

Maximizing the Quality, Efficiency and Information Content

*Parthys*  
**Reverse Informatics**  
*The Art of Generating New Knowledge*



**Presentation at ICIC 2010, Vienna, Austria**

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# The Art Of Generating New Knowledge

Data



*Forward*



*Informatics*

Knowledge



*Reverse*



*Informatics*

Curated Data



Normalized Data



*Re-Informatics*



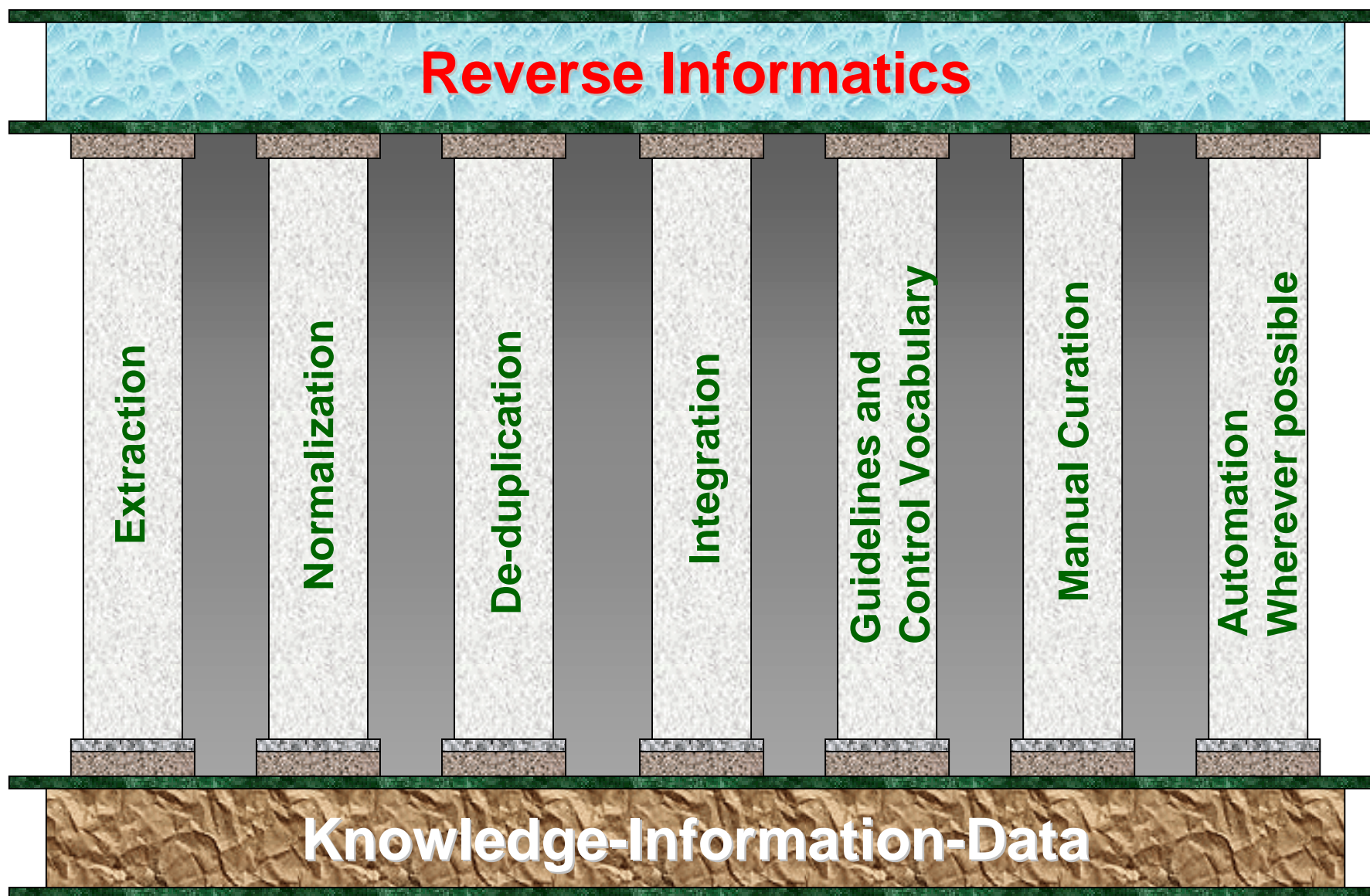
Synthetic  
Knowledge



"Those who cannot remember the past are condemned to repeat it." George Santayana. The Life of Reason



# The Pillars of Reverse Informatics



# Identifying Relevance

[Home](#) [Create set](#) [File labeling](#) [Entity tagging](#) [Entity linking](#) [Compare files](#) [Tutorial](#) [Feedback](#) [Links](#)

## Word Highlighter.

### Positive words

(please fill in one word or expression by line)

ubiquitinates  
ubiquitination  
targets  
associates tightly

### Negative words

(please fill in one word or expression by line)

regenerative  
transplanted  
preclinical  
outbreed  
somatosensory

GO!

## Article to curate.

Remaining items :13

Item identifier :19414597

### Title :

Identification of the serine 307 of LKB1 as a novel phosphorylation site essential for its nucleocytoplasmic transport and endothelial cell angiogenesis.

### Content :

LKB1, a master kinase that controls at least 13 downstream protein kinases including the AMP-activated protein kinase (AMPK), resides mainly in the nucleus. A key step in LKB1 activation is its export from the nucleus to the cytoplasm. Here, we identified S307 of LKB1 as a putative novel phosphorylation site which is essential for its nucleocytoplasmic transport. In a cell-free system, recombinant PKC-zeta phosphorylates LKB1 at S307. AMPK-activating agents stimulate PKC-zeta activity and LKB1 phosphorylation at S307 in endothelial cells, hepatocytes, skeletal muscle cells, and vascular smooth muscle cells. Like the kinase-dead LKB1 D194A mutant (mutation of Asp194 to Ala), the constitutively nucleus-localized LKB1 SL26 mutant and the LKB1 S307A mutant (Ser307 to Ala) exhibit a decreased association with STRAD alpha. Interestingly, the PKC-zeta consensus sequence surrounding LKB1 S307 is disrupted in the LKB1 SL26 mutant, thus providing a likely molecular explanation for this mutation causing LKB1 dysfunction. In addition, LKB1 nucleocytoplasmic transport and AMPK activation in response to peroxynitrite are markedly reduced by pharmacological inhibition of CRM1, which normally facilitates nuclear export of LKB1-STRAD complexes. In comparison to the LKB1 wild type, the S307A mutant complexes show reduced association with CRM1. Finally, adenoviral overexpression of wild-type LKB1 suppresses, while the LKB1 S307A mutant increases, tube formation and hydrogen peroxide-enhanced apoptosis in cultured endothelial cells. Taken together, our results suggest that, in multiple cell types the signaling pathways engaged by several physiological stimuli converge upon PKC-zeta-dependent LKB1 phosphorylation at S307, which directs the nucleocytoplasmic transport of LKB1 and consequent AMPK activation.

not ppi

→ Protein- Protein Interaction  
Swiss-Prot ID: Protein  
Normalization




[illegible]

← **Unstructured Knowledge**

TBdb [Compatibility Mode] - Microsoft Excel


B	C	D	E	F	G
PubMed Link	PubMed ID (PMID)	Given Name	IUPAC Name	SMILES	Assay Type
med.org/11796333	11796333	Compound 1h	(E)-N-(1-	O=C(N/N=C(C)/C2=CC=CC=C2)	Invitro
med.org/11796333	11796333	Compound 1h	(E)-N-(1-	O=C(N/N=C(C)/C2=CC=CC=C2)	Invitro
med.org/11796333	11796333	Compound 1i	(E)-N-(1-2	O=C(N/N=C(C)/C2=CC=CC=C2F	Invitro
med.org/11796333	11796333	Compound 1i	(E)-N-(1-2	O=C(N/N=C(C)/C2=CC=CC=C2F	Invitro
med.org/11796333	11796333	Compound 1i	(E)-N-(1-2	O=C(N/N=C(C)/C2=CC=CC=C2F	Invitro
med.org/11796333	11796333	Compound 1i	(E)-N-(1-2	O=C(N/N=C(C)/C2=CC=CC=C2F	Invitro
med.org/11796333	11796333	Compound 1i	(E)-N-(1-2	O=C(N/N=C(C)/C2=CC=CC=C2F	Invitro
med.org/11796333	11796333	Compound 1i	(E)-N-(1-2	O=C(N/N=C(C)/C2=CC=CC=C2F	Invitro
med.org/11796333	11796333	Compound 1i	(E)-N-(1-2	O=C(N/N=C(C)/C2=CC=CC=C2F	Invitro
med.org/11796333	11796333	Compound 1i	(E)-N-(1-2	O=C(N/N=C(C)/C2=CC=CC=C2F	Invitro
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med.org/11796333	11796333	Compound 1i	(E)-N-(1-2	O=C(N/N=C(C)/C2=CC=CC=C2F	Invitro
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med.org/11796333	11796333	Compound 1i	(E)-N-(1-2	O=C(N/N=C(C)/C2=CC=CC=C2F	Invitro
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med.org/11796333	11796333	Compound 1k	(E)-N-(1-4	O=C(N/N=C(C)/C2=CC=CC=C2F	Invitro



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The Art of Generating New Knowledge

et5 Sheet4 Sheet2 final

**Structured Data** ➡

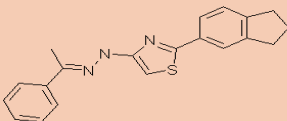


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# Tuberculosis-Database

ID3

Structure



Reference

Turan-Zitouni G, Eur J Med Chem. 2008 May;43(5):981-5

PubMed\_Link

<http://pubmed.org/17719146>

PubMed\_ID

17719146

Given\_Name

Compound 3a

SMILES

C/C(C)=CC=C=C1=MNNC2=CSC(C3=CC(CCC4)=C4=C3)=N2

IUPAC\_Name

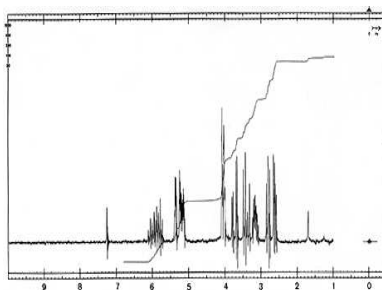
N-(2-Indan-5-yl-thiazol-4-yl)-N'-(1-phenyl-eth-(E)-ylidene)-hydrazine

Assay_Type	Assay	Target_Name	Target_Normalized Name	Cells/Organism	Assay_Dose_Range	Conc./Conc_Range	M_Volume/Parameter	Value	SD	Unit
1	Invitro	Antimycobacterial activity	-	Mycobacterium	-	-	MIC	>6.25	-	µg/mL
2	Invitro	Antimycobacterial activity	-	Mycobacterium	6.25 µg/mL	-	-	89	-	%
3	Invitro	Cytotoxicity against	-	NIH/3T3 cells	-	-	IC50	200	9.1	µg/mL
4	Invitro	Cytotoxicity against	-	NIH/3T3 cells	49 µg/mL	-	Toxicity	Non-toxic	-	-

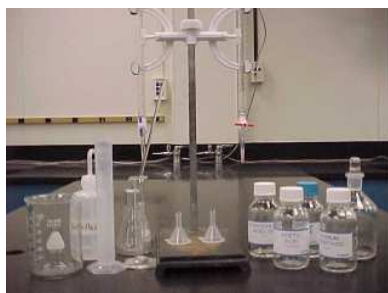


# Thematic Databases

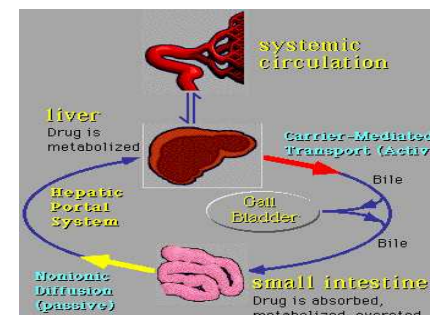
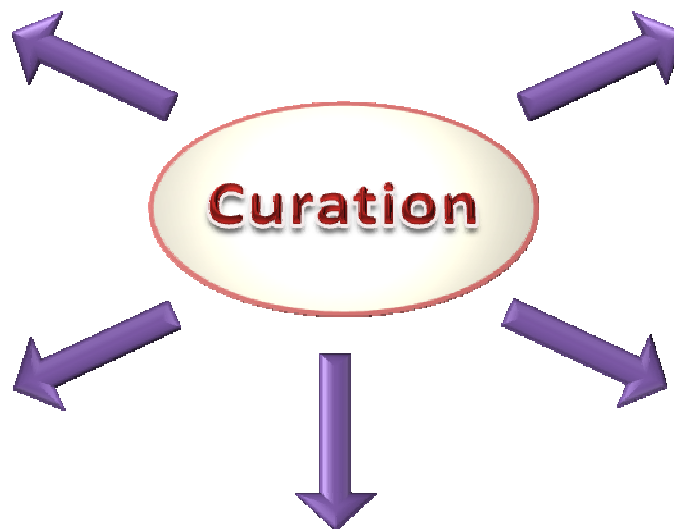
Reverse Informatics has the capability to extract relevant information as per the Guidelines and Control Vocabulary in all the Scientific areas: Pharmacological, Chemical, Biological, and toxicity information from scientific literatures/articles for each component and its relating facts.



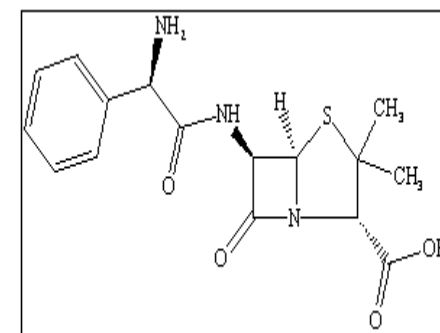
Physicochemical properties



Chemical Synthesis



Pharmacology



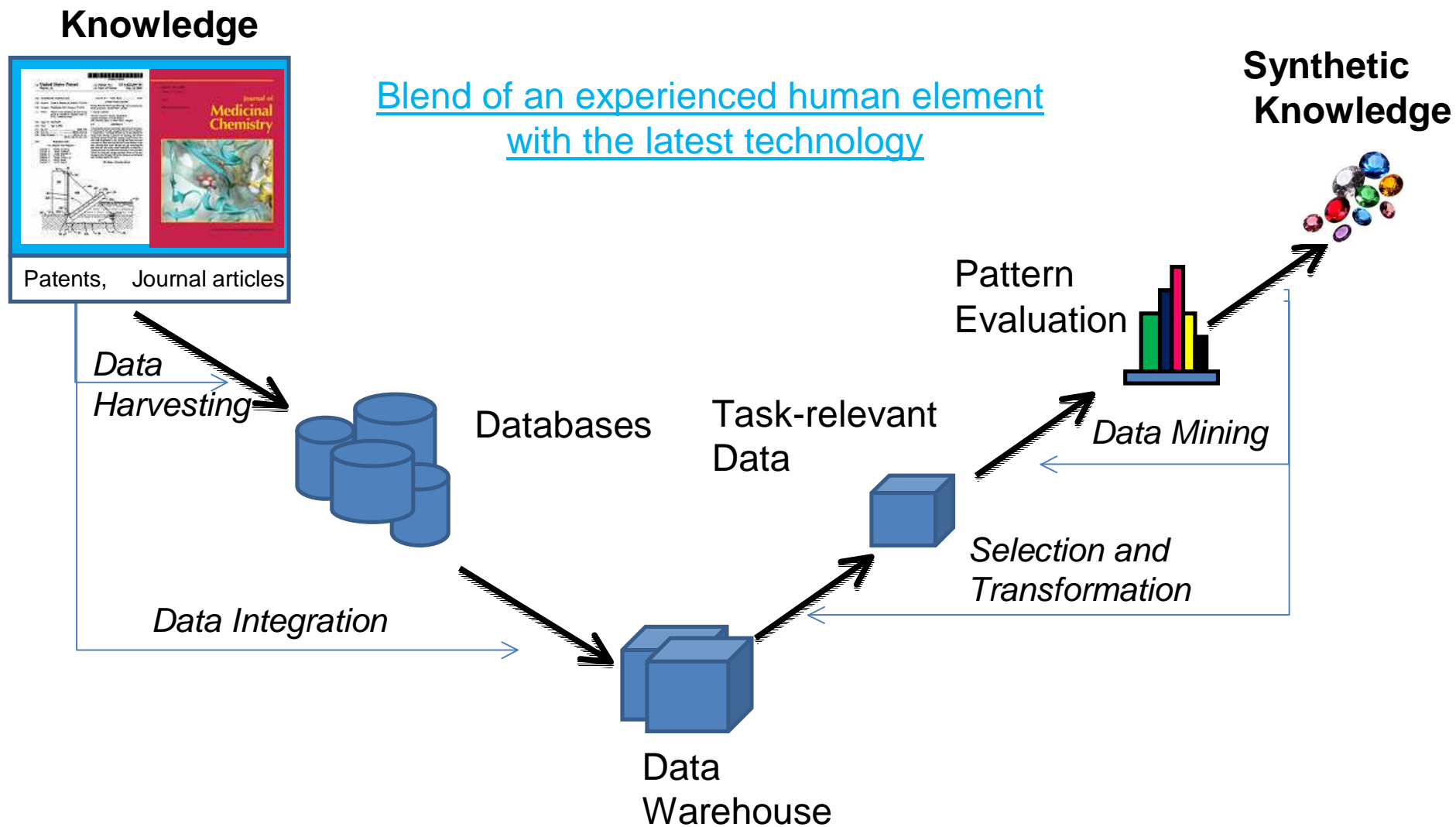
Structure

...AAATCGTCAA GATTGAGGCG...

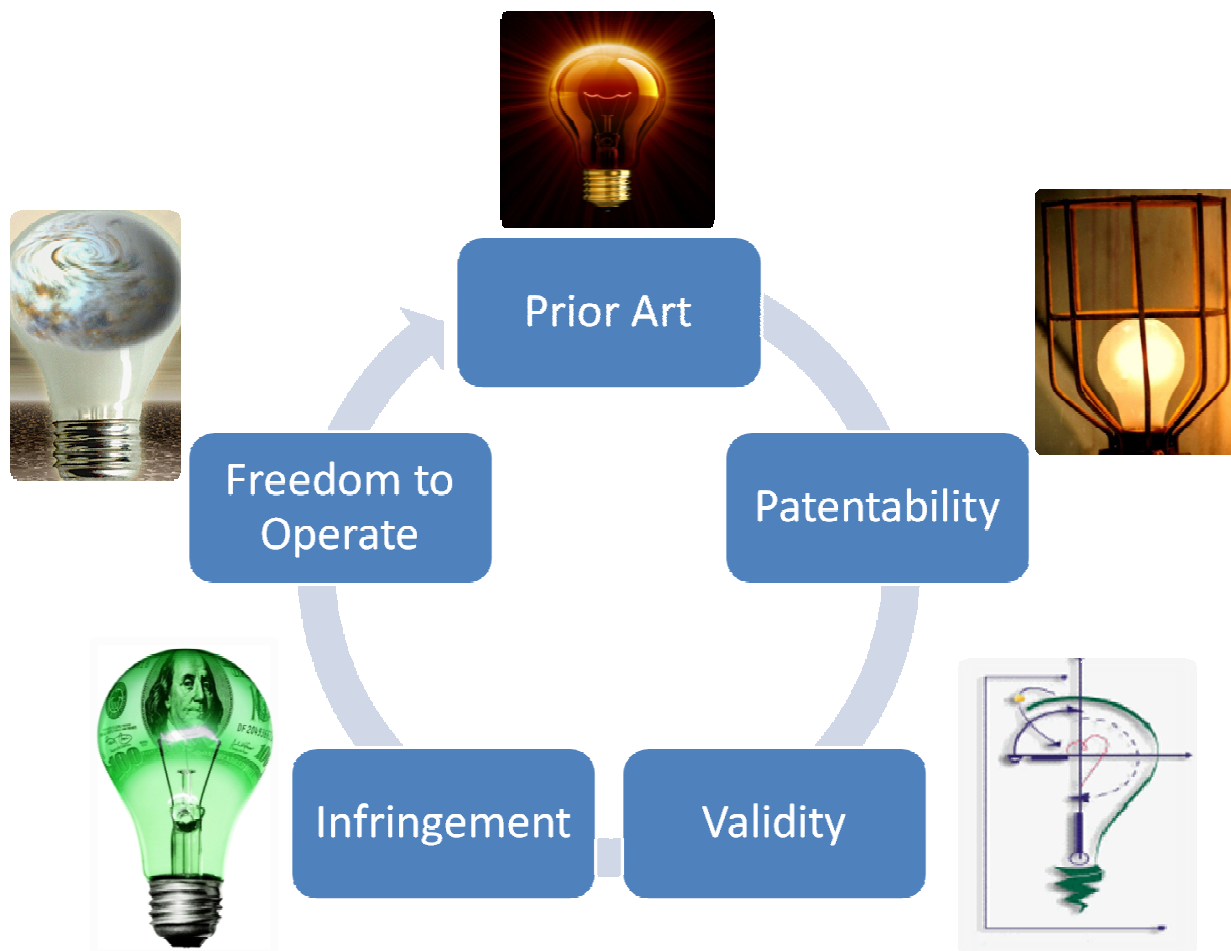
Gene Sequences from literature



# The Reverse Informatics Steps



# Patent Search Services



## Technology Coverage

Chemistry  
Biotechnology  
Pharmaceuticals  
Medical Devices

Electrical  
Electronics  
Mechanical  
Consumer Products





# ***Leveraging Literature Information***



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# ***Thank You!***



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