP2* and *PCDH15* are downstream...

All figures (7)

Similar articles

SIMILAR ARTICLES (METADATA)

LncRNA MIR22HG inhibits growth, migration and invasion through regulating the miR-10a-5p/NCOR2 axis in hepatocellular carcinoma cells.
Wu Y, Zhou Y, Huan L, Xu L, Shen M, Huang S, Liang L.
Cancer Sci. 2019 Mar;110(3):973-984. doi: 10.1111/cas.13950. Epub 2019 Feb 23.
PMID: 30680848 Free PMC article.

Long non-coding RNA MIR22HG inhibits cell proliferation and migration in cholangiocarcinoma by negatively regulating the Wnt/β-catenin signaling pathway.
Hu X, Tan Z, Yang Y, Yang P.
J Gene Med. 2019 May;21(5):e3085. doi: 10.1002/jgm.3085. Epub 2019 Apr 15.
PMID: 30856284

Upregulated lncRNA SNHG1 contributes to progression of non-small cell lung cancer through inhibition of miR-101-3p and activation of Wnt/β-catenin signaling pathway.
Cui Y, Zhang F, Zhu C, Geng L, Tian T, Liu H.
Oncotarget. 2017 Mar 14;8(11):17785-17794. doi: 10.18632/oncotarget.14854.
PMID: 28147312 Free PMC article.

Wnt/β-catenin signaling cascade: A promising target for glioma therapy.
He L, Zhou H, Zeng Z, Yao H, Jiang W, Qu H.
J Cell Physiol. 2019 Mar;234(3):2217-2228. doi: 10.1002/jcp.27186. Epub 2018 Sep 17.
PMID: 30277583 Review.

Crosstalk between long non-coding RNAs and Wnt/β-catenin signalling in cancer.
Yang G, Shen T, Yi X, Zhang Z, Tang C, Wang L, Zhou Y, Zhou W.
J Cell Mol Med. 2018 Apr;22(4):2062-2070. doi: 10.1111/jcmm.13522. Epub 2018 Feb 1.
PMID: 29392884 Free PMC article. Review.

See all similar articles

Publication types

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› Glioma / genetics
› Male
› Mice, Nude
› MicroRNAs / genetics*
› RNA, Long Noncoding / genetics
› Wnt Signaling Pathway / genetics*
› beta Catenin / genetics*

LABEL HIERAHCY

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› RNA, Long Noncoding
› beta Catenin

Related information

GEO Profiles
Gene
Gene (GeneRIF)
MedGen
Nucleotide (RefSeq)
Nucleotide (RefSeq)
Taxonomy via GenBank

