



REUTERS/Wolfgang Rattay

## Intellectual Property and Science

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# ***THOMSON REUTERS IP & SCIENCE: APOIO TOTAL À INOVAÇÃO CIENTÍFICA E TECNOLÓGICA***

Antero Macedo, PhD  
[antero.macedo@thomsonreuters.com](mailto:antero.macedo@thomsonreuters.com)



**THOMSON REUTERS**

# MARKET TRENDS

# Big Data



THOMSON REUTERS

# Trends in Biological Information Generation – How to Keep Updated?

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**13.149**

Publications with  
“EGFR” &  
“Cancer” in  
title/abstract\*

EGFR



**28.961**

Publications with  
“EGFR” in  
title/abstract\*



~1 hour per paper  
= 548 days  
without sleep/rest!

~1 hour per paper  
= 1.206 days  
without sleep/rest!



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\*Searches performed 3<sup>rd</sup> of Set 2014 in Pubmed

Understanding molecular basis of  
disease = understanding whole  
GENOME & how it all interacts!

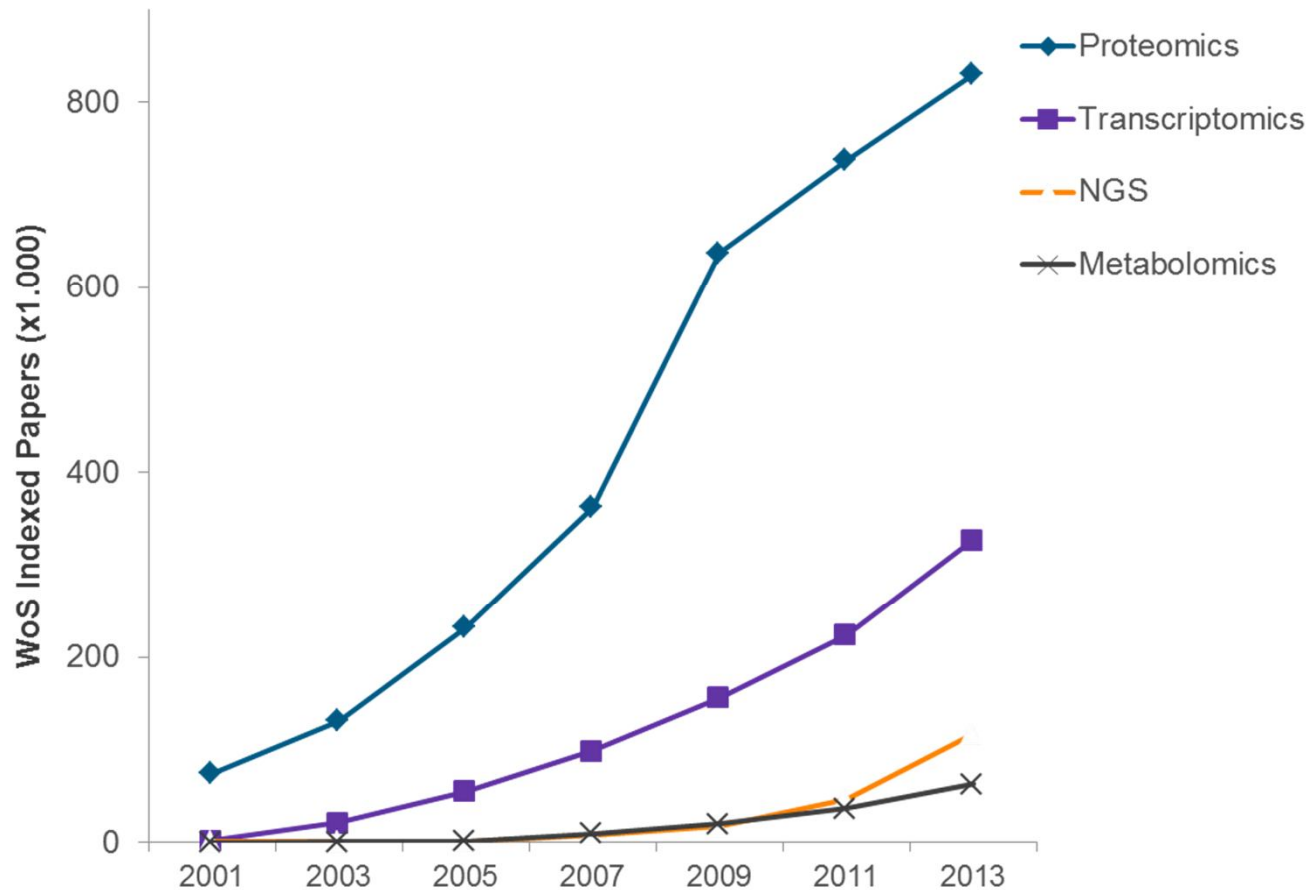


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# Trends in Biological Information Generation – How to Keep Updated?

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**+229 Million  
Scientific Papers in  
the last 100 years**



# How to Structure Information?

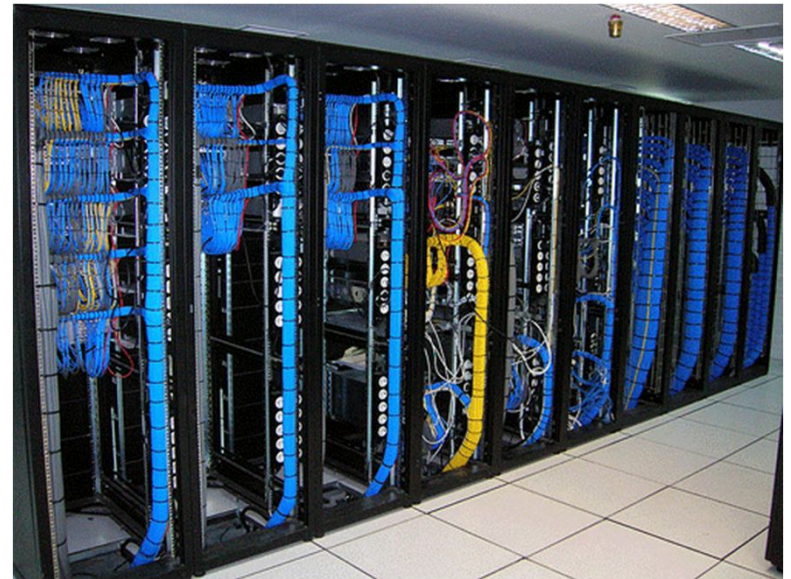
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**Unstructured**

**80%**

**VS**



**Structured**

**20%**



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# THOMSON REUTERS

is the largest provider of  
intelligent information

*to business and professional  
customers around the world.*

*Generating a total revenue of  
\$12.5 billion.*

## GLOBAL PRESENCE

*We operate in 300 cities  
in over 100 countries.*

## PUBLICLY TRADED

*We hold ourselves  
accountable through  
compliance with  
Sarbanes Oxley and a  
stringent code of  
business ethics.*

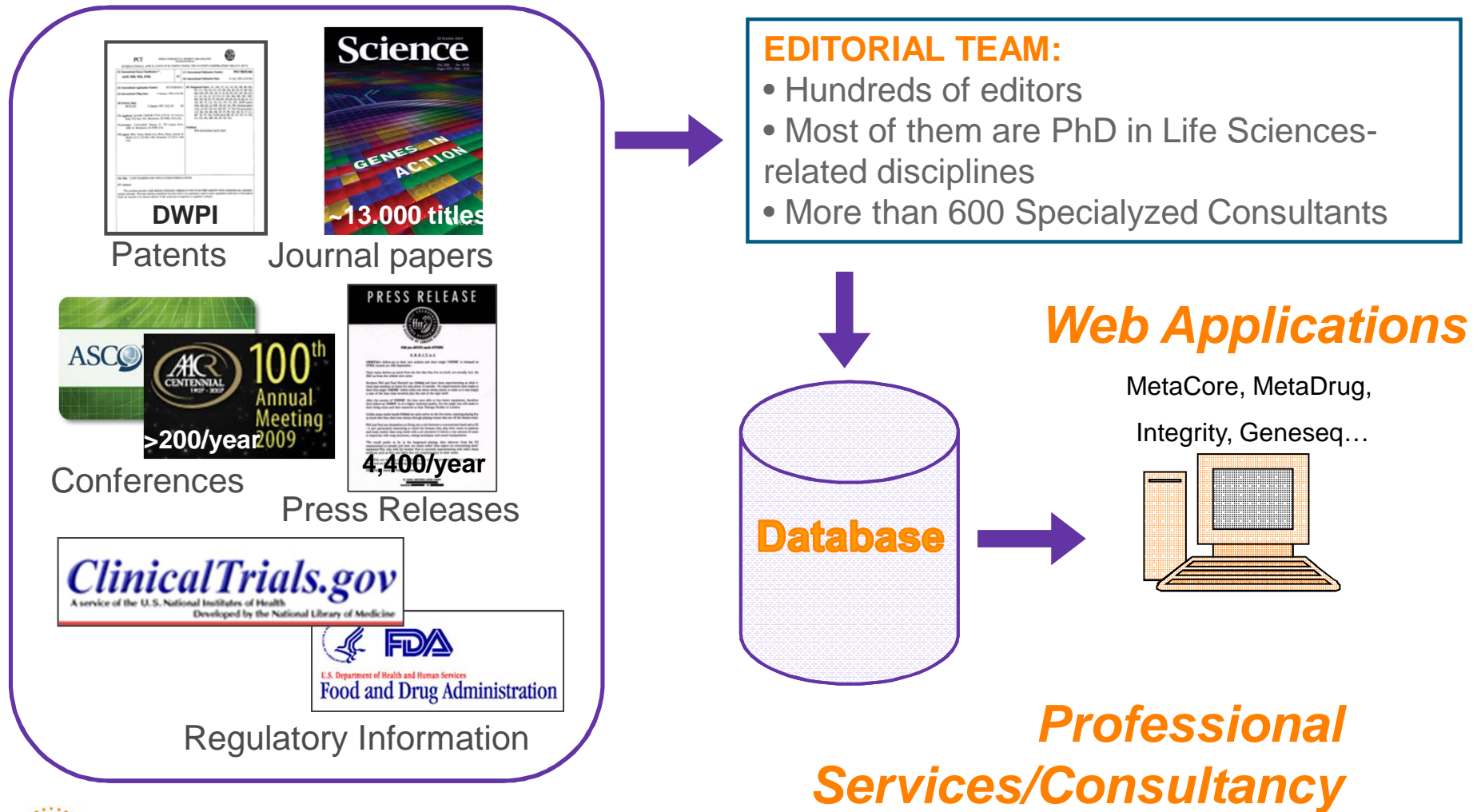
## STRONG BRAND

*Named 57th Best  
Global Brand of 100 as  
ranked by InterBrand.*



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# Thomson Reuter Strategy for Information Management – Road to Knowledge





