Understanding Biological Research Documents using a Neural Network

Varun Mittal

Motivation: Assist researchers in literature search by annotating entities and establishing a relation type between them.

Stimulation of glioma cell motility by expression, proteolysis, and release of the L1 neural cell recognition molecule

PUBLISHED IN **BIOMED CENTRAL**

Contributers:

Muhua Yang • Shalini Adla • Murali K Temburni • Vivek P Patel • Errin L Lagow • Owen A Brady • Jing Tian • Magdy I Boulos • Deni S Galileo

Bookmark

Legend: CELL PROTEIN GENE PLACES PEOPLE

Background

Malignant glioma cells are particularly motile and can travel diffusely through the brain parenchyma, apparently without following anatomical structures to guide their migration. The neural adhesion/recognition protein L1 (L1CAM; CD171) has been implicated in contributing to stimulation of motility and metastasis of several non-neural cancer types. We explored the expression and function of L1 protein as a stimulator of glioma cell motility using human high-grade glioma surgical specimens and established rat and human glioma cell lines.

Results

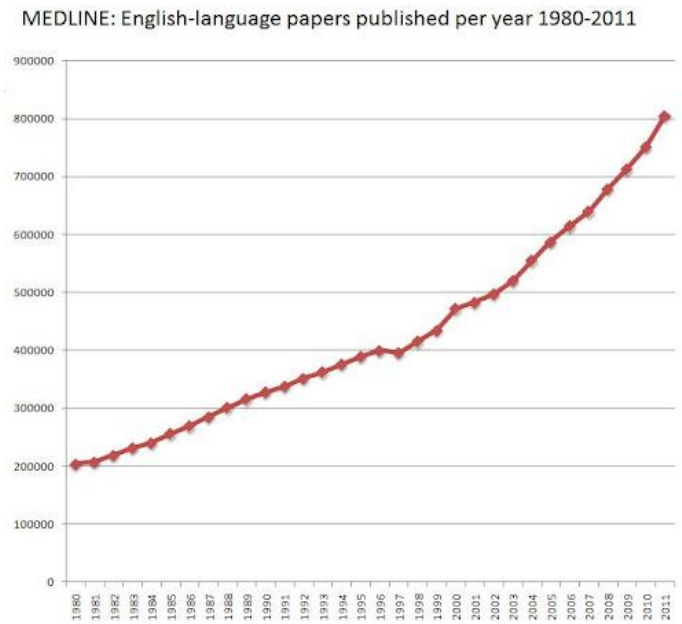
L1 protein expression was found in 17 out of 18 human high-grade glioma surgical specimens by western blotting. L1 mRNA was found to be present in human U-87/LacZ and rat C6 and 9L glioma cell lines. The glioma cell lines were negative for surface full length L1 by flow cytometry and high resolution immunocytochemistry of live cells. However, fixed and permeablized cells exhibited positive staining as numerous intracellular puncta. Western blots of cell line extracts revealed L1 proteolysis into a large soluble ectodomain (~180 kDa) and a smaller transmembrane proteolytic fragment (~32 kDa). Exosomal vesicles released by the glioma cell lines were purified and contained both full-length L1 and the proteolyzed transmembrane fragment. Glioma cell lines expressed L1-binding αvβ5 integrin cell surface receptors. Quantitative time-lapse analyses showed that motility was reduced significantly in glioma cell lines by 1) infection with an antisense-L1 retroviral vector and 2) L1 ectodomain-binding antibodies.

Conclusion

Our novel results support a model of autocrine/paracrine stimulation of cell motility in glioma cells by a cleaved L1 ectodomain and/or released exosomal vesicles containing L1. This mechanism could explain the diffuse migratory behavior of high-grade glioma cancer cells within the brain.

Challenges faced by researchers

1.



Exponentially increasing number of articles.
Reference: http://blogs.discovermagazine.com/neuroskeptic/

2.

Literature search

3.

