

Agile Chemistry-Enabled Text Mining

Peter Corbett

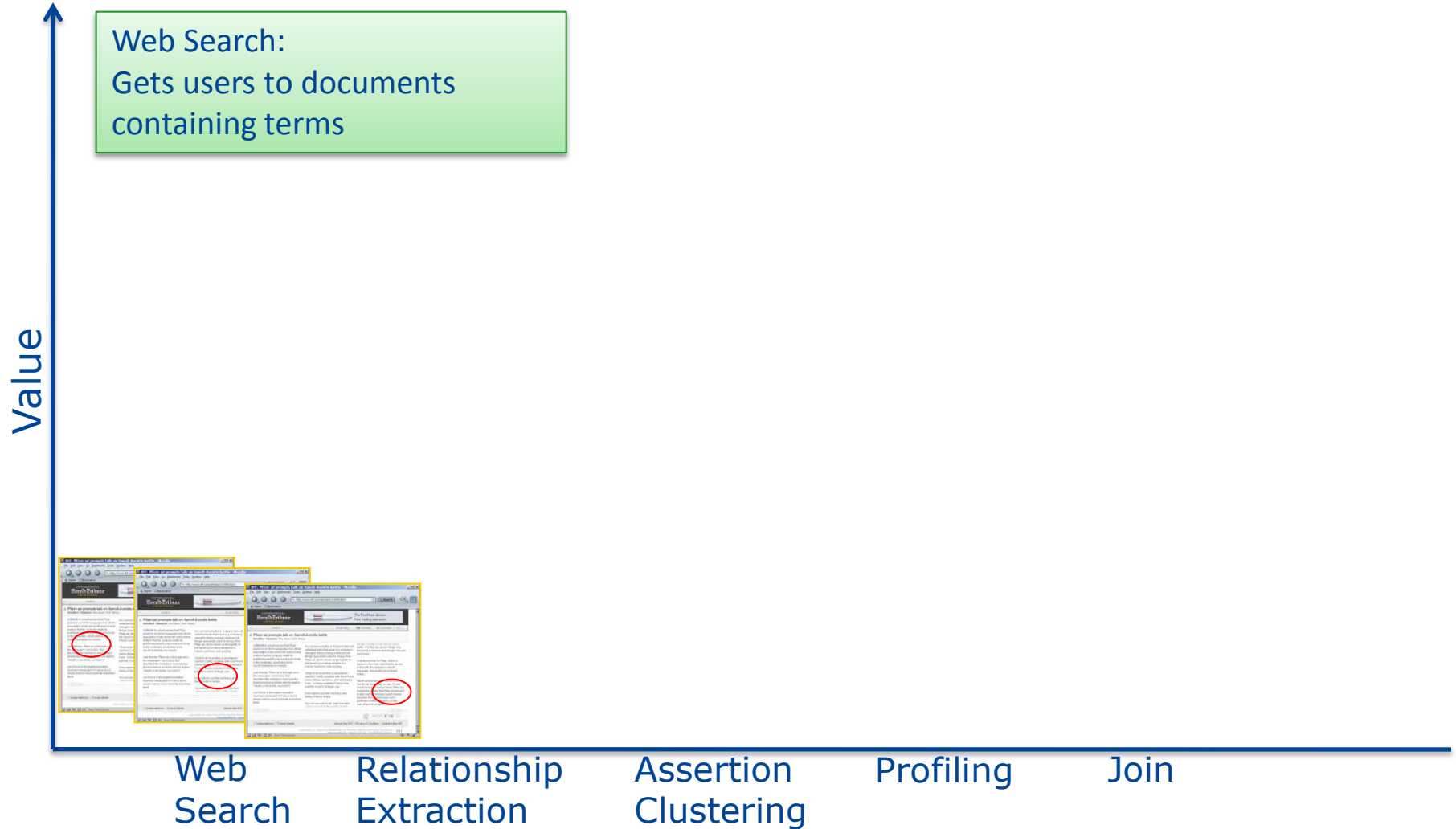
Research Scientist, Linguamatics

May 2011

Flexible and scalable text mining for business-critical knowledge discovery

- Natural language processing (NLP)-based knowledge discovery platform
- Rapidly reveals structured facts and relationships by understanding meaning
- Delivers relevant, high quality results in real-time

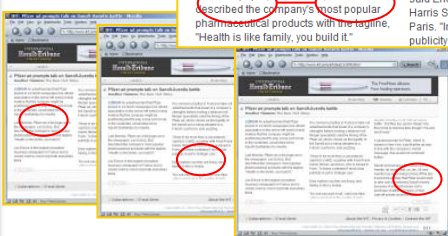
From Documents to Knowledge



From Documents to Knowledge

Value

Relationship Extraction:
Finds relationships within
documents



LONDON An advertisement that Pfizer placed in a French newspaper has stirred speculation in the rumor-rife world of deal makers that the company might be positioning itself to play some sort of role in the contested, unsolicited bid by Sanofi-Synthelabo for Aventis.