# Thomson Reuters IP&Science: Full Support to Scientific Innovation

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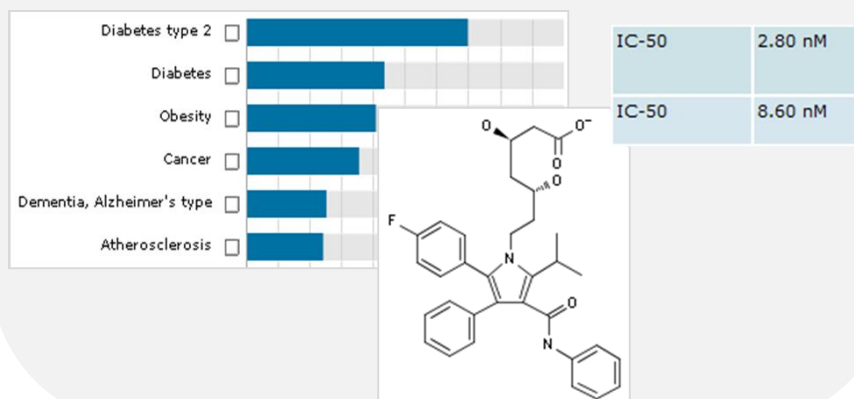
- How to make a comprehensive **technological prospection** to better position your research?
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- **Predict** the therapeutic **effect**, **toxic** potential and **mechanisms of action** of your chemical compounds
- Explore what has been **patented** in your innovation area
- Define the **most impactful journal** to publish your data



# Scientific and Strategic Overview of Drug Research & Development

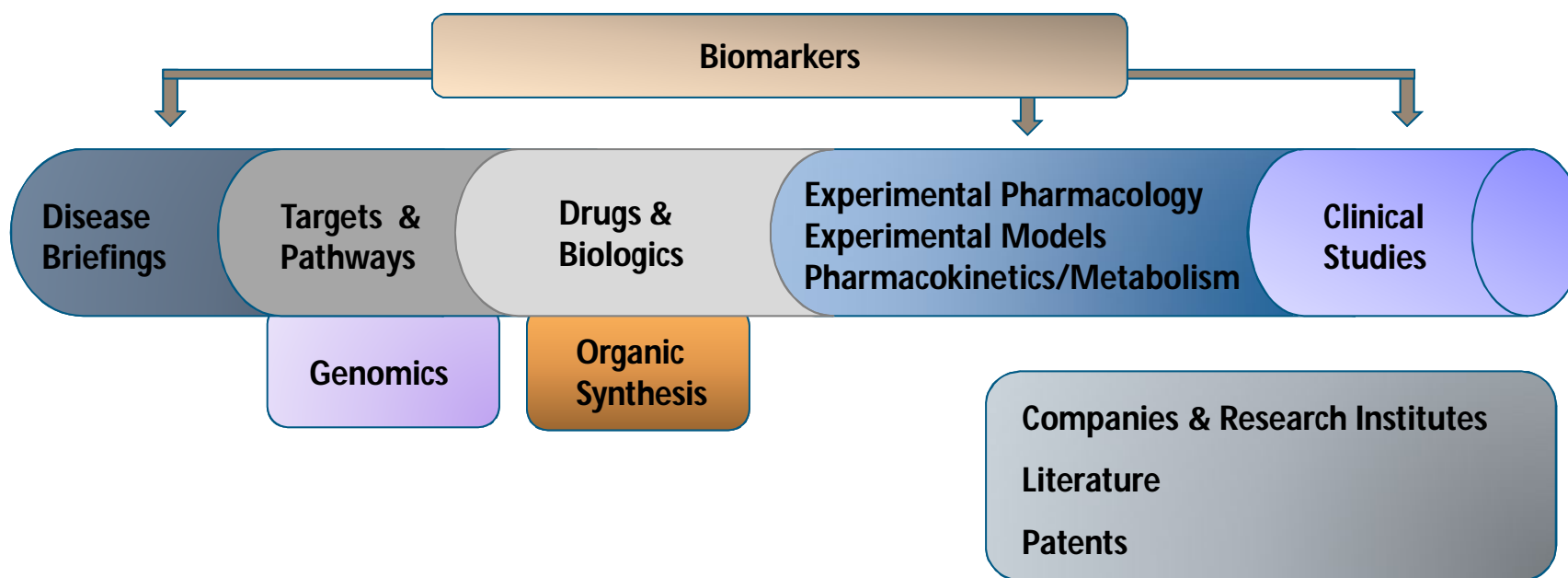
## INTEGRITY

- Provides pharmaceutical pipeline competitor intelligence for the scientific researcher
- Prioritize research activities with evaluation of prior art and competitors
- Validate hypotheses with biomarker, drug, chemistry, pharmacology and PK content



# Integrity: All the Most Relevant Data to Support Drug R&D Integrated in a Single Source

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# Integrity Concept

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## Thomson Reuters IP&Science: Full Support to Scientific Innovation

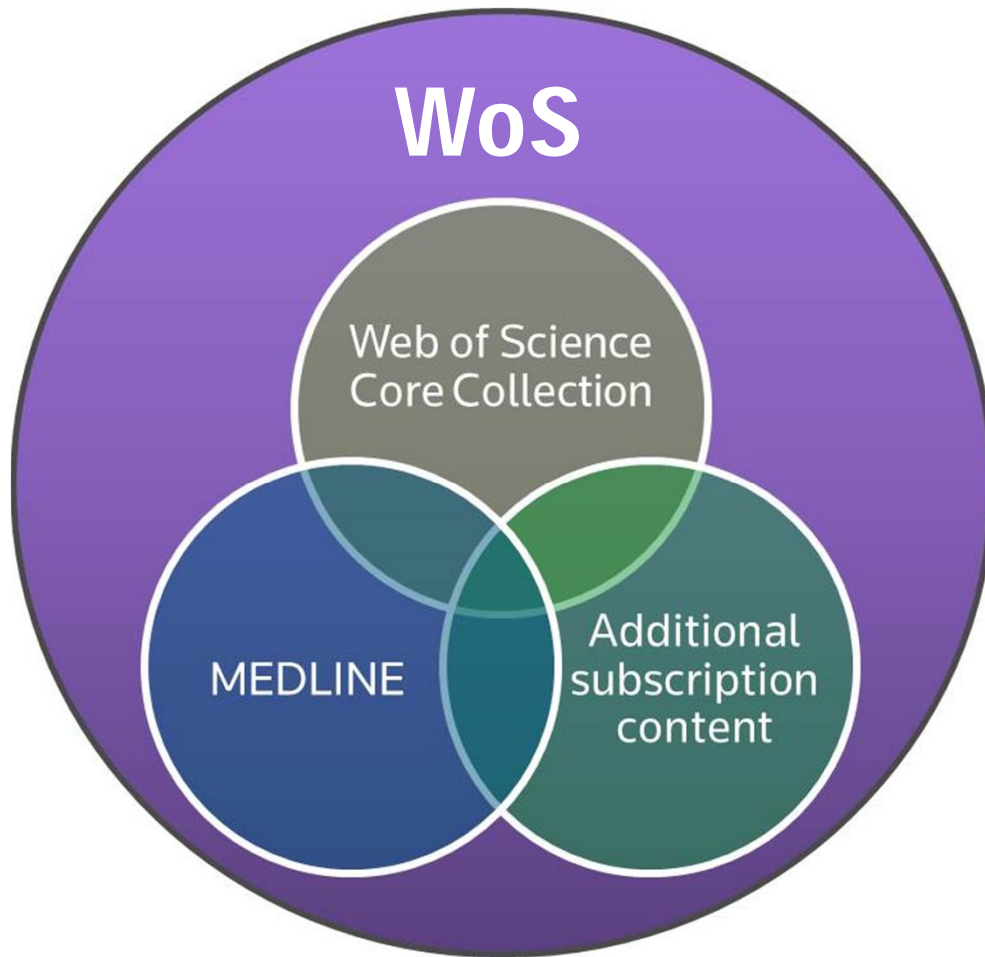
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# The Web of Science platform

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- The Web of Science platform includes papers from:
  1. Web of Science Core Collection indexed journals, books and conferences
  2. MEDLINE indexed journals
  3. Literature, datasets, and patents from 11 additional databases (by subscription)
- You can refine an All Databases search to see which papers are unique to one database, or to see which papers are covered in both the Core Collection and Medline.

