The anti-intellectual effects of intellectual property

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Intellectual property dynamics

• Academic sector
  — becoming more business like
  — getting into drug discovery

• Chemistry databases
  — private / public synergy

• Precompetitive initiatives
  — can compounds be shared?

• Conclusion
Where did this title come from?

The anti-intellectual effects of intellectual property
Christopher A Lipinski

Intellectual property considerations decrease research productivity in subtle and unanticipated ways. Chemical probe exchange between Pharma and academia is hindered by academic IP interests. These are perceived as a subtle nuisance by the academic researcher. Novel ligands for oral targets are historically few and numbers of economically attractive oral drug targets are limited. Economically speculative targets lie in the academic domain but the medicinal chemistry to explore these in a drug discovery sense lies in Pharma and cooperation between the two is hindered by very different academic and Pharma views on chemical quality. Tools and probes for academic target validation can accommodate looser chemical quality criteria as opposed to the very strict chemical quality criteria required in Pharma drug discovery.

Libraries Screening Center Network and associated Molecular Library Repository of screening compounds exemplify important efforts to address this deficit [2]. The anti-intellectual effects of intellectual property (IP) considerations are the topics broadly covered by this commentary. Too often