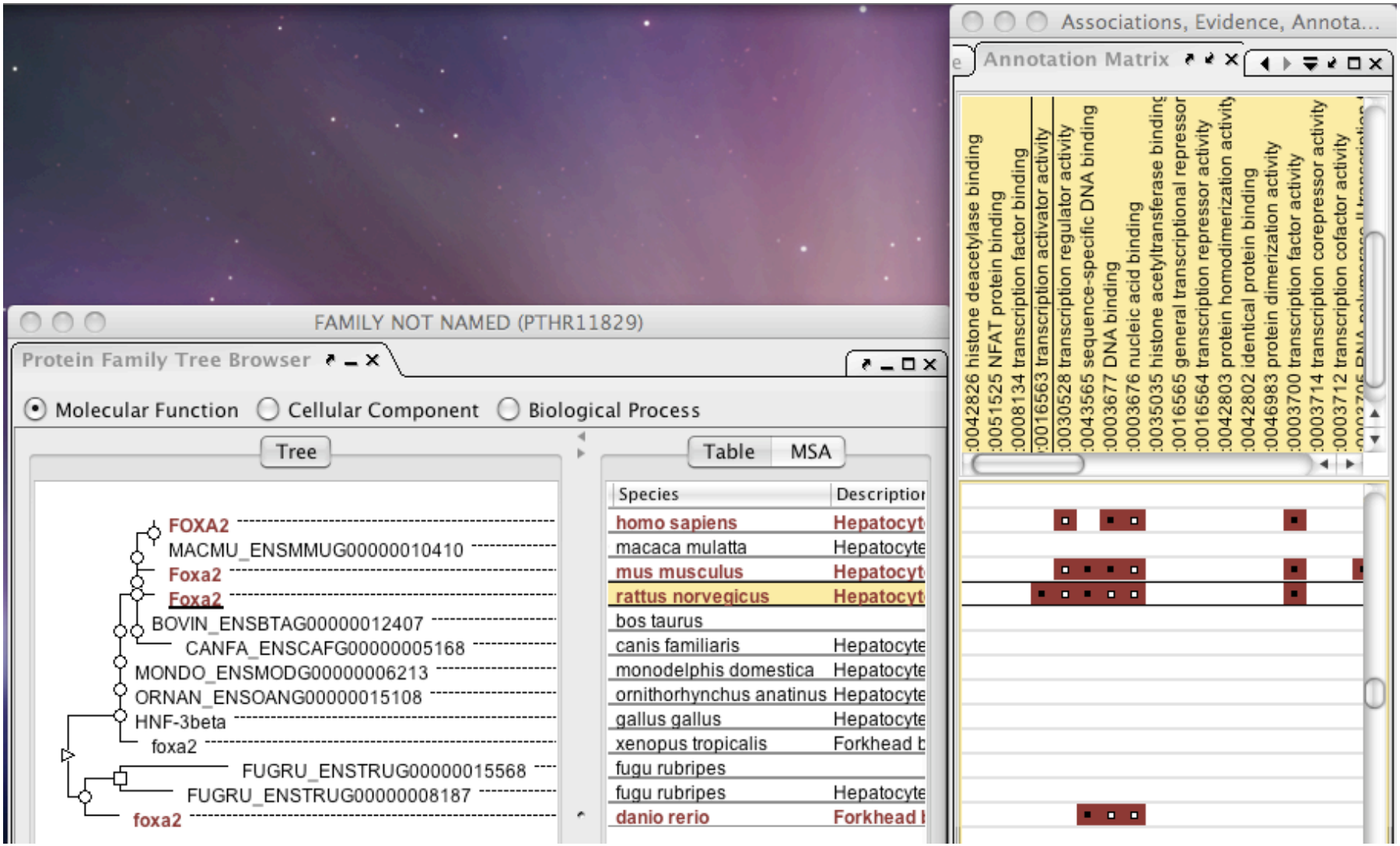
Progress in PAINT-Powered Protein Property Propagation

Mike Livstone

Transfer ("Propagate") GO terms from annotated proteins to less-annotated homologs



PAINT Products

- GAF file
  - Annotations to extant proteins (RefGenome & non-RG)
  - 1° annotations to ancestral nodes
  - 2° annotations inherited by ancestral nodes
- Evidence file
  - Brief description of phylogeny & scope of annotations
  - Reasoning behind annotations
  - Questions
    - MOD curators
    - Ontology curators

These and some other accessory files are deposited in CVS.

http://cvsweb.geneontology.org/cgi-bin/cvsweb.cgi/go/gene-associations/submission/paint/

Initial SOP

http://gocwiki.geneontology.org/index.php/RefG_Princeton_April_12-13_2010

- Select the most specific GO term possible.
- Apply the term as widely as possible.
- When necessary, suggest changes to annotations or ontologies
- Use or address *every* experimental annotation.

Initial effort: Forkhead family (PTHR11829)

- Originally chosen for the lung development project.
- Large family (672 proteins) of transcription factors involved in multiple developmental pathways.
- Generated ~15,000 new annotations
- Time required to annotate with PAINT:
  - MF: 3 days
  - CC: 2 days
  - BP: 4 weeks
- *Highly productive, but much too slow*

Q: What was the major obstacle?
A: The need to address *every* annotation (especially in BP), often by reading the paper.

