Topics

Market Drivers

- Euretos
- BRAIN
- Use cases
- Close
Key drivers

The Data Tsunami

Datarrhoeia

Standards?

Needle Transport

DIY Data
"Data is just like crude. It’s valuable, but if unrefined it cannot really be used. It has to be changed into gas, plastic, chemicals, etc., to create a valuable entity that drives profitable activity."

* 2013: Ann Winblad
legendary investor and senior partner at Hummer-Winblad
Big data is like teenage sex:
everyone talks about it,
obody really knows how to do it,
everyone thinks everyone else is
doing it, so everyone claims they
are doing it...

(Dan Ariely)
Life sciences – the perfect storm?

- The easy ‘low hanging fruit’ medical discoveries have been made.
- New ‘higher hanging fruit’ research is orders of magnitude more complex.

Drowning in data
- 1.5 new article published every minute
- Massive multi-omics output data (genome data alone doubles per 8 months)

Lost in data
- Many databases are consulted daily
- Each only have a fragment of the puzzle
- Each have specific classifications, terms
- Google as the only integrative tool
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Addressing researchers’ needs

ChEMBL
UniProt
PubMed
GWAS
OMIM
DrugBank
USPTO
Google
Elsevier
PubChem
ChemSpider
Euretost Product Solution: BRAIN

- Many online resources
- Look **through** data
- **Discover** new relations
- Instantly **evaluate** evidence
- **Personalise** alerts
- **Minimise** Time to knowledge
Products & Services

KaaS
Overview
• Knowledge as a Service
• User friendly application
• Instant access
• Public & private data
• Secure
• Up to date
• Easy collaboration
• Alerts

License
• Monthly subscription
• Integration services

Reports
Overview
• Standard reports
• Custom reports

License
• Fixed price per report /
  • Subscription

API
Overview
• Access to BRAIN database
• Develop own applications

License
• Annual base license &
  • Per transaction fee

Private Instance
Overview
• On-site BRAIN install
• Behind own firewall
• Public & private data
• Frequent updates
• Tailored pricing
• Full integration into local environment

License
• Annual base license &
  • Support fee &
  • Professional services
Selected references

KaaS

Overview
- HQ Kopenhagen, DK
- Listed company
- Development of human antibody therapeutics for cancer treatment

We provide
- BRAIN KaaS to the pre-clinical research team

Reports

Overview
- Based in Leiden, NL
- Bayer, Lundbeck, Merck, AstraZeneca, Janssen, Sanofi, UCB Consortium
- Target screening

We provide
- Target dossiers for target owners and internal review panel

API

Overview
- HQ San Diego, US
- Agricultural, industrial and healthcare markets
- Plant and yeast genetics & trait development

We provide
- API for in-house solution development including project support

Private Instance

Overview
- HQ Hinxston, UK
- Official EU infrastructure for life sciences data
- ‘FAIR’ datapublishing of public research data

We provide
- In-house installation of key elements of BRAIN to support data indexing & publishing
Topics

Market Drivers

Euretos

BRAIN

Use cases

Close

Copyright Euretos b.v. 2014
Disambiguation – By knowing all terms, their synonyms and storing them as a single concept. Whatever term you enter, we always find what you mean

Look through data – By connecting these Nanopublications and thus ‘look through’ all the data sources at once

Data reduction – By taking only Nanopublications from raw data and ‘zip up’ all identical ones in a single ‘Cardinal Assertion’.

Performance – the result: high performance at a very low footprint
Here, we reveal that β-parvin binds directly and specifically to leucine-aspartic acid repeat (LD) motif of paxillin.

The luciferase complementation assay showed that Akt1

**PMID: 22869380**

Structural basis for paxillin binding and focal adhesion turnover in β-parvin.

β-parvin is a cytoplasmic adapter protein that localizes to focal adhesions where it associates with inositol triphosphate kinase and is involved in integrin signaling to the cytoskeleton. It has been reported that elevated β-parvin levels in cancer cells lead to increased cell motility and migration. Here, we show that β-parvin binds directly and specifically to leucine-aspartic acid repeat (LD) motif of paxillin. We also present crystal structures of paxillin, β-parvin, and β-parvin-LD motif of paxillin, each in complex with LD motif.  