Last Monday, Pfizer ran a full-page ad in the newspaper, as Eche, that described the company's most popular pharmaceutical products with the tagline, "Health is like family, you build it."

It is common practice in France to take out advertisements that boast of a company's strengths before making a takeover bid. Merger specialists said the timing of the Pfizer ad, which comes as the legality of the Sanofi bid is being debated in a French courtroom, was puzzling.

"It has to be more than a coincidence," said Eric Cafritz, a partner with Fried Frank Harris Shriver Jacobson, who is based in Paris. "In these contested French bids, publicity is put to strategic use."

super involved in the Pfizer-Sanofi battle. "Did they buy space cheap? Are they trying to improve their image? We just don't know."

A spokeswoman for Pfizer, which is based in New York, said that the ad was in line with the company's overall message. She would not comment further.

Sanofi announced a \$60 billion bid for Aventis, its larger rival, on Jan. 18 and Aventis has been driving to fend off the bid.

Web
Search

Relationship
Extraction

Assertion
Clustering

Profiling

Join

From Documents to Knowledge

Value

Assertion Clustering:
Gets users directly to lists of interest, or assertions and the evidence for them

Drug	Dosage	Doc	Hit
Cyclosporine	5 mg/kg/day	131552052	3 Alterations in renal function in psoriasis patients treated with cyclosporine, 5 mg/kg/day.
	2.5 mg/kg/day	51732342	2 Patients were first treated with cyclosporine either 1.25 or 2.5 mg/kg/day (Sandimmune), in case of inadequate response the dosage was increased to a maximum of 5 mg/kg/day.
	3 mg/kg/day	510824492	1 His headache continued even after tonsillectomy and was effectively treated with cyclosporine A (3 mg/kg/day).
	2 mg/kg/day	38021375	3 OBJECTIVE: The objective of this study was to evaluate the efficacy and safety of the combination of 2 mg/kg/day of cyclosporine with calcipotriol ointment (50 micrograms/gm) in the treatment of severe plaque psoriasis.
	4 mg/kg/day	211208503	1 After the unsuccessful use of non-steroidal antiinflammatory drugs a combination therapy with cyclosporin (4 mg/kg/day) and azapropazone (300 mg t.i.d.) was introduced.
20 mg/kg/day	115093258	2 Male rats (10 per group) were orally administered pimecrolimus at 10 or 30 mg/kg/day, tacrolimus at 3 mg/kg/day or CSA at 20 mg/kg/day for 4 weeks.	

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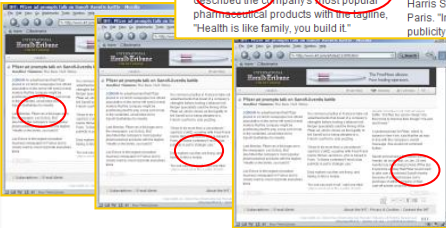
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Web Search

Relationship Extraction

Assertion Clustering

Profiling

Join

From Documents to Knowledge

Value

Profiling:
Summarizes different kinds of information about a compound, person etc.

Pharmacologic Substance	Relation	Entity	Doc	Hit	qID
▼ Etanercept	► treats	Psoriasis	► 1216485060	► 2 Etanercept for the treatment of psoriasis	7
	▼ causes	Injection site reaction	111453808	2 Clinical, histological, and immunophenotypic characteristics of injection site reactions associated with etanercept: a recombinant tumor necrosis factor alpha receptor. Fc fusion protein.	4
		Lymphoma	116454534	1 An increased incidence of lymphomas has been postulated to be associated with etanercept, infliximab and adalimumab; serious infections, such as tuberculosis, have also been reported with these three biologicals, all of which target TNF-alpha.	4
	inhibit	TNF	111961039	1 Although both infliximab and etanercept inhibited transmembrane TNF-mediated activation of human endothelial cells, infliximab was significantly more effective.	1