# WoS: Track the Main Publications and Authors in Your Field

Web of Science™ | InCites™ | Journal Citation Reports® | Essential Science Indicators™ | EndNote™

## WEB OF SCIENCE™

**Pesquisa** | Minhas ferramentas ▼ | Histórico de pesquisa | Lista marcada

**Resultados: 226.409** (de Todas as publicações) (Número de citações)

Classificar por: **Data de publicação -- mais recente para mais antiga** ▼

Página 1 de 10.000

Use as caixas de seleção para remover itens individuais deste relatório de citações ou para restringir a itens publicados entre 1864 e 2015 Ir

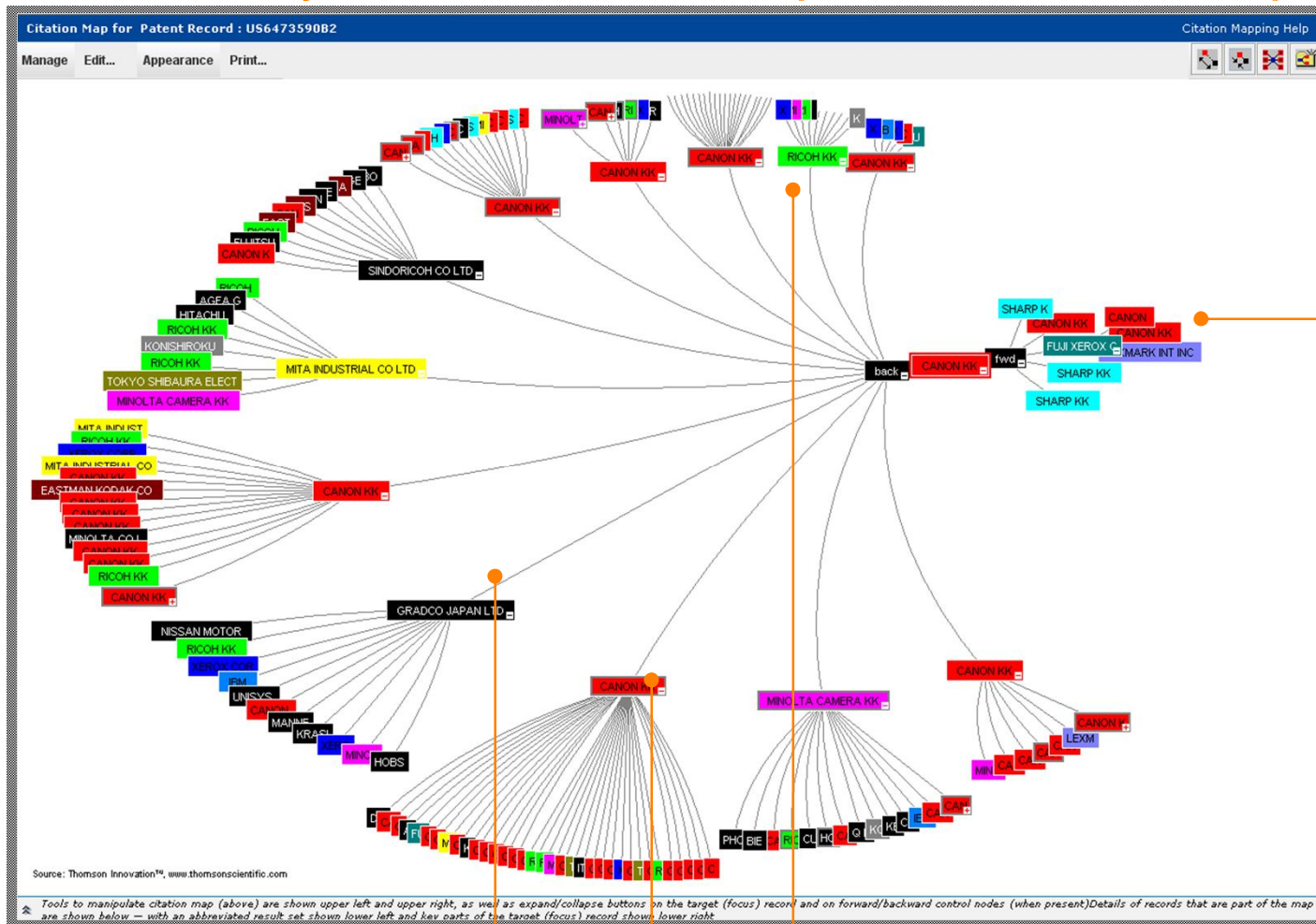
**Refinar**

Procurar

Bases de dados

	2011	2012	2013	2014	2015	Total	Média de citações por ano
1. <b>WAF1, A POTENTIAL MEDIATOR OF P53 TUMOR SUPPRESSION</b> Por: ELDEIRY, WS; TOKINO, T; VELCULESCU, VE; et al. CELL Volume: 75 Edição: 4 Páginas: 817-825 Publicado: NOV 19 1993	2124	2091	1995	1905	998	44180	1472.67
2. <b>Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib</b> Por: Lynch, TJ; Bell, DW; Sordella, R; et al. NEW ENGLAND JOURNAL OF MEDICINE Volume: 350 Edição: 21 Páginas: 2129-2139 Publicado: MAY 20 2004	194	181	149	138	97	6796	295.57
3. <b>EGFR mutations in lung cancer: Correlation with clinical response to gefitinib therapy</b> Por: Paez, JG; Janne, PA; Lee, JC; et al. SCIENCE Volume: 304 Edição: 5676 Páginas: 1497-1500 Publicado: JUN 4 2004	533	548	561	560	273	5840	486.75
	441	469	478	477	236	4965	413.75

# CITATION MAP ANALYSIS: Easily Track the Development of a Concept



FUTURE: THE  
IMPACT OF AN  
IDEA ON THE  
SCIENTIFIC  
COMMUNITY

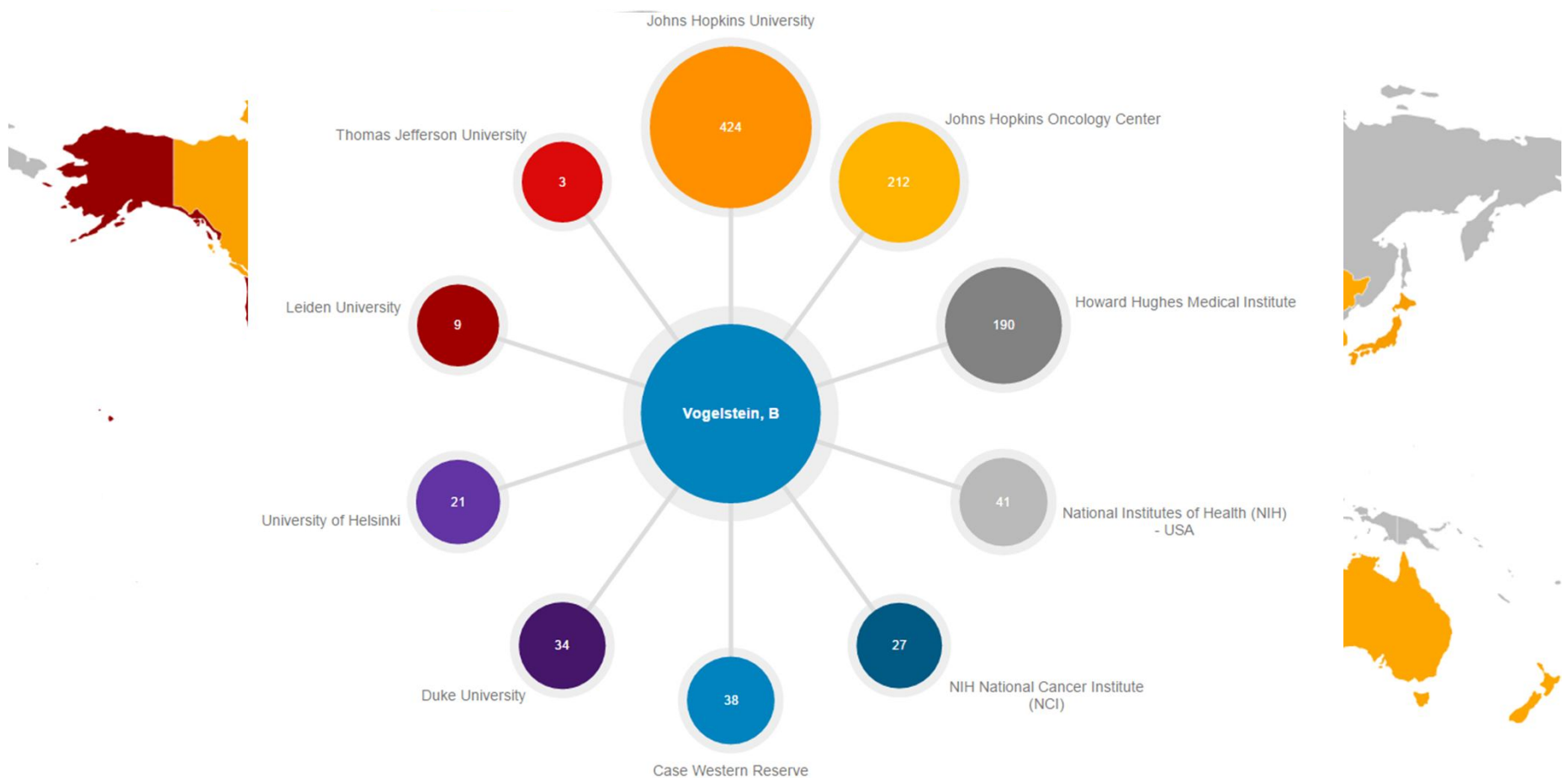
PAST: UNDERSTAND THE  
EVOLUTION OF AN INVENTION