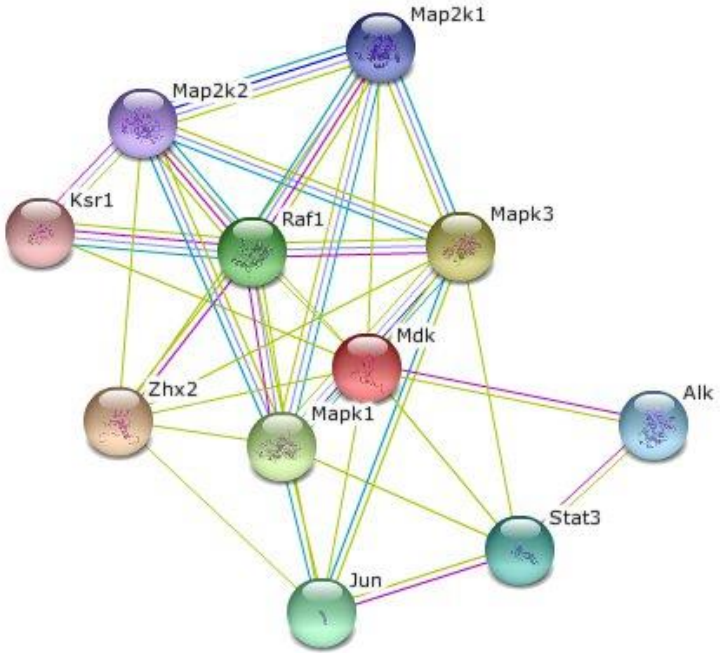
Analyzing articles
Image Credit: Google.com

Importance of annotations in Biology

There are several matches for 'map'.
Please select one from the list below and press Continue to proceed.