Drug	Dosage	Doc	Hit
▼ Cyclosporine	5 mg/kg/day	► 131552052	► 3
	2.5 mg/kg/day	► 51732342	2 Patients were first treated with cyclosporine either 1.25 or 2.5 mg/kg/day (Sandimmune), in case of inadequate response the dosage was increased to a maximum of 5 mg/kg/day.
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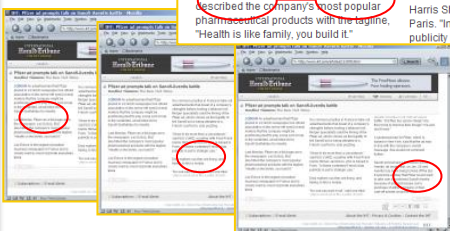
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Web Search

Relationship Extraction

Assertion Clustering

Profiling

Join

From Documents to Knowledge

Join:
Creates indirect correlations
and connections

Value

Cyclosporine	Compound-Gene	Entrez	Genes	Gene-Disease	Psoriasis	Doc	Hit	Doc	Hit
Cyclosporine	inhibit		Interferon	affect	Psoriasis	11789988	1 In addition, cyclosporin blocked the interferon-gamma-induced increase in epidermal 12(S)-HETE binding.	99856816	1... helper 1-type cytokines such as interleukin gamma in psoriasis.
Cyclosporine	inhibit		IL8	affect	Psoriasis	29588080	1 It was found out that CSA inhibits IL-8 production by stimulated THP-1 monocyte cell	811376329	2 Interleukin-8 positive neutrophils in psoriasis.
Cyclosporine	affect		CALM3	affect	Psoriasis	12277142	1 Cyclosporine binds to calmodulin with low affinity, and ...	71879887	1 Epidermal calmodulin levels in psoriasis before & after therapy.

▼ Etanercept	▼ causes	Injection site reaction	111453808	2	Clinical, histological, and immunophenotypic characteristics of injection site reactions associated with etanercept: a recombinant tumor necrosis factor alpha receptor. Fc fusion protein.	4
		Lymphoma	116454534	1	An increased incidence of lymphomas has been postulated to be associated with etanercept, infliximab and adalimumab; serious infections, such as tuberculosis, have also been reported with these three biologicals, all of which target TNF-alpha.	4
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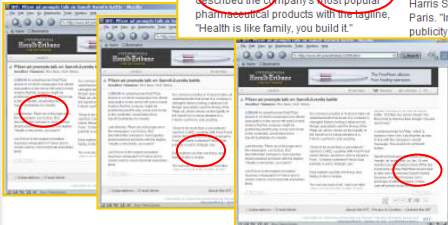
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Web Search

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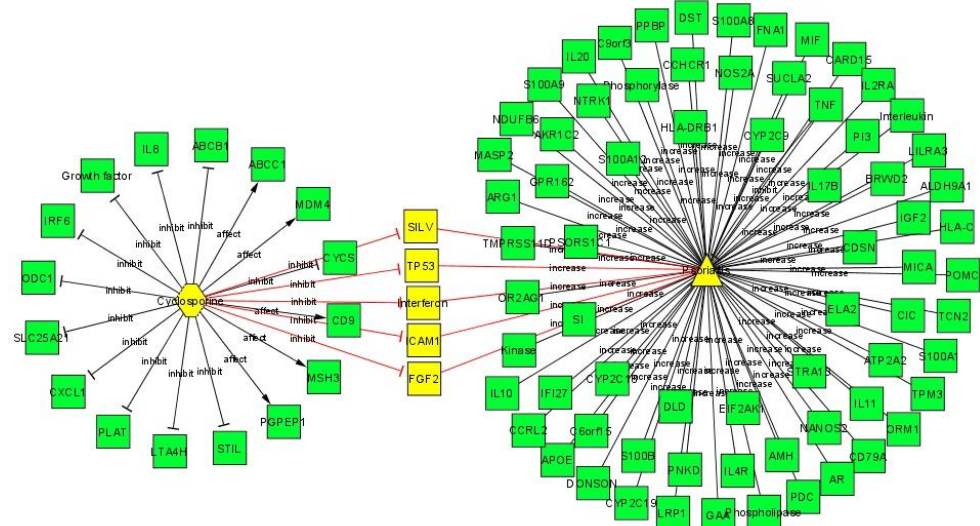
Assertion Clustering