LinkOut - more resources

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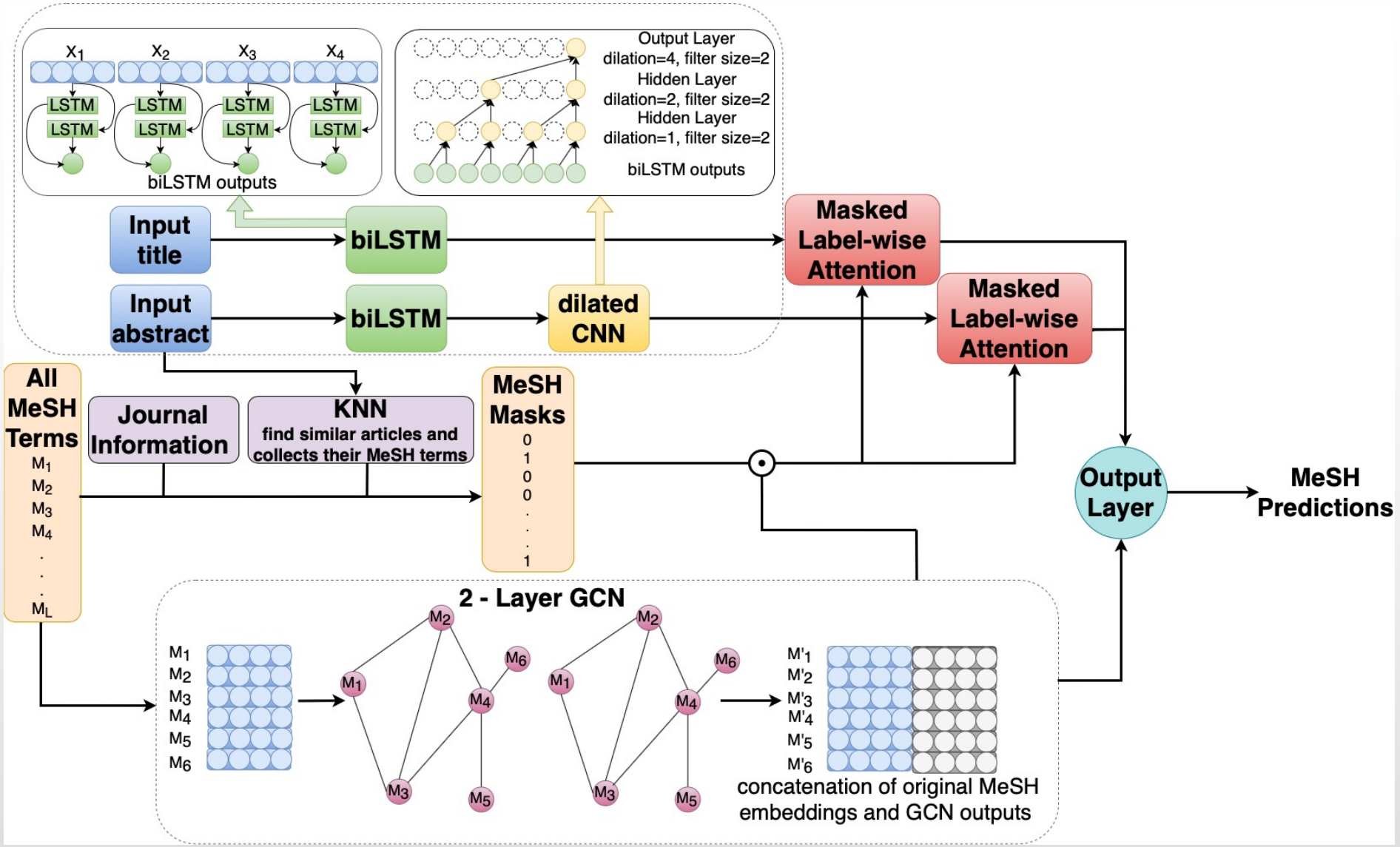
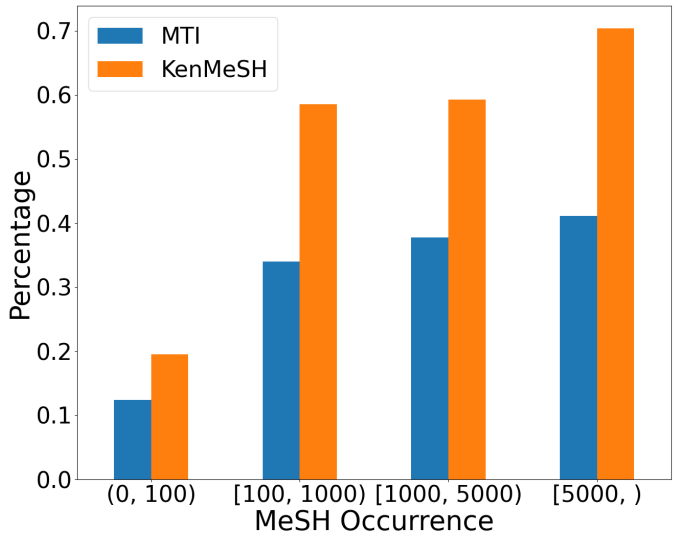
KenMeSH


x1 x2 x3 x4
LSTM
biLSTM outputs
Output Layer
dilation=4, filter size=2
Hidden Layer
dilation=2, filter size=2
Hidden Layer
dilation=1, filter size=2
biLSTM outputs
Input title
Input abstract
biLSTM
biLSTM
dilated CNN
Masked Label-wise Attention
Masked Label-wise Attention
All MeSH Terms
M1
M2
M3
M4
ML
Journal Information
KNN
find similar articles and collects their MeSH terms
MeSH Masks
0
1
0
0
1
Output Layer
MeSH Predictions
2 - Layer GCN
M1
M2
M3
M4
M5
M6
M'1
M'2
M'3
M'4
M'5
M'6
concatenation of original MeSH embeddings and GCN outputs

Results

Method	*Micro-average Measure*			*Example Based Measure*		
	MiF	*MiP*	*MiR*	*EBF*	*EBP*	*EBR*
MTI	0.390	0.379	0.402	0.393	0.378	0.408
HGCN4MeSH	0.524	0.763	0.399	0.529	0.762	0.405
DeepMeSH	0.639	0.669	0.612	0.631	0.667	0.627
BERTMeSH	0.667	0.696	0.640	0.657	0.700	0.650
FullMeSH (Full)	0.651	0.683	0.623	0.643	0.680	0.639
BERTMeSH (Full)	0.685	0.713	**0.659**	0.675	0.717	**0.667**
KenMeSH	**0.745** ±0.021	**0.864** ±0.011	0.655 ±0.027	**0.738** ±0.018	**0.863** ±0.011	0.644 ±0.022

Table 1: Comparison to previous methods across two main evaluation metrics. Methods marked as *Full* are trained on entire PMC articles, others on abstracts and titles only. Bold: best scores in each column.



Thank you!

Codes are available at:

https://github.com/xdwang0726/KenMeSH