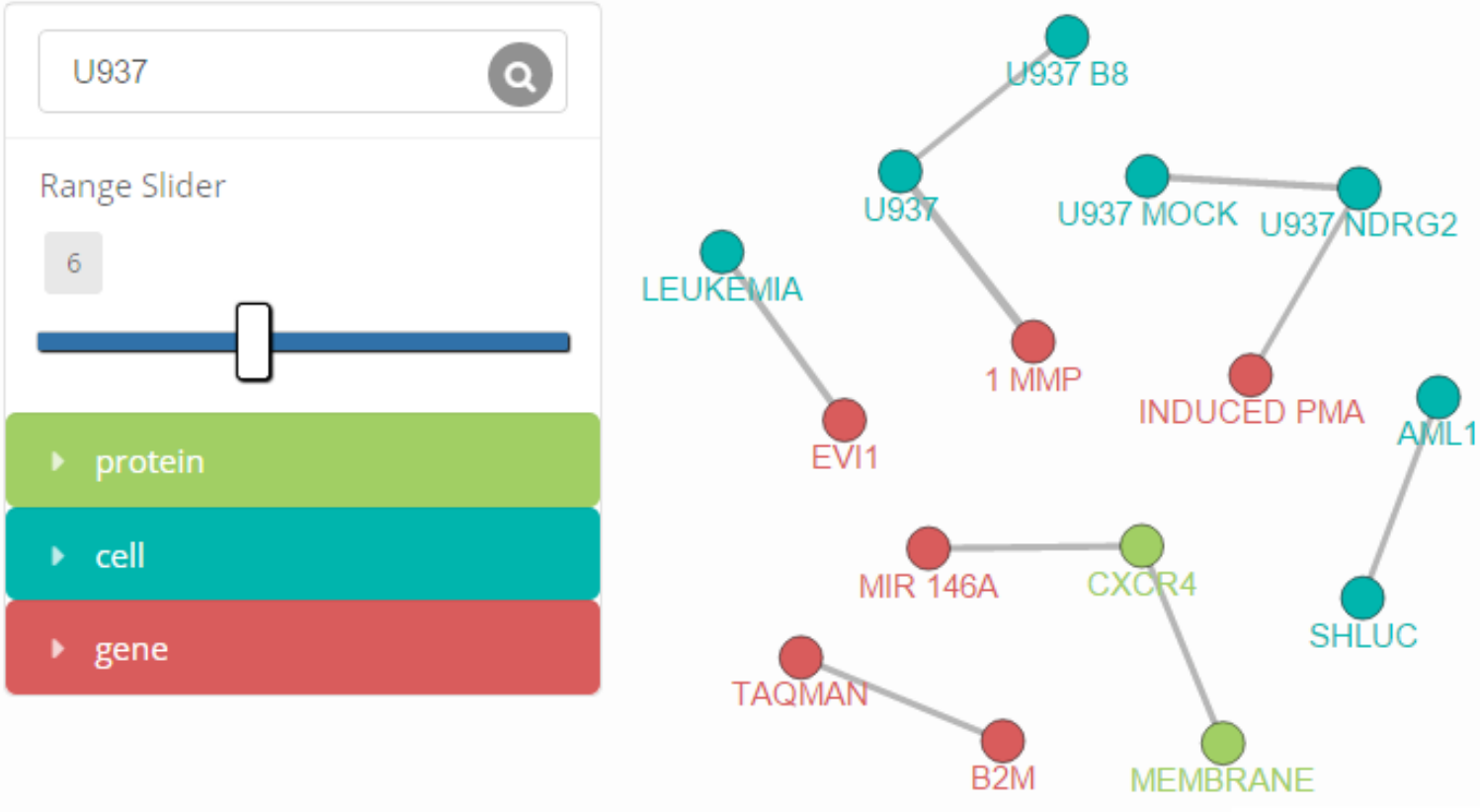
<- BACK | CONTINUE ->

organism	protein
Escherichia coli K12 MG1655	map - methionine aminopeptidase; Removes the N-terminal methionine from nascent proteins (By similarity)
Homo sapiens	SGSM3 - small G protein signaling modulator 3; May play a cooperative role in NF2-mediated growth suppression of cells
Mus musculus	H2-DMa - histocompatibility 2, class II, locus DMa; Plays a critical role in catalyzing the release of class II HLA-associated invariant chain-derived peptides (CLIP) from newly synthesized class II HLA molecules and freeing the peptide binding site for acquisition of antigenic peptides
Homo sapiens	MAP2K6 - mitogen-activated protein kinase kinase 6; Dual specificity protein kinase which acts as an essential component of the MAP kinase signal transduction pathway. With MAP3K3/MKK3, catalyzes the concomitant phosphorylation of a threonine and a tyrosine residue in the MAP kinases p38 MAPK11, MAPK12, MAPK13 and MAPK14 and plays an important role in the regulation of cellular responses to cytokines and all kinds of stresses. Especially, MAP2K3/MKK3 and MAP2K6/MKK6 are both essential for the activation of MAPK11 and MAPK13 induced by environmental stress, whereas MAP2K6/MKK6 is the major MAPK1 [...]
Homo sapiens	MAP2K2 - mitogen-activated protein kinase kinase 2; Catalyzes the concomitant phosphorylation of a threonine and a tyrosine residue in a Thr-Glu-Tyr sequence located in MAP kinases. Activates the ERK1 and ERK2 MAP kinases (By similarity)
Homo sapiens	DUSP14 - dual specificity phosphatase 14; Involved in the inactivation of MAP kinases. Dephosphorylates ERK, JNK and p38 MAP-kinases
Homo sapiens	PPP2CA - protein phosphatase 2, catalytic subunit, alpha isozyme; PP2A is the major phosphatase for microtubule-associated proteins (MAPs). PP2A can modulate the activity of phosphorylase B kinase casein kinase 2, mitogen-stimulated S6 kinase, and MAP-2 kinase. Cooperates with SGOL2 to protect centromeric cohesin from separase-mediated cleavage in oocytes specifically during meiosis I (By similarity). Can dephosphorylate SV40 large T antigen and p53/TP53. Activates RAF1 by dephosphorylating it at 'Ser-259'
Homo sapiens	DUSP26 - dual specificity phosphatase 26 (putative); Inactivates MAPK1 and MAPK3 which leads to dephosphorylation of heat shock factor protein 4 and a reduction in its DNA-binding activity. Inhibits MAP kinase p38 by dephosphorylating it and inhibits p38-mediated apoptosis in anaplastic thyroid cancer cells. Can also induce activation of MAP kinase p38 and c-Jun N-terminal kinase (JNK)