Solutions

- Abandon the need to address every unused EXP annotation.
  - "response to" IEP's
  - Downstream effects (IMP's)
- Impose deadlines: Keep pace with the literature curation. Don't PAINT for longer than the curation period.
- Prioritize the most important EXP annotations

Impose deadlines

Active annotation period (Dates)	Panther Family	Gene Symbol (Human protein ID)	PAINT due to begin
Week 1-2 (1st-16th July)	PTHR12027:SF15, PTHR12027:SF18, PTHR12027:SF25	wnt1 (P04628) wnt3 (P56703)	Week 5
	PTHR12027:SF21, PTHR12027:SF23	wnt2 (P09544) wnt5 (P41221, Q9H1J7)	Week 5
	PTHR12027:SF4, PTHR12027:SF6, PTHR12027:SF7, PTHR12027:SF19	wnt4 (P56705) wnt8 (Q9H1J5, Q93098) wnt9 (O14904, O14905) wnt11 (O96014)	Week 5
	PTHR12027:SF14	wnt6 (Q9Y6F9)	Week 5
	PTHR12027:SF16, PTHR12027:SF22, PTHR12027:SF26	wnt7 (O00755, P56706) wnt16 (Q9UBV4)	Week 5
	PTHR12027:SF11	wnt10 (WNT10A Q9GZT5, WNT10B O00744)	Week 5
Week 3 (17th-23rd July)	PTHR23315	CTNNB1 (P35222)	Week 7
	PTHR16505	CTNNBIP1 (Q9NSA3)	Week 7
Week 4 (24th-31st July)	PTHR10845:SF11	Axin1 (O15169)	Week 8
	PTHR10845:SF103	Axin2 (Q9Y2T1)	Week 8
Week 5-6 (1st-13th August)	PTHR11309:SF31, PTHR11309:SF32, PTHR11309:SF33, PTHR11309:SF34, PTHR11309:SF49	fzd1 (Q9UP38) fzd2 (Q14332) fzd7 (O75084)	Week 9
	PTHR11309:SF28, PTHR11309:SF29	fzd5 (Q13467) fzd8 (Q9H461)	Week 9
	PTHR11309:SF23	fzd4 (Q9ULV1)	Week 9
	PTHR11309:SF24	fzd10 (Q9ULW2)	Week 9
	PTHR11309:SF25	fzd9 (O00144) fzd3 (Q9NPG1)	Week 9
	PTHR11309:SF21	fzd6 (O60353)	Week 9
Week 6-7 (14th-20th August)	PTHR11309:SF7, PTHR11309:SF10	SFRP1 (Q8N474) SFRP2 (Q96HF1) SFRP4 (Q6FHJ7)	Week 10
	PTHR11309:SF10	SFRP5 (Q5T4F7)	Week 10
Week 8 (21st-31st August)	PTHR10878	dvl1 (O14640) dvl2 (O14641) dvl3 (Q92997)	Week 11
Week 9-10 (1st-10th September)	PTHR10529:SF108	LRP5 (O75197)	Week 13
	PTHR10529:SF109	LRP6 (O75581)	Week 13
Week 11 (11th-17th September)	PTHR12607	APC (P25054) APC2 (O95996)	Week 14
	PTHR10373:SF11	LEF1 (Q9UJU2)	Week 15
Week 12-16 (18th September - 22nd October)	Review annotations with respect to PAINT inferences)		

http://gocwiki.geneontology.org/index.php/Wnt_signaling_Pathway#Families_to_annotate_.28BATCH_1.29

Establish Priorities
Example: the Wnt family

1) Signaling pathways (especially those mentioning "Wnt" by name, such as GO:0060070 "canonical Wnt receptor signaling pathway")
2) Signaling pathway/developmental pathway cross-products
3) Regulation of transcription as a result of signaling
4) Developmental terms
   a) organs and tissues
   b) high-level pattern formation

New handling of questions: Wiki instead of SourceForge

- Easier access
- All discussions are public
- Better structure and organization
- Easily exported to Evidence file

PTHR23315

Questions that arose during PAINT curation

Contents [hide]

Examples:

http://gocwiki.geneontology.org/index.php/PTHR23315

http://gocwiki.geneontology.org/index.php/PTHR12027

Statistics
April-August 2010

Family	Description	# proteins	Inferences	Annotations	Time elapsed
PTHR10046	LonP	115	20	1085	(SOP exemplar)
PTHR22573	HPRT	233	46	1900	MF+CC 3 days, BP 1 week
PTHR11829	Forkhead	672	387	14858	5 weeks
PTHR11447	p53	43	30	973	1 week
PTHR10202	presenilin	42	26	784	1 week
PTHR11361	MutS & MSH's	203	57	557	3 days
PTHR24221	TAP2	434	44	2492	1 week
PTHR12027	Wnt's	294	241	5151	2 weeks
PTHR23315	Beta-catenin	172	94	1796	4 days
PTHR16505	Beta-catenin interacting protein	32 (15)	7	98	1 day
PTHR10845	Axin1 & -2	383 (29)		1735	1 day