Profiling

Join

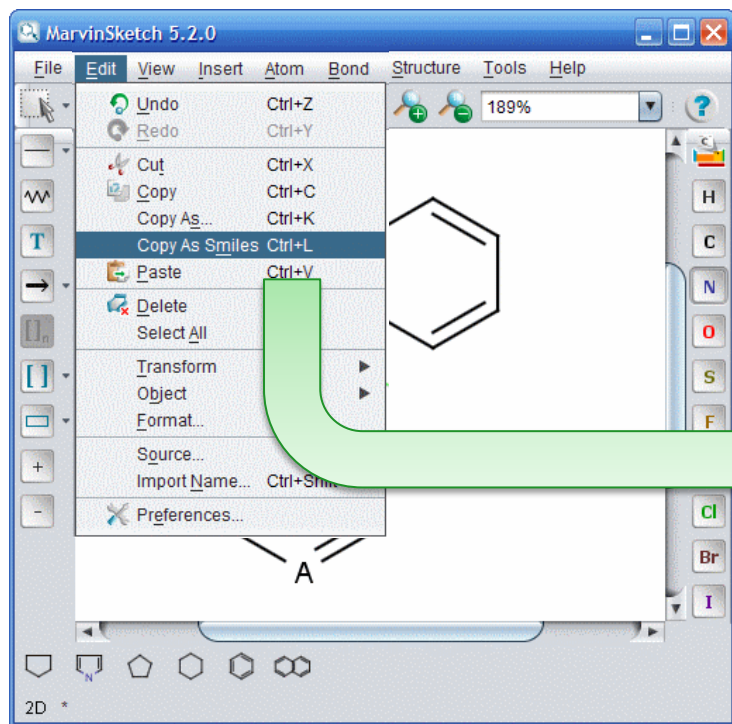
Finding Potential Mechanisms

Discover indirect associations across multiple documents



Cyclosporine	Compound-Gene	Entrez Genes	Gene-Disease	Psoriasis	Doc	Hit	Doc	Hit
Cyclosporine	inhibit	Interferon	affect	Psoriasis	1 1789988	1 In addition, ciclosporin blocked the interferon-gamma-induced increase in epidermal 12(S)-HETE binding.	9 9856816	1 ... helper 1-type cytokines such as interferon-gamma in psoriasis.
Cyclosporine	inhibit	IL8	affect	Psoriasis	2 9588080	1 It was found out that CsA inhibits IL-8 production by stimulated THP-1 monocyte cell ...	8 11378328	2 Interleukin-8-positive neutrophils in psoriasis.
Cyclosporine	affect	CALM3	affect	Psoriasis	1 2277142	1 Cyclosporine binds to calmodulin with low affinity, and ...	7 1879887	1 Epidermal calmodulin levels in psoriasis before & after therapy.
Cyclosporine	inhibit	Growth factor	affect	Psoriasis	2 8884530	1 FK506 and cyclosporin A inhibit growth factor-stimulated human keratinocyte proliferation by blocking cells in the ...	6 14962110	1 Single-nucleotide polymorphisms of vascular endothelial growth factor in psoriasis of early onset.

Using ChemAxon Substructure/Similarity Search to Extract Information Based on Chemical Structure



Class Properties

Chooser Advanced

molecular entity
oral product
phenylpropanoid
stilbenoid
stilbene
4,4-bis-((4-anilino-6-[bis(2-hydroxyethyl)amino]-1,3,5-triazin-2-yl)amino)stilbene-2,2'-disulfonic acid
inorganic entities
organohalogen compound
organofluorine compounds
nilotinib
molecular entities
molecular entities
oxide salt
organic chloride salt
hydrochloride
pirenzepine hydrochloride

Look for: N(C1=CC=CC=C1)C1=CC=C(N1) as: Substructure in: SMILES Search

Case sensitive Below selection Find leaves only Less

More 30 results found (SMILES string match)

Name/synonyms found	Path to parent
nilotinib	...> heterocyclic ...> halogenated ...> heterocyclic ...> fluorinated ...> drug ...> bioactive ...> inhibitor
4,4-bis-((4-anilino-6-[bis(2-hydroxyethyl)amino]-1,3,5-triazin-2-yl)amino)stilbene-2,2'-disulfonic acid	...> natural product ...> secondary amine ...> chlorinated ...> halogenated ...> heterocyclic ...> salt ...> organofluorine
pirenzepine hydrochloride	...> chlorinated ...> halogenated ...> heterocyclic ...> salt ...> organofluorine