Reference: http://string-db.org/cgi/network.pl

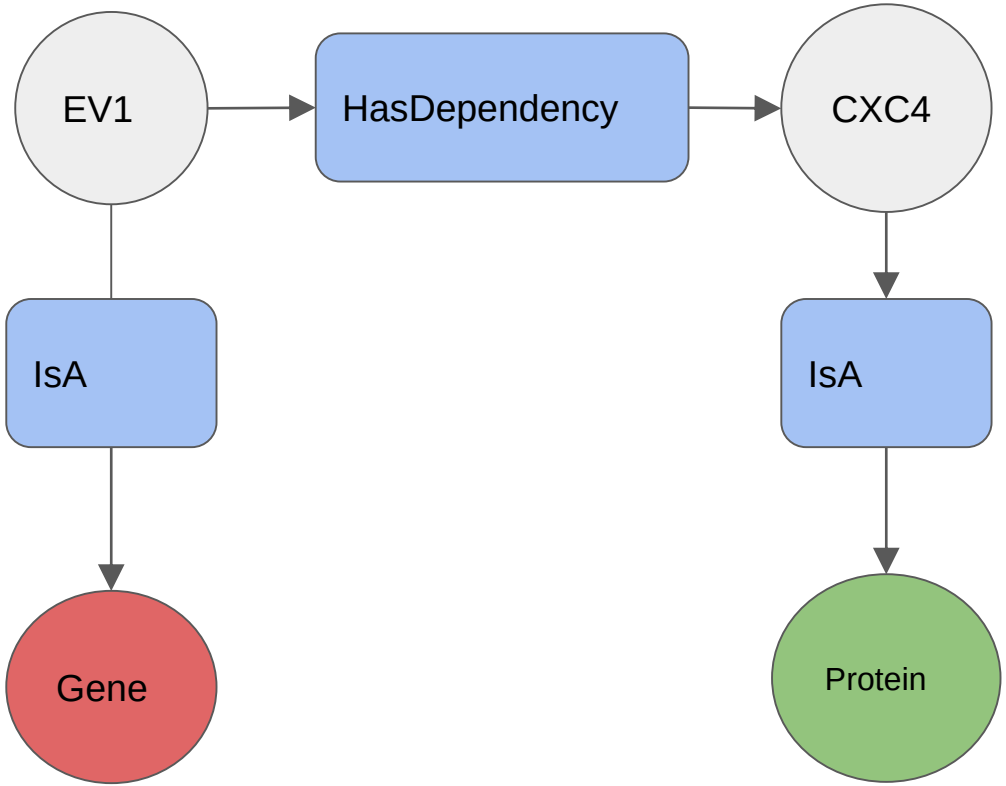
Current state of art - Statistical method



Challenges in the current approach

Different word, same meaning(Synonyms) Protein names	Different expression, common meaning Non-smoker Does not smoke
Different notations 5mg/kg of cyclosporine per day Cyclosporine 5mg/kg per day	Same word, different content Learning rate - research time Learning rate - machine learning