**PMID: 20164304**

Functional molecular imaging of S6K-mediated Akt/PKB signaling cascades and the associated role of beta-parvin.

β-parvin preferentially binds to beta-parvin, which is involved in ALK-mediated Akt/PKB signaling cascades. These data from functional molecular imaging demonstrated that preferential binding of β-parvin to β-parvin is a specific mediator of cell survival.
## Comprehensive

<table>
<thead>
<tr>
<th>Biological pathways</th>
<th>H1 2014</th>
<th>H2 2014</th>
<th>H1 2015</th>
</tr>
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<tbody>
<tr>
<td>Gene Ontology</td>
<td>HMDB</td>
<td>WikiPW</td>
<td>Reactome</td>
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<td>Uniprot</td>
<td>Protein Atlas</td>
<td>Protein Data bank</td>
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<td>Phenotypes</td>
<td>NCI/UMLS</td>
<td>Genes / Diseases</td>
<td>DBGaP</td>
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<td>CTD</td>
<td>PubChem</td>
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<tr>
<td>Other</td>
<td>Pubmed</td>
<td>Clinicaltrial</td>
<td>NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Foodb</td>
</tr>
</tbody>
</table>

**Genetics**
- EntrezGene
- SNP db
- GWAS
- Jaspar DB
- Tiger Epigenomics
- LOVD ENCODE

**Proteins**
- Uniprot
- Protein Atlas
- Protein Data bank
- Secreted Protein db
- Binding db
- Enzyme

**Phenotypes**
- NCI/UMLS
- Genes / Diseases
- DBGaP

**Other**
- Pubmed
- Clinicaltrial
- NCI
- Foodb
- USPTO

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In summary: Value to the researcher

First to Knowledge...

- Create a single view on private & public data
- See all existing knowledge in all sources at once
- Discover ‘potential’ relations
- Collaborate on specific hypotheses
- Keep up to date via alerts

....First to Market

- Find more leads for research
- Increase quality of research
- Decrease late stage attrition of leads
- Accelerate end to end development process
- Save time, cost & money
Topics

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- BRAIN
- Use cases – Time to knowledge
- Close
Immune activation and collateral damage in AIDS pathogenesis

Frank Miedema¹ *, Mette D. Hazenberg², Kiki Tesselaar¹, Debbie van Baarle¹, Rob J. de Boer³ and Jose A. M. Borghans¹

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² Department of Internal Medicine and Hematology, Academic Medical Center, Amsterdam, Netherlands
³ Theoretical Biology and Bioinformatics, Utrecht University, Utrecht, Netherlands

In the past decade, evidence has accumulated that human immunodeficiency virus (HIV)-induced chronic immune activation drives progression to AIDS. Studies among different monkey species have shown that the difference between pathological and non-pathological infection is determined by the response of the immune system to the virus, rather than its cytopathicity. Here we review the current understanding of the various mechanisms driving chronic immune activation in HIV infection, the cell types involved, its effects on HIV-specific immunity, and how persistent inflammation may cause AIDS and the wide spectrum of non-AIDS related pathology. We argue that therapeutic relief of inflammation may be beneficial to delay HIV-disease progression and to reduce non-AIDS related pathological side effects of HIV-induced chronic immune stimulation.

Keywords: AIDS, pathogenesis, immune activation, TLR, Immunity, therapy

Based on meticulous reading of 221 articles
Using BRAIN Path predictor function
Using BRAIN Shortest Path function
Detail statement and provenance

Not mentioned in the Miedema paper.

Deleterious genetic influence of CX3CR1 genotypes on HIV-1 disease progression.


Abstract

We previously reported that patients homozygous for a specific mutation (M280) in the chemokine receptor CX3CR1 progressed to AIDS more rapidly than those with other genotypes. This deleterious effect would predict that a cohort of prevalent patients would be depleted in M280 carriers, because these patients would have disappeared before recruitment. This hypothesis is confirmed in this new study based on the French SEROCO cohort showing that patients homozygous for the M280 allele were rare among the seroprevalent group. These results may explain the conflicting results published on the impact of CX3CR1 polymorphism in seroconverters.

