Argudas: arguing with gene expression information

Kenneth McLeod

kcm1@hw.ac.uk

Overview

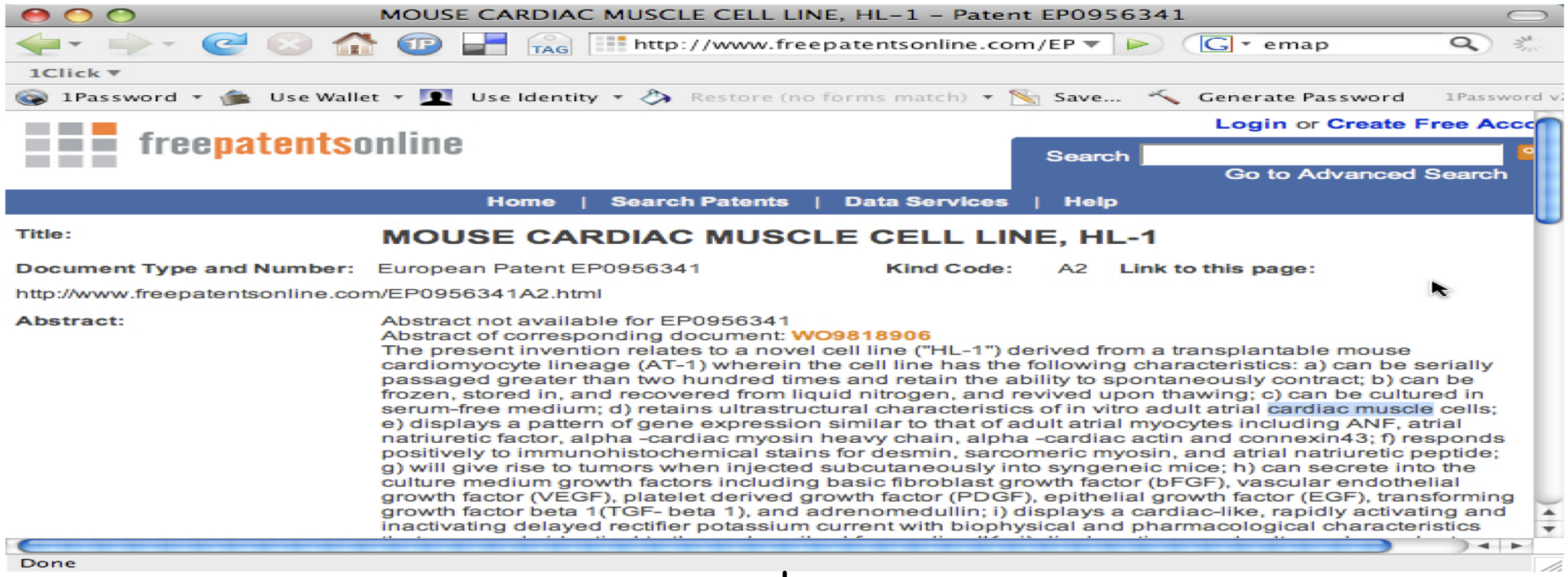
- Motivation – Sealife Project
- Evolution of tool to resolve inconsistencies in gene expression information
- Future work