Proposed state of Art: Suggest relations between entities



Note:
EV1 : Gene
CXC4: Protein

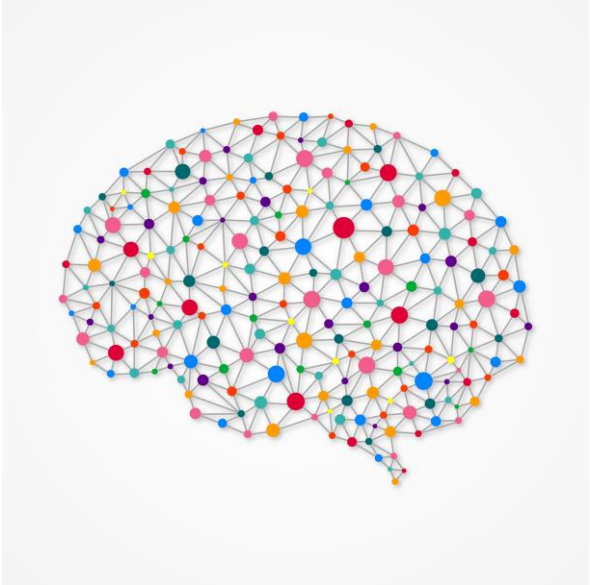
Methodology

A saxophone is used for jazz.

Extract Part of Speech Tags from example

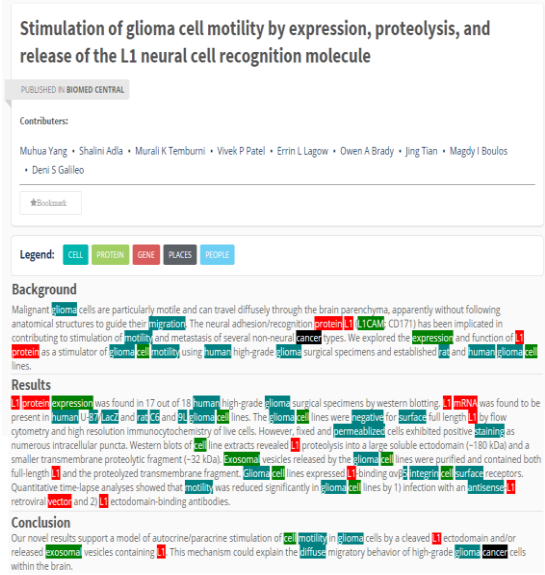
A/DT saxophone/NN is/VBZ used/VBN for/IN jazz/NN ./.

Collect samples and train a neural network



Summary

PROBLEM



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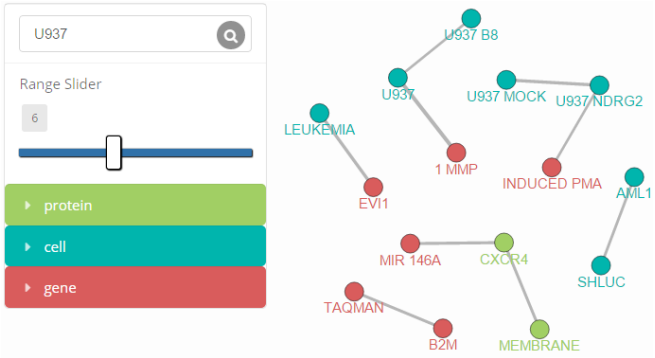
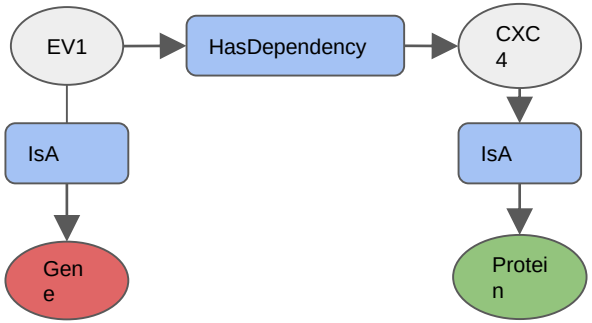
PROPOSED SOLUTION





CURRENT CHALLENGES

Acknowledgment

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