OK Cancel

Link Results to Outside Sources

Pharmacologic Substance	Targets	Entrez Genes	Doc	Hit
▼ gefitinib	▶ inhibit	AHSA1	1 17205515	Inversely, in IC1LC131, Erk and Akt pathways remained active, while Jnk and P38 pathways were inhibited by gefitinib.
	▶ treats	Dependents	1 17237287	Gefitinib inhibited DNA synthesis in a concentration-dependent fashion in 6 of 17 lines.
▼ imatinib	▶ dosage	200 mg/day	1 17386117	Three years after treatment with different chemotherapeutic agents for progressive cutaneous Kaposi's Sarcoma with no visceral involvement, he was prescribed imatinib (200 mg/day for two weeks followed by 400 mg/day) after four weeks of treatment he developed anasarca, further progression of KS and agranulocytosis.
	▶ increase	DCX	1 17064569	CONCLUSION: STI571 could promote the activation/maturation of DC derived from BMMNCs of patients with CML in vitro, which might be partially responsible for the fact that the inhibitory effect of VEGF on DC NF- κ B activation was relieved through STI571 inhibiting the overproduction of VEGF in CML.
	▶ inhibit	ABL1	1 17603257	Imatinib also inhibited signaling in the presence of imatinib.
▼ imatinib methanesulfonate	▶ dosage	400 mg/day	1 15161340	In patients with new the chronic phase, resulted in higher progression to the
	▶ increase	AIF1	1 16885745	Gleevec alone res G2 arrest.
	▶ inhibit	ABL1	2 17436575	Gleevec inhibits th
	▶ treats	Adhesion	1 17289809	Depletion of endog of EPCs to activate
▼ lapatinib	▶ inhibit	AKT1	1 17283152	In addition, lapatin non-overexpressin
	▶ treats	Insulin-like growth factor	1 17308062	Importantly, lapatin parental and resist blocking antibody ?
▼ nilotinib	▶ inhibit	ABL1	1 17106016	Nilotinib inhibits BC
	▶ treats	International normalised ratio	1 17106016	Nilotinib inhibits BC
▼ vandetanib	▶ increase	ABCB1	1 17912240	In addition, ZD647 by enhancing the t
	▶ inhibit	EGFR	2 17308046	In vitro, ZD6474 ini and VEGF-inducec

chemicalize.org^{alpha}

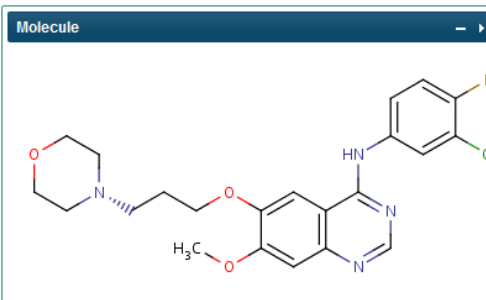
Open All Close All

Manage calculations

Layout: Medicinal Chemist

gefitinib

Search



logP

logP: 3.88

Polar Surface Area

Polar surface area: 68.74

Molecular Surface Area

Calculate Molecular Surface Area

Name

IUPAC name: N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[3-(morpholin-4-yl)propoxy]quinazolin-4-amine

Traditional name: Iressa

Elemental Analysis

Formula: C₂₂H₂₄ClFN₄O₃

Isotope formula: C₂₂H₂₄ClFN₄O₃

Composition: C (59.13%), H (5.41%), Cl (7.93%), F (4.25%), N (12.54%), O (10.74%)

Isotope composition: C (59.13%), H (5.41%), Cl (7.93%), F (4.25%), N (12.54%), O (10.74%)

Mass: 446.902

Exact mass: 446.152096566

Topology Analysis

Simple Ring Counts Path and distance

Atom count: 55

Bond count: 58

Cyclomatic number: 4

Chain atom count: 9

Chain bond count: 11

Asymmetric atom count: 0

Rotatable bond count: 8

ChiKEL: EU Research Project

- Linguamatics and ChemAxon
- Name-to-Structure
 - Evaluation
 - Integration with I2E
 - chemical names
 - proprietary drug names
 - names based on structures (IUPAC names)
- Enhanced output including structures
- Research
 - Image recognition integration
 - Automated generation of ontology hierarchy for structures found
 - Markush search integration
 - Integration of chemical knowledge for text mining e.g. for ranking according to molecular weight