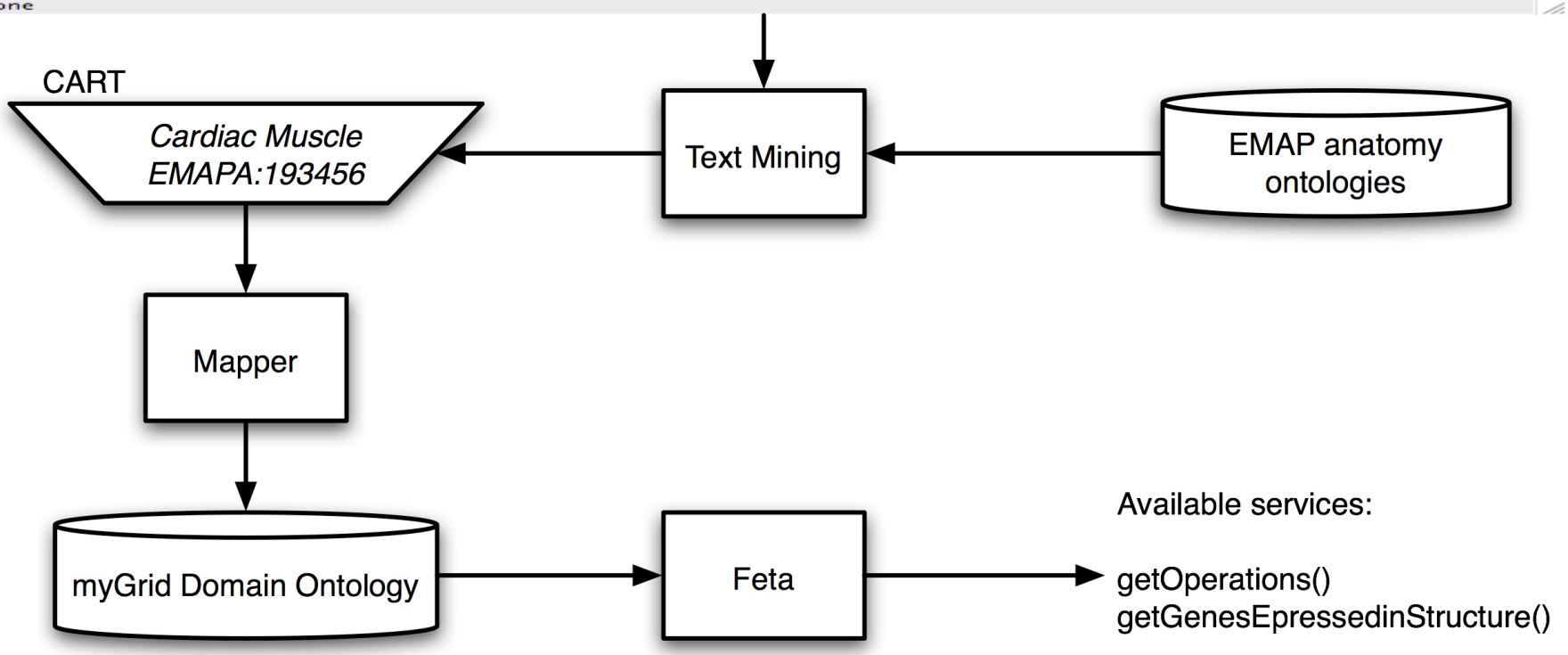
HERIOT WATT UNIVERSITY

Relationship between tissues & genes

Described in terms of expression strength

absent, present (weak, moderate, strong)


MOUSE CARDIAC MUSCLE CELL LINE, HL-1 – Patent EP0956341
http://www.freepatentsonline.com/EP
freepatentsonline
Search
Go to Advanced Search
Home | Search Patents | Data Services | Help
Title:
MOUSE CARDIAC MUSCLE CELL LINE, HL-1
Document Type and Number: European Patent EP0956341
Kind Code: A2
Link to this page:
http://www.freepatentsonline.com/EP0956341A2.html
Abstract:
Abstract not available for EP0956341
Abstract of corresponding document: WO9818906
The present invention relates to a novel cell line ("HL-1") derived from a transplantable mouse cardiomyocyte lineage (AT-1) wherein the cell line has the following characteristics: a) can be serially passaged greater than two hundred times and retain the ability to spontaneously contract; b) can be frozen, stored in, and recovered from liquid nitrogen, and revived upon thawing; c) can be cultured in serum-free medium; d) retains ultrastructural characteristics of in vitro adult atrial cardiac muscle cells; e) displays a pattern of gene expression similar to that of adult atrial myocytes including ANF, atrial natriuretic factor, alpha -cardiac myosin heavy chain, alpha -cardiac actin and connexin43; f) responds positively to immunohistochemical stains for desmin, sarcomeric myosin, and atrial natriuretic peptide; g) will give rise to tumors when injected subcutaneously into syngeneic mice; h) can secrete into the culture medium growth factors including basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), platelet derived growth factor (PDGF), epithelial growth factor (EGF), transforming growth factor beta 1(TGF- beta 1), and adrenomedullin; i) displays a cardiac-like, rapidly activating and inactivating delayed rectifier potassium current with biophysical and pharmacological characteristics
Done


CART
Cardiac Muscle
EMAPA:193456
Text Mining
EMAP anatomy ontologies
Mapper
myGrid Domain Ontology
Feta
Available services:
getOperations()
getGenesEpressedinStructure()
...