PMID: 12626895 [PubMed - indexed for MEDLINE]
Significant Time-to-Knowledge saving

Reading 221 papers: WEEKS

4 minutes....in BRAIN
Topics

Market Drivers

Euretos

BRAIN

Use cases – Knowledge Prediction

Close
Also just saw this article on ALS and Retigabine, a drug that affects Potassium channels and might work for ALS. Would BRAIN have predicted this relationship?
Store terms and statements in project folder
Select statements with relevant relations

- Motor neurons -> neg_location_of -> amyotrophic lateral sclerosis
- Nerve tissue -> location_of -> spinal cord diseases
- Neurons -> location_of -> amyotrophic lateral sclerosis
- Motor neurons -> location_of -> potassium channels
- Polyglutamine -> coexists_with -> potassium channels
- Motor neurons -> location_of -> amyotrophic lateral sclerosis
- Potassium channels -> affects -> nerve tissue
- Motor nerves -> location_of -> potassium channels
- Motor nerves -> location_of -> amyotrophic lateral sclerosis
- Embryonic stem cells -> location_of -> potassium channels
- Nerve tissue -> location_of -> amyotrophic lateral sclerosis
- Embryonic stem cells -> location_of -> amyotrophic lateral sclerosis
- Polyglutamine -> associated_with -> amyotrophic lateral sclerosis

- Retigabine -> stimulates -> potassium channels
- Retigabine -> interacts_with -> potassium channels
- Thallium hydride -> causes -> amyotrophic lateral sclerosis
- Motor neurons -> location_of -> thallium hydride
- Retigabine -> affects -> thallium hydride
- Retigabine -> stimulates -> receptors, glutamate
- Receptors, adrenergic -> interacts_with -> retigabine
- Receptors, glutamate -> causes -> amyotrophic lateral sclerosis
- Receptors, glutamate -> associated_with -> amyotrophic lateral sclerosis
- Receptors, adrenergic -> associated_with -> amyotrophic lateral sclerosis
Before this paper was published, BRAIN contained sufficient indirect relationships between Retigabine and ALS to predict it as a potential drug.

Discovery that several mutations associated with ALS cause abnormally high activity in motor neurons > early degradation. There is a deficit in open potassium channels in ALS motor neurons. Retigabine, a drug that opens potassium channels and approved for human use, seems to normalize ALS cells in vitro, reducing their hyperexcitability > clinical trials in preparation.
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One click target dossiers

Reports

Overview

• Based in Leiden, NL
• Bayer, Lundbeck, Merck, AstraZeneca, Janssen, Sanofi, UCB Consortium
• Target screening

We provide

• Target dossiers for target owners and internal review panel

Key functions

• Target – disease association (predict function)
• Drugability analysis of a compound
• Indepth compound analysis ranked by QeD
10 – Druglikeness Properties

Figure 4 -- QED Score

Figure 5 -- Ro3 violations

Figure 6 -- Rule of 5 violations

Figure 7 – Structural Alerts

11 – Top 5 Drugable Compounds

<table>
<thead>
<tr>
<th>QED</th>
<th>Interaction</th>
<th>Detailed information</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.91</td>
<td>IC50 &gt; 6290 nM</td>
<td>4′-Hydroxy-3′-methoxyflavone</td>
</tr>
</tbody>
</table>

https://www.eb.ac.uk/chembl/assay/inspect/CHEMBL1614462

http://www.chemspider.com/Chemical-Structure.588784.html
Topics

Market Drivers

Euretos

BRAIN

Use cases – Adverse Drug Reaction

Close
Adverse drug reaction assessment

**Rosiglitazone** (trade name *Avandia*, GlaxoSmithKline) is an antidiabetic drug in the thiazolidinedione class of drugs.

A meta-analysis of 16 observational studies released in March, **2011**, provides evidence that *rosiglitazone* is associated with a higher risk of heart failure, *myocardial infarction* and *death* than a similar agent, pioglitazone in real life.
Connect the key concepts
Review the evidence
Topics

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