tumor  
but not  
structure, ar  
s in cultu  
this p53.  
ectly indu

# InCites: Map the Scientific Networks

## Bert Vogelstein Collaborative Network



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Source: TR InCites

# Thomson Innovation: Complete Coverage of Innovative Technologies

WORLD-  
CLASS  
CONTENT

Patents



Scientific  
Literature



News



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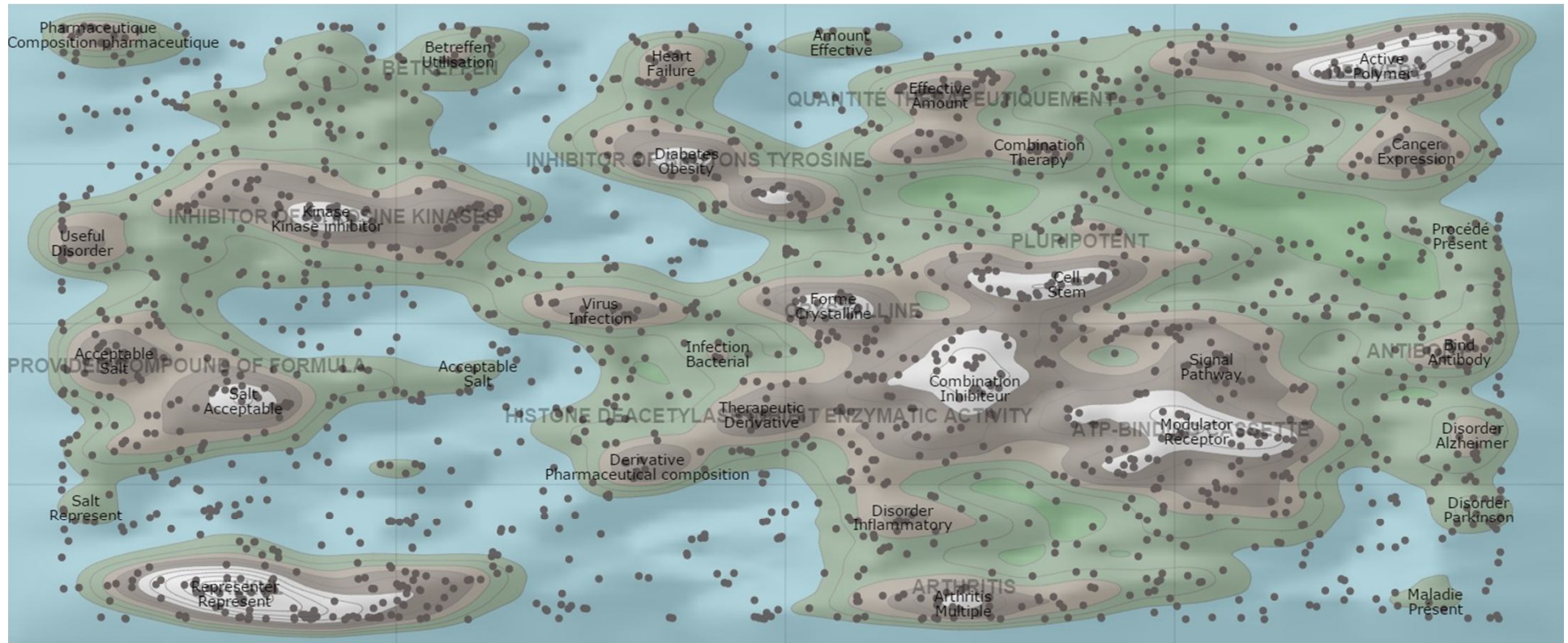


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# Themescape Map: Innovation Under a Different Perspective

Query: Kinase Inhibitors



Source: Thomson Innovation®, [www.thomsoninnovation.com](http://www.thomsoninnovation.com)



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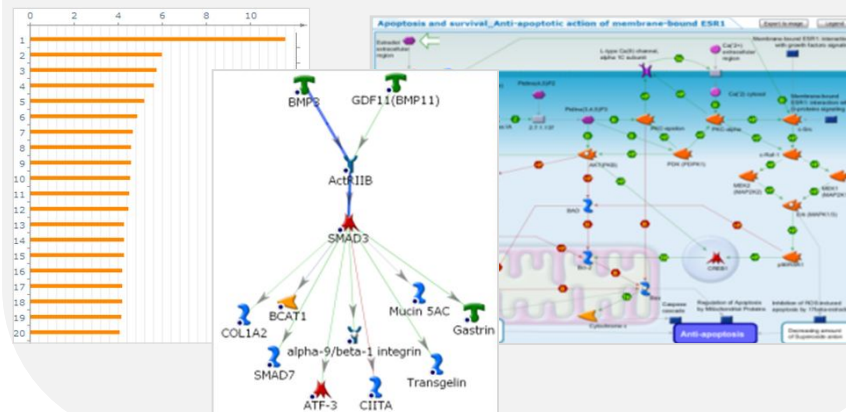
- How to make a comprehensive **technological prospection** to better position your research?
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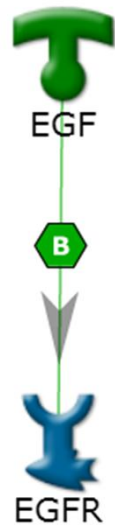
# LINKING BIOLOGICAL INSIGHTS WITH DRUG DISCOVERY KNOWLEDGE

## METACORE

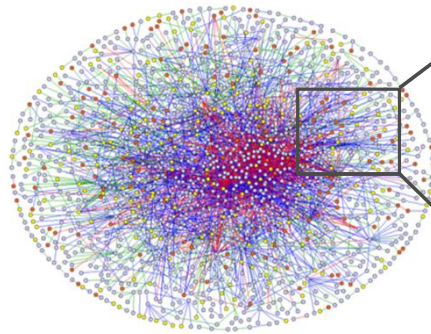
- Provides molecular understanding of disease
- Analyze and understand experimental findings (Omics data) in the context of validated biological pathways.
- Generate hypotheses around novel targets, biomarkers, mechanisms of action



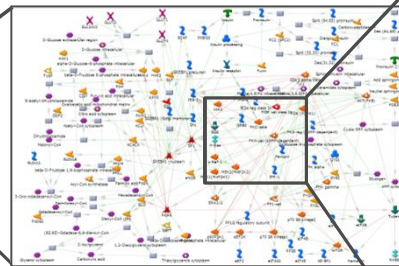
# HIERARCHY OF INFORMATION: FROM INTERACTIONS TO PATHWAYS



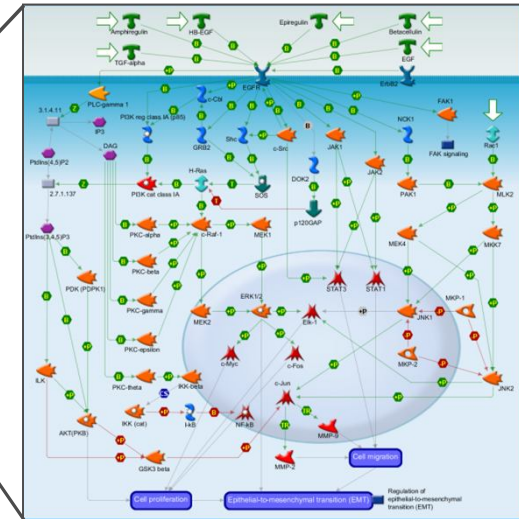
**MOLECULAR  
INTERACTION**



**NETWORK:**  
~ 1,500,000  
molecular interactions



**PROCESS NETWORK**  
~1,103 process networks



**PATHWAY**  
~ 3,000 pathways

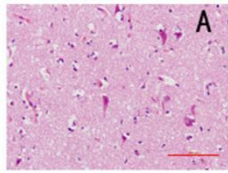


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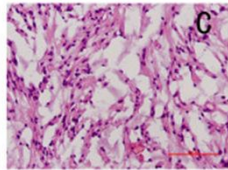
# MetaCore – Molecular Understanding of Diseases

## GBM-HE

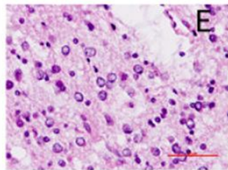
Normal



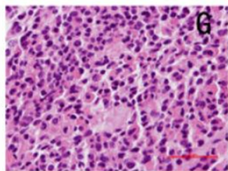
Grade1



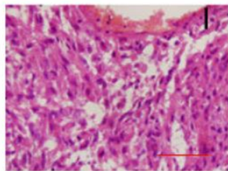
Grade2



Grade3



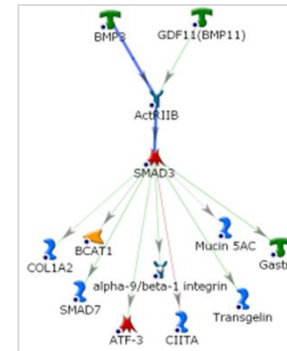
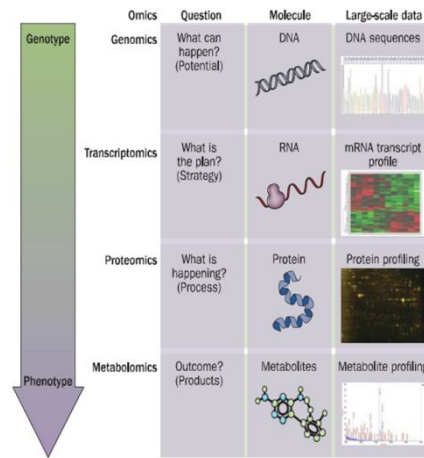
Grade4