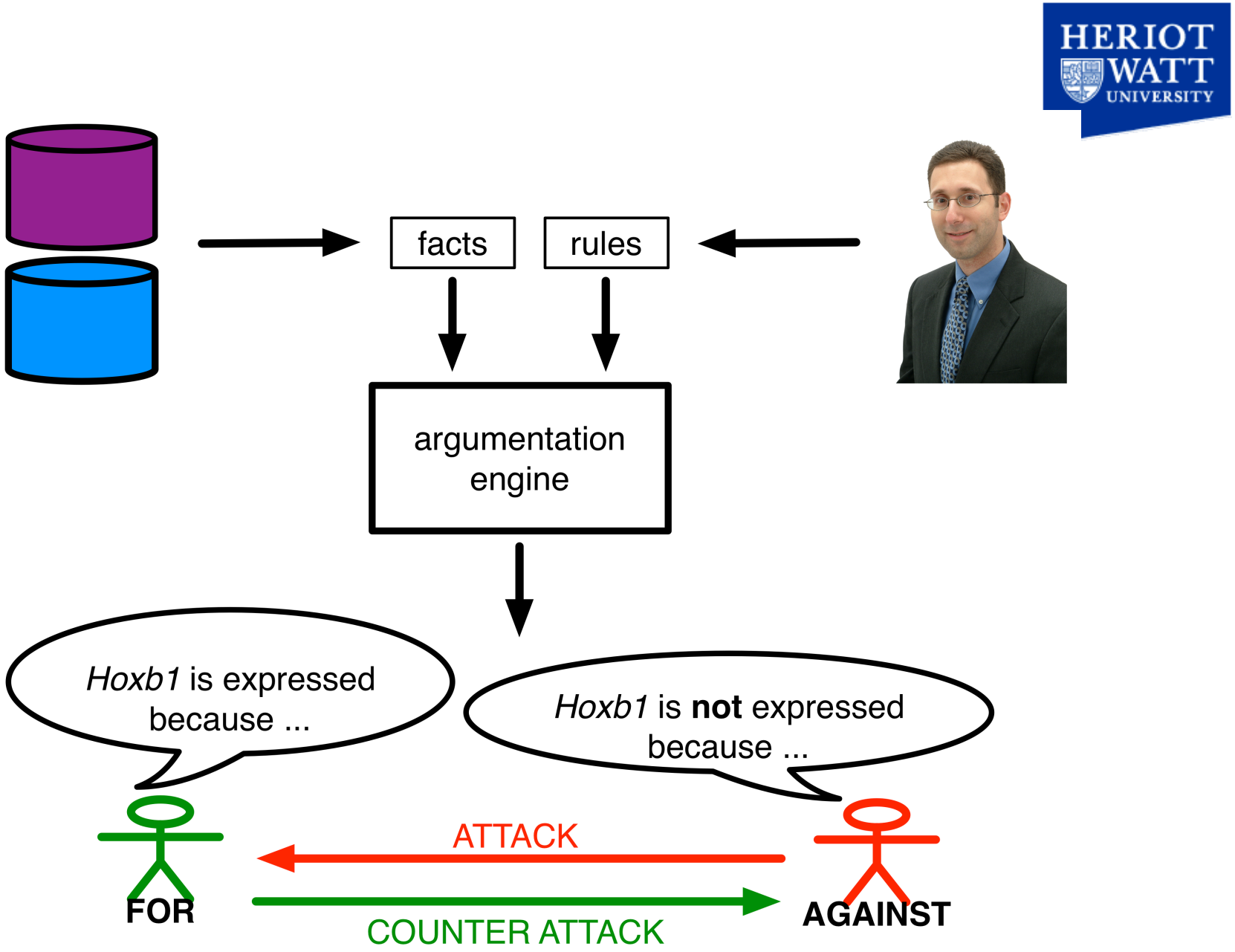
HERIOT WATT UNIVERSITY

Argument = reason to believe something is true

It is raining is a reason to believe I will get wet

Argumentation = debate using arguments

Computational argumentation = automated debate


HERIOT WATT UNIVERSITY
facts
rules
argumentation engine
Hoxb1 is expressed because ...
Hoxb1 is **not** expressed because ...
ATTACK
COUNTER ATTACK
FOR
AGAINST

SeaLife – Argumentation Interface 3

SeaLife - Argumentation Interface

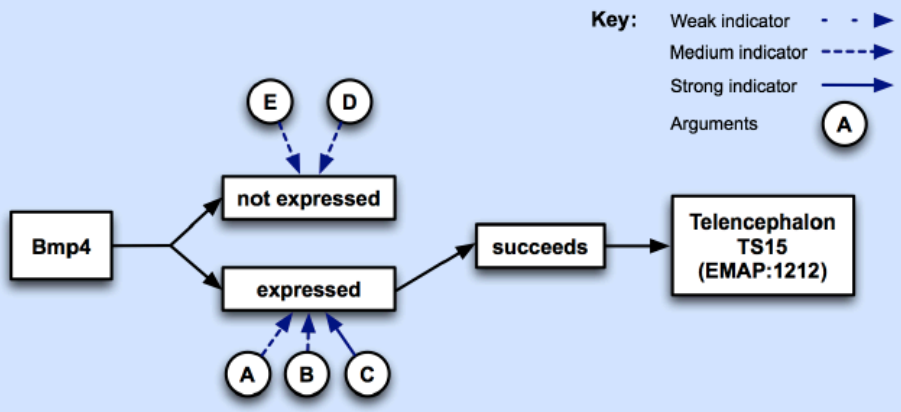
Close Window

You have selected the following structure, gene and database/s for the argumentation:

Structure:	Telencephalon TS15
Structure ID:	EMAP:1212
Gene:	Bmp4
Database/s:	EMAGE + GXD + CGAP

Conclusion →

Summary: The arguments appear to suggest the gene is expressed.



Arguments →

Why the gene may be expressed:

A. There is experimental evidence of expression. There is no reason to doubt the annotation: EMAGE:1049 has a textual annotation showing MODERATE expression for Bmp4 in TELENCEPHALON TS15 (EMAP:1212). STRENGTH=79%.

B. There is experimental evidence of expression. There is no reason to doubt the annotation: MGI:1276853 has a textual annotation showing PRESENT expression for Bmp4 in TELENCEPHALON TS15 (EMAP:1212). STRENGTH=79%.

C. CGAP reports that the SAGE experiments suggests expression. SAGE library SM070 shows that Bmp4 is found in EMAP:1212 1 times. STRENGTH=83%.

Why the gene may be not expressed:

D. There is experimental evidence the gene is not expressed. There is no reason to doubt the annotation: (Negative expression can be propagated down). EMAP:1212 is part of EMAP:1199. EMAGE:998 has a textual annotation showing Bmp4 is not expressed in FUTURE BRAIN TS15 (EMAP:1199). STRENGTH=79%.

E. There is experimental evidence the gene is not expressed. There is no reason to doubt the annotation: (Negative expression can be propagated down). EMAP:1212 is part of EMAP:1199. MGI:2158675 has a spatial annotation showing Bmp4 is not expressed in FUTURE BRAIN TS15 (EMAP:1199). STRENGTH=79%.

HERIOT WATT UNIVERSITY

OK, BUT…

ARGUMENTS TOO SUBJECTIVE

AUTOMATED DECISION BAD

CLEANER, SIMPLER INTERFACE

Too subjective

Tried to have multiple experts reassign degrees of belief to domain knowledge

Experts struggled to agree

Should have used Bayesian Net?

Basic approach of modeling expert knowledge & assigning degrees of belief works in medicine

Medics can work from clinical guidelines

Biologists have no published, accepted foundations

HERIOT WATT UNIVERSITY

SO…

NEW DEGREES OF BELIEF

CLEANER INTERFACE

NO AUTOMATED DECISION

HERIOT WATT UNIVERSITY

BETTER, BUT…

PROCESS TOO LONG

TOO MANY ARGUMETS

ARGUMENTS TOO NEGATIVE

Fewer arguments

Many arguments look semantically equivalent

Yet, equivalence depends on

- Individual user
- Task

If a gene is expressed in the finger, then it is also expressed in the hand.

General principle of propagation

Experiment A shows the gene is weakly expressed in the heart

Experiment A shows the gene is strongly expressed in the heart

HERIOT WATT UNIVERSITY

"ARGUMENT" BECOMES A METAPHOR

	Multiple annotations agree:	Annotation in next stage agree:	Annotation in previous stage agree:
STRONG	✔	✘	✔ Details ...
MODERATE	✔	✘	✘
WEAK			
PRESENT	✔	✔ Details ...	✔ Details ...
ABSENT	✔	✘	✘

HERIOT WATT UNIVERSITY

NEED MORE RESOURCES, BUT…

DIFFERENT ONTOLOGIES

NO ACCEPTED MAPPING

HERIOT WATT UNIVERSITY

SEMANTIC WEB & BUSINESS INTELLIGENCE

EU FP7 PROJECT FP7-ICT-2010-257403

Conclusion

Argumentation useful because it is intuitive

Technology / methodology needs to improve

Current funding:

BBSRC project Argudas (BB/G024162/1)

Biological data & knowledge:

www.emouseatlas.org