Wang M *et al* - BMC Cancer (2011)

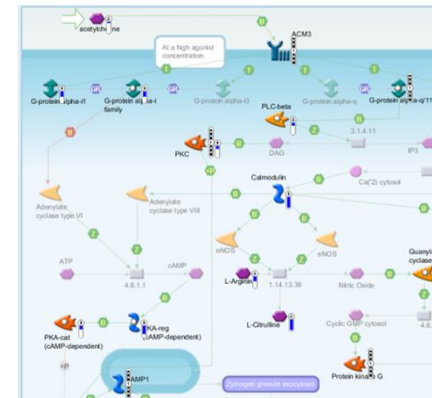


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## Network Reconstruction

- Mechanism of Action
- Onthology
- Biomarker Identification
- Therapeutical Targets

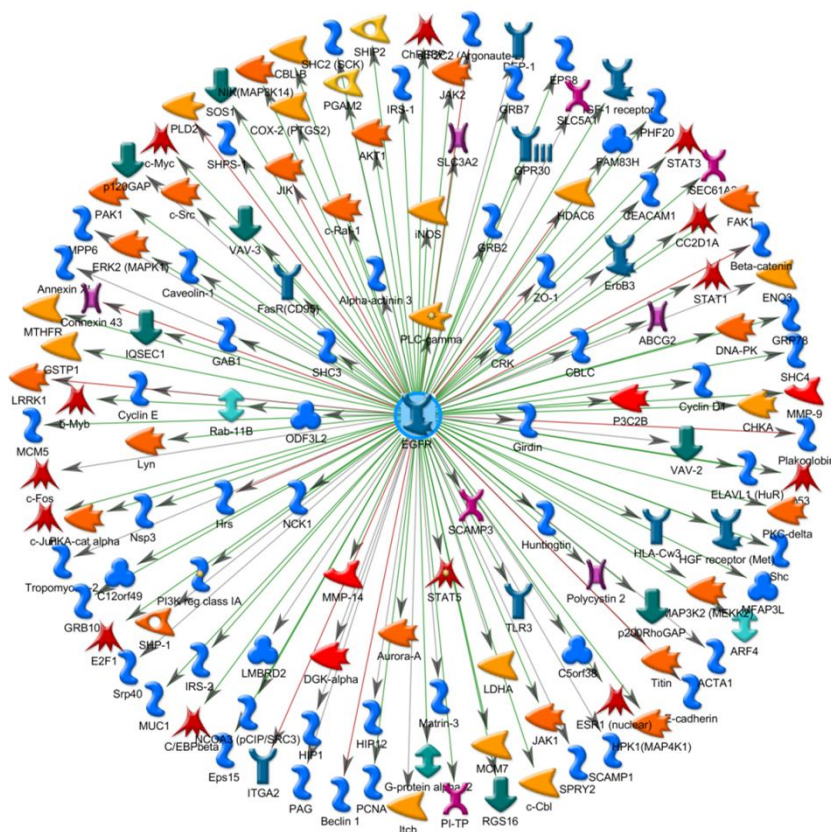


## Functional Enrichment

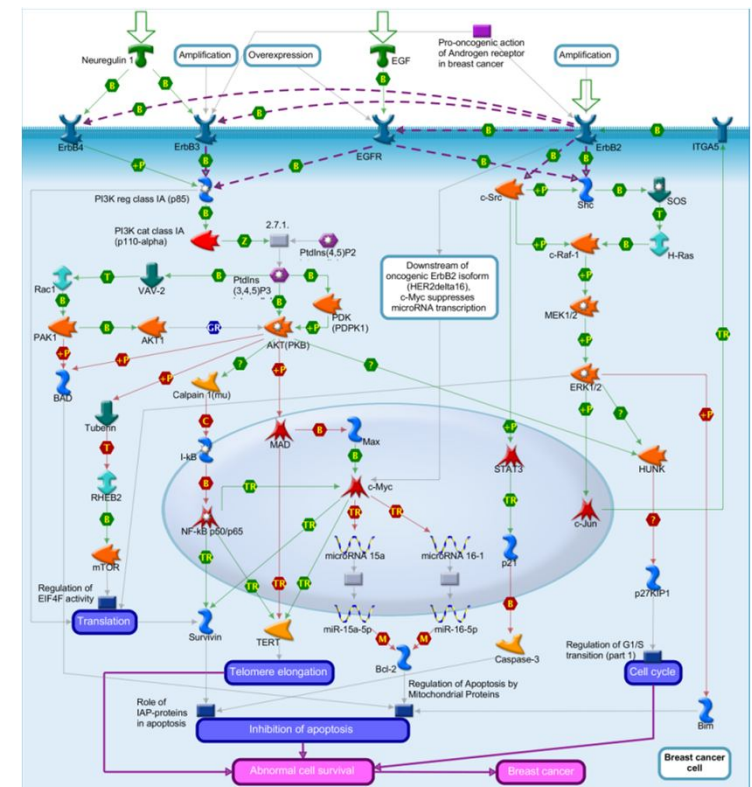


# What's the Functional Consequences of Modulating my Favourite Target?

## Downstream EGFR Effectors



## Functional Outcome



# Patient Stratification – Beneficial Strategy for Drug Development and Use

---

## Blockbuster strategy

“One drug for all patients”



New strategy is needed

Marginal Efficacy

Higher risk of toxicity/side effects

## Patient stratification

“The most efficient and safe drug for a cohort of patients”



Good Efficacy

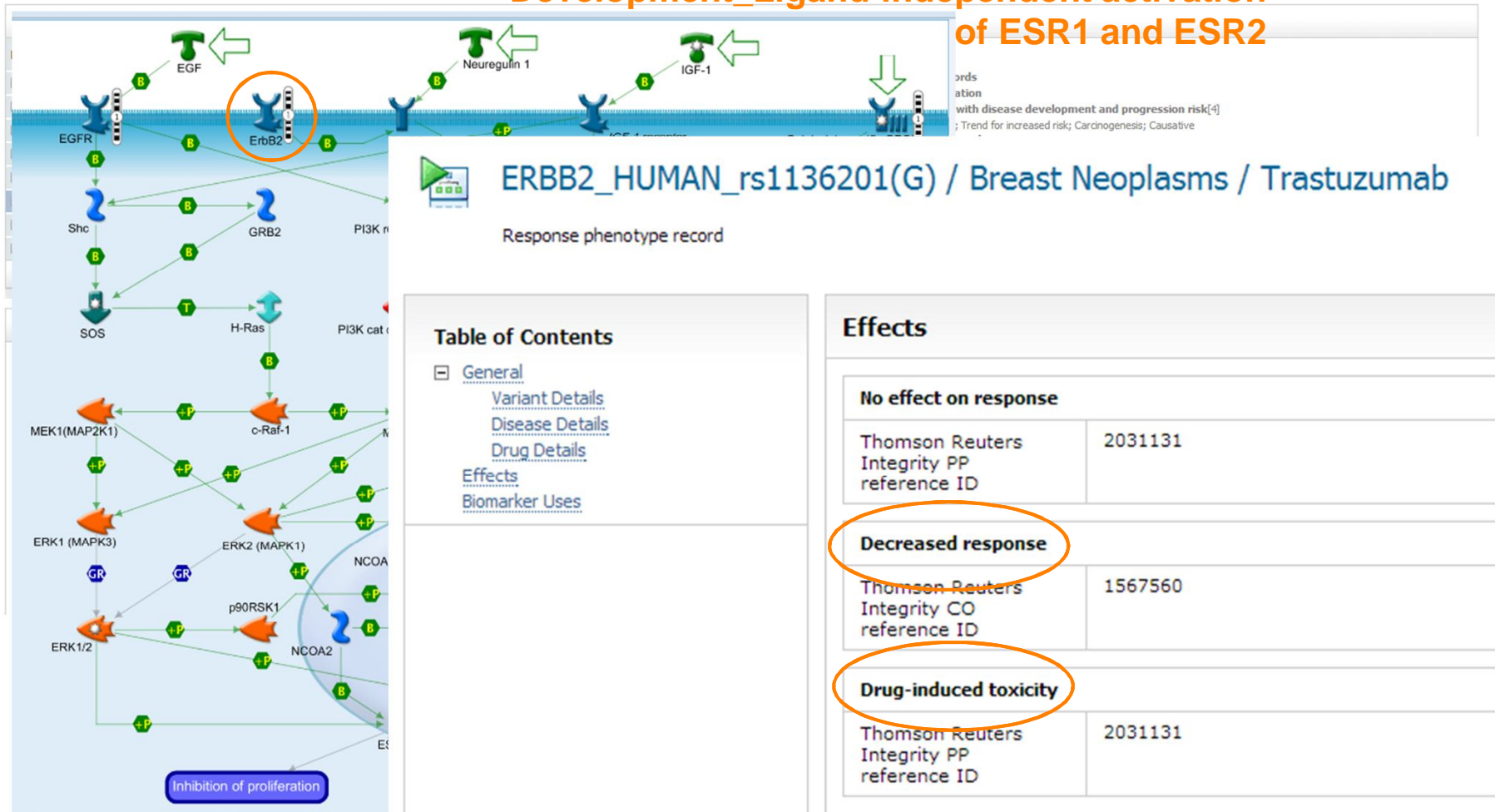
Lower risk of toxicity/side effects



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# Metacore NGS Analysis

## Development\_Ligand-independent activation of ESR1 and ESR2



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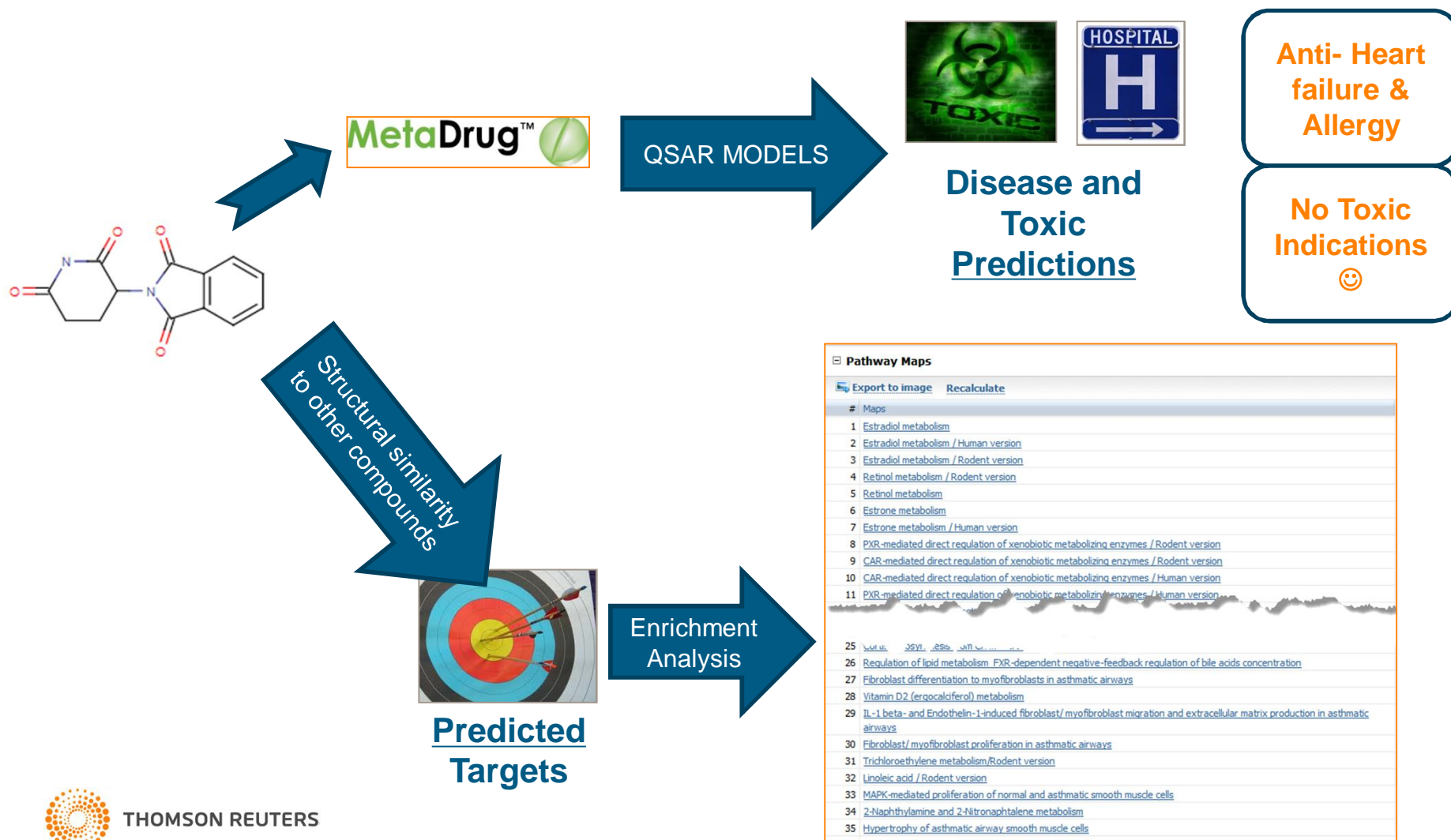
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# METADRUG - PREDICTING COMPOUND ACTIVITY FROM CHEMICAL STRUCTURES



# DRUG TARGETS/TOX/EFFECT PREDICTION

## Possible targets for input molecule

	Check	Type	Target	Interactions	Database compound	Similarity, %	Input molecule	Link Info
	<a href="#">Check all</a>	<a href="#">Uncheck all</a>	<a href="#">Invert all</a>				<a href="#">Group proteins by class</a>	
1	<input checked="" type="checkbox"/>	 <b>AKT1</b>			(S)-Thalidomide Thalidomide	100.00 100.00 100.00 100.00		
<b>▼ Pathway Maps</b>								
2	<a href="#">Export to image</a>	<a href="#">Recalculate</a>						
3	# Maps							
4	1	<a href="#">Muscle contraction Relxin signaling pathway</a>						
5	2	<a href="#">Immune response Inhibitory action of Lipoxins on pro-inflammatory TNF-alpha signaling</a>						
6	3	<a href="#">Immune response C3a signaling</a>						
7	4	<a href="#">Development PEDF signaling</a>						
8	5	<a href="#">Apoptosis and survival Role of PKR in stress-induced apoptosis</a>						
9	6	<a href="#">Immune response Role of PKR in stress-induced antiviral cell response</a>						
10	6	 <b>PERM</b>			(S)-Thalidomide (R)-Thalidomide Thalidomide			
11	7	 <b>Cereblon</b>			Thalidomide (R)-Thalidomide (S)-Thalidomide S-3APG R-3APG Pomalidomide Lenalidomide			

## Functional Enrichment

Export to image Recalculate

# Maps

- 1 Muscle contraction Relxin signaling pathway
- 2 Immune response Inhibitory action of Lipoxins on pro-inflammatory TNF-alpha signaling
- 3 Immune response C3a signaling
- 4 Development PEDF signaling
- 5 Apoptosis and survival Role of PKR in stress-induced apoptosis
- 6 Immune response Role of PKR in stress-induced antiviral cell response

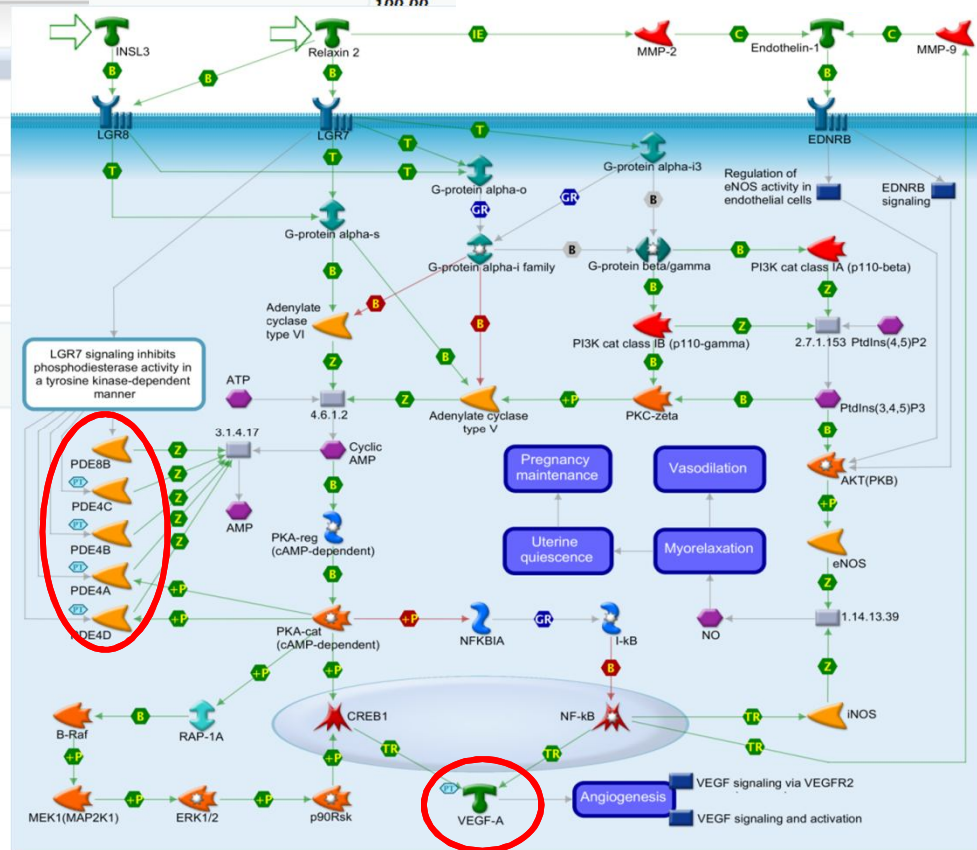
## Mechanism of Action

The diagram illustrates the mechanism of action of thalidomide, focusing on its inhibition of the Relxin signaling pathway. Key components include:

- Receptors:** LGR7, LGR8, Relaxin 2, and Endothelin-1 (EDNRB).
- Signaling Pathways:**
  - Relxin Pathway:** Relaxin 2 binds to LGR7, activating G-protein alpha-s, which then activates Adenylate cyclase type VI, leading to the production of cyclic AMP (cAMP). cAMP activates PKA-reg (cAMP-dependent), which in turn activates Akt (PKB).
  - Endothelin-1 Pathway:** Endothelin-1 binds to EDNRB, activating G-protein alpha-13, which then activates G-protein beta/gamma, leading to the activation of PI3K cat class IB (p110-gamma) and PI3K cat class IA (p110-beta). These activate Akt (PKB).
- Thalidomide Inhibition:** Thalidomide inhibits LGR7 signaling, which in turn inhibits the Relxin signaling pathway. This leads to the inhibition of endothelial cells, resulting in the inhibition of eNOS activity and the inhibition of vasodilation.
- Other Effects:** The diagram also shows the inhibition of PKC-zeta and the inhibition of Akt (PKB).

## Functional Enrichment

## Mechanism of Action



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# BIOTECH REVOLUTION

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*Bt-cry1Ac Gene*



**Transgenic**

**Control**

*GFP Mice*



*Lupus:  
Rituximab*

-



+



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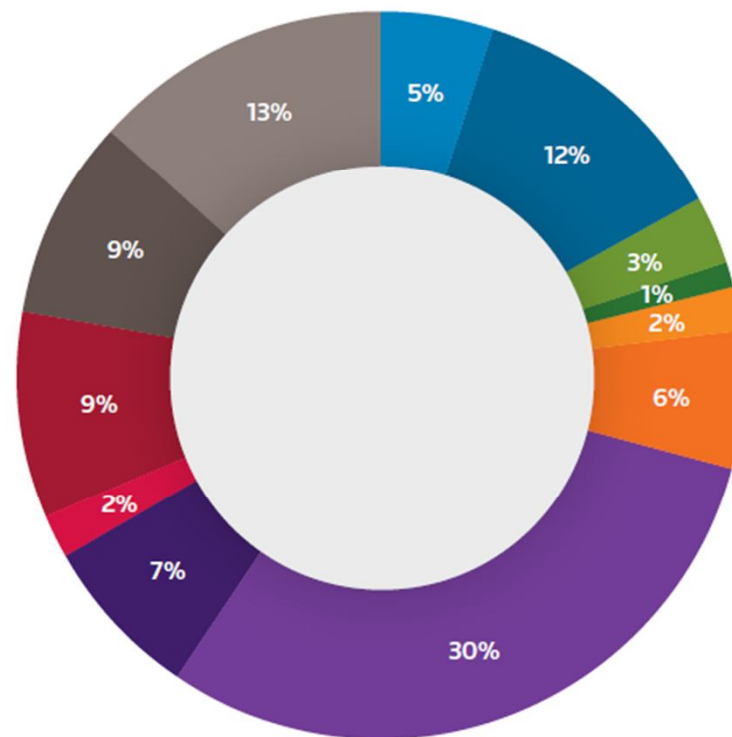


# BIOTECH INNOVATION

## Overall View of Innovation

%	Industry	2014 Volume	2013 Volume	% Change
5%	Aerospace & Defense	62,162	63,080	-1%
12%	Automotive	153,872	152,221	1%
3%	Biotechnology	42,584	39,685	7%
1%	Cosmetics & Well Being	11,017	10,197	8%
2%	Food, Tobacco & Beverage Fermentation	26,333	21,758	21%
6%	Home Appliances	71,278	71,118	0%
30%	Information Technology	380,325	367,028	4%
7%	Medical Devices	93,462	99,290	-6%
2%	Oil & Gas	24,158	23,925	1%
9%	Pharmaceuticals	111,479	99,950	12%
9%	Semiconductors	112,625	119,099	-5%
13%	Telecommunications	161,739	153,153	6%

Source: Thomson Reuters Derwent World Patents Index

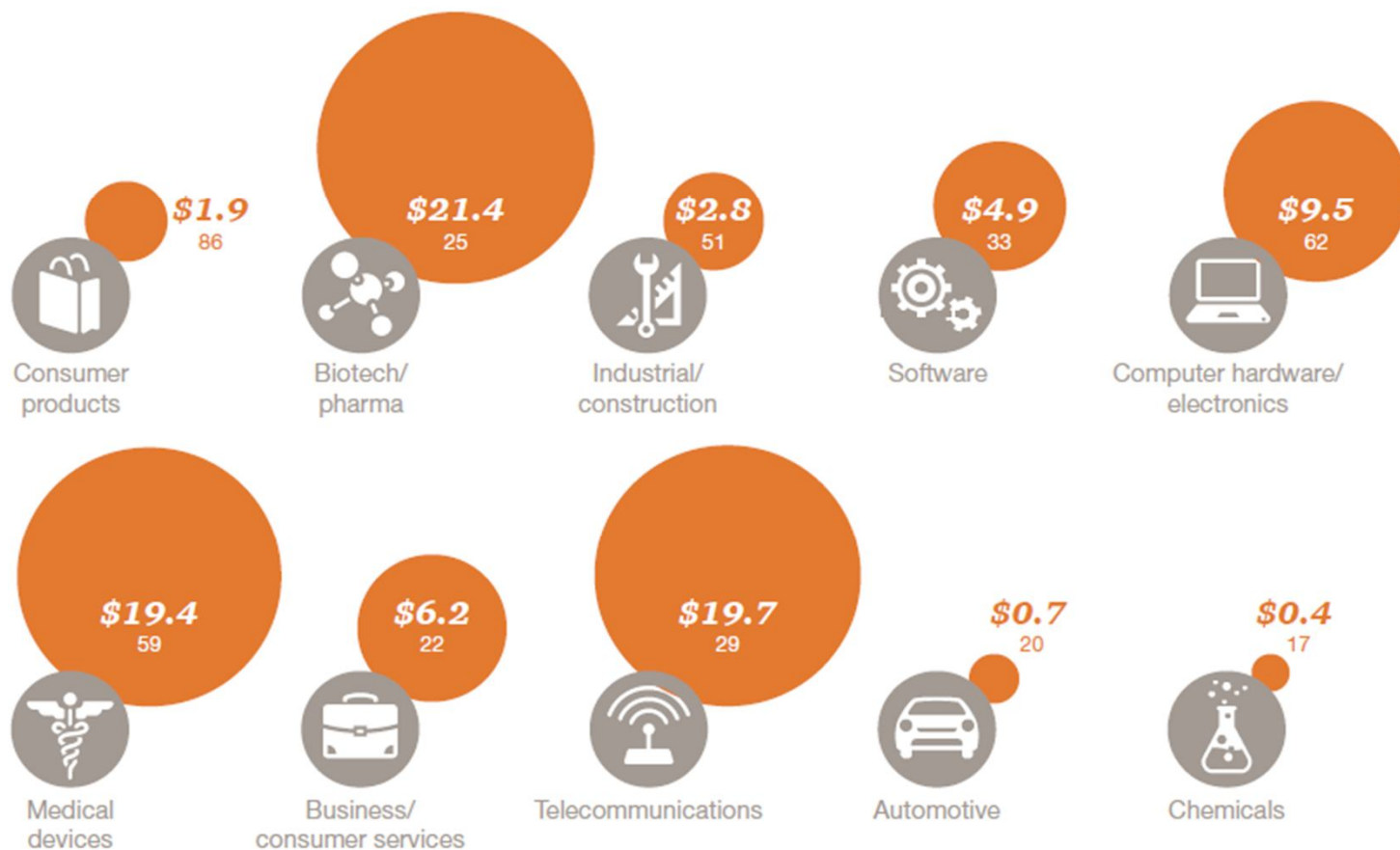


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Thomson Reuters 2015 State of Innovation

# How to Avoid Damages Awards with the Biotech Industry?

Overall median damages award for all industries is about \$5.4M



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Source: PCW 2015 – Patent litigation study

# Explore Biological Products Innovation Scenery Through Sequence-Search Within Patents

## GENESEQ

- The world's largest database of biological sequences from patents
- Prioritize research activities with evaluation of prior art and competitors
- Efficiently find patents containing any related biological sequence of your interest

Query: 1 EVQLVESGGGLVQPGGSLRLSCAASGFINIKDTYIHAVRQAPGKGLNVARITYPTNGYTRY 60  
 EVQLVESGGGLVQPGGSLRLSCAASGFINIKDTYIHAVRQAPGKGLNVARITYPTNGYTRY  
 Sbjct: 344 EVQLVESGGGLVQPGGSLRLSCAASGFINIKDTYIHAVRQAPGKGLNVARITYPTNGYTRY 403

Query: 61 ADSVKGRFTISADTSKNTAYLQMNLSRAEDTAVYYCSRNGGDFYAMDYWGQGLTVTVSS 120  
 ADSVKGRFTISADTSKNTAYLQMNLSRAEDTAVYYCSRNGGDFYAMDYWGQGLTVTVSS  
 Sbjct: 404 ADSVKGRFTISADTSKNTAYLQMNLSRAEDTAVYYCSRNGGDFYAMDYWGQGLTVTVSS 463

Query: 121 ASTKGPSVFPLAPSSKSTSGGT 1  
 ASTKGPSVFPLAPSSKSTSGGT 1  
 Sbjct: 464 ASTKGPSVFPLAPSSKSTSGGT 1

Query: 181 GLYLSVVTVPSSSLGTQTYIC 1  
 GLYLSVVTVPSSSLGTQTYIC 1

Sequence number	First << AZX02941 >> Last
Sequence key	First << SBNP0003TYYQ >> Last
Sequence description	Anti-EGFR-2 (Her-2) human antibody, SEQ ID NO 20
Keywords	EGFR-2; Her-2; SectM; antibody; antibody production; drug screening
Sequence location	Example 5; SEQ ID NO 20; 95pp; English
Title	New polynucleotide construct useful for screening fragment antigen-binding (Fab) against target antigen, comprises Fab chain-coding sequence, and linker peptide-coding sequence.
Inventor(s)	Fujino Y; Fujita R; Wada K; Oda K; Ueda T; Shimizu Y; Kanamori T
Applicant	MITSUBISHI TANABE PHARMA CORP; UNIV TOKYO
Pub No	WO2012074029 A1
Pub Date	2012-06-07
Download	(Download XML, Thomson Innovation, PatentScope)
N-PSDB	AZX02940; WPI 2012-G42232/43

The present invention relates to a novel polynucleotide construct comprising a first fragment antigen-binding (Fab) chain-coding sequence, a linker peptide-coding sequence, and a second Fab chain-coding sequence. The invention also includes: (1) a method for screening Fab, which involves: (a) introducing the above-mentioned polynucleotide construct comprising the Fab into a cellular translation system; (b) contacting the Fab with an antigen; (c) selecting the antigen and a target Fab; and (d) amplifying the polynucleotide which codes the target Fab; (2) a method for producing Fab, which involves: introducing the polynucleotide construct into an in-vitro translation system; and producing the Fab; (3) a kit for performing the above-mentioned methods; and (4) a method for increasing affinity of a target substance binding protein. The polynucleotide construct of the invention is useful for screening the Fab against target antigen for diagnosis, medical treatment, research, and in the fields of genetic engineering a...



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# GENESEQ Record - Manual Annotations – Added Value Content

GENESEQ™ Copyright 2014 Thomson Reuters			
Sequence number	AYN23213		
Sequence key	SBNP0001M3B9		
Sequence description	Human G-protein- coupled receptor (hRUP3) mutein L224K.		
Keywords	G-protein coupled receptor; GPCR; RUP3; diagnostic test; drug discovery; drug screening; mutein; therapeutic		
Sequence location	Example 2; Page; 146pp; English.		
Enhanced title – Rewritten to be more informative than the original patent title.	Screening candidate compound to identify pharmaceutical agent specific cell endogenous human, involves contacting candidate compound with host cell or their membrane comprising ligand-independent active hTDAG8; and (b) measuring the ability of the compound or compounds to inhibit functionality of the receptor, where the method involves identifying an inverse agonist of the receptor. The host cell is a mammalian host cell or a yeast host cell. The method of the invention is useful: for the direct identification of candidate compounds as receptor agonists, inverse agonists or partial agonists having potential applicability as therapeutic agents; to determine related disease/disorder states which are associated with the expression and/or over-expression of the		
Chen R; Lowitz K; Behan DP; Liaw CW; Chalmers DT			
ARENA PHARM INC			
Publication information (More)	EP2264068	A1	2010-12-22
Cross references	WPI 2010-Q55957/01		
Comments (Less)	The present invention relates to a method for screening candidate compounds to identify a pharmaceutical agent for decreasing campthothecin (cAMP) in cells endogenous T-cell death associated gene 8 (TDAG8), a G-protein- coupled receptor (GPCR). The method involves contacting the candidate compounds with host cell or their membrane comprising ligand-independent active hTDAG8; and (b) measuring the ability of the compound or compounds to inhibit functionality of the receptor, where the method involves identifying an inverse agonist of the receptor. The host cell is a mammalian host cell or a yeast host cell. The method of the invention is useful: for the direct identification of candidate compounds as receptor agonists, inverse agonists or partial agonists having potential applicability as therapeutic agents; to determine related disease/disorder states which are associated with the expression and/or over-expression of the		

Description of sequence - understand at a glance what the sequence is.

Searchable keywords based on controlled vocabularies – for more reliable retrieval and to filter results to focus on the most relevant.

Sequence location within the specification – it is important to know if a sequence is in the claims of a patent. Also save time by going straight to the right page.

Cross references to internal and external sources – for easy linking to the DWPI record to see the full patent family.

Mini abstract for each sequence – saves time in trying to understand the I.P. and biological context of the sequence



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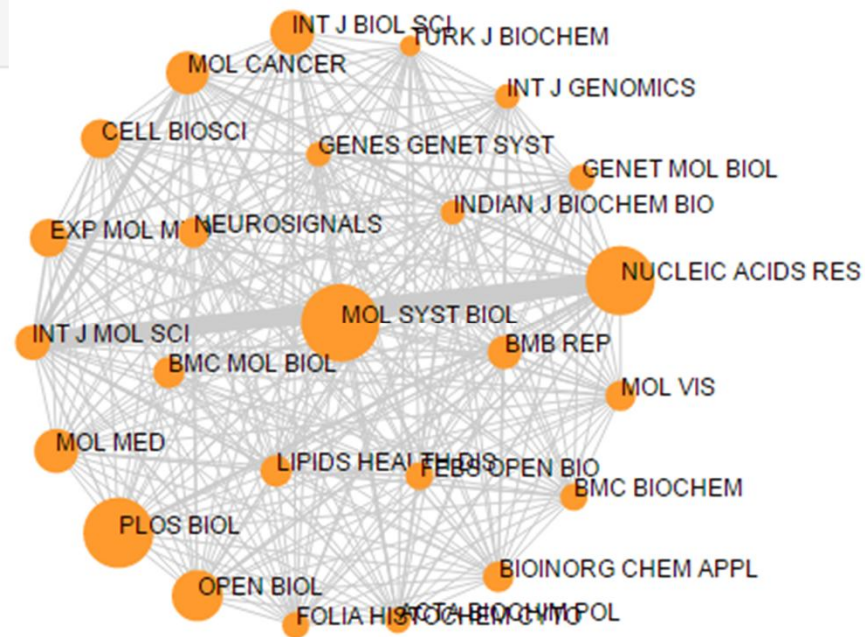
- How to make a comprehensive **technological prospection** to better **position your research**?
- Find the **most influent authors** on your field – define possible **competitors** and **collaborators**
- Find the most accepted **cellular and animal models** to your studies
- Discover the **molecular mechanisms** and main **biomarkers** related to the **disease** of your interest or your **omics data**
- **Predict** the therapeutic **effect**, **toxic** potential and **mechanisms of action** of your chemical compounds
- Explore what has been **patented** in your innovation area
- Define the **most impactful journal** to publish your data



# JCR: Defining the Impact Factor of Scientific Journals

$$\text{Impact Factor}^{\text{®}}_{2010\text{-JCR}} = \frac{\text{number of citations in 2009 of articles published in 2007-2008}}{\text{number of articles published in the journal in 2007-2008}}$$

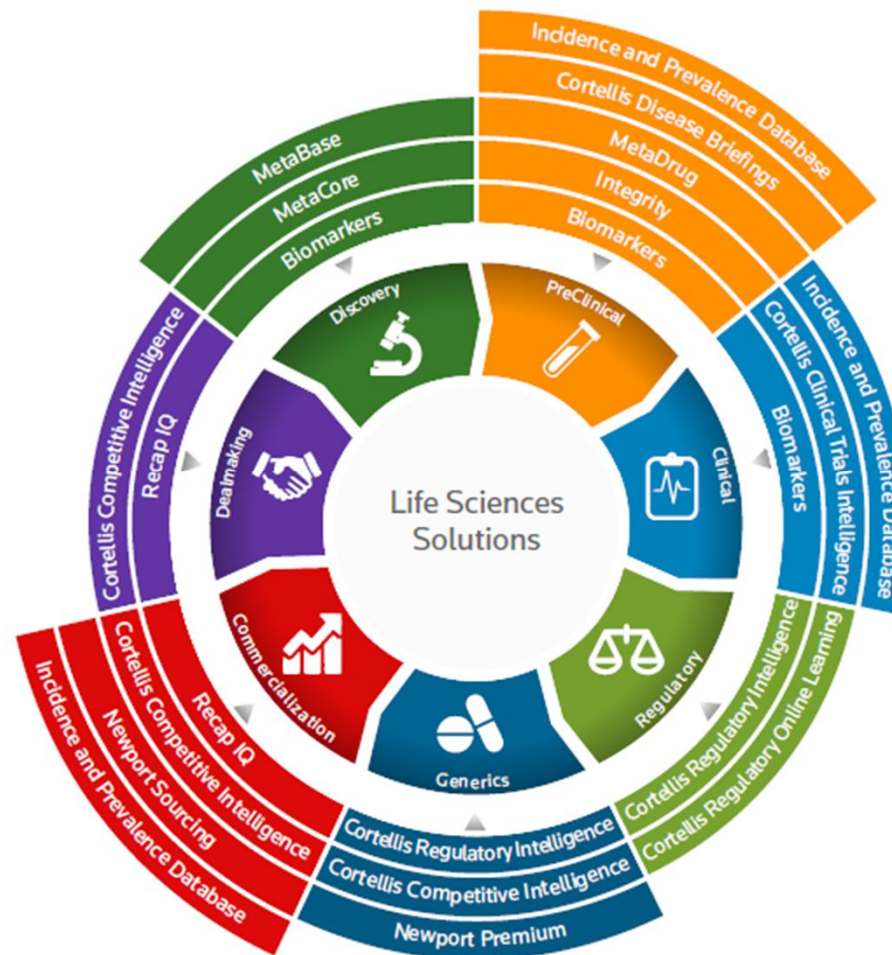
	Full Journal Title	Total Cites	Journal Impact Factor 	Eigenfactor Score
1	Molecular Systems Biology	7,644	10.872	0.03895
2	PLOS BIOLOGY	25,729	9.343	0.09309
3	NUCLEIC ACIDS RESEARCH	136,883	9.112	0.34417
4	Open Biology	833	5.784	0.00555
5	International Journal of Biological Sciences	2,611	4.509	0.00936



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# Innovation Cycle - Drug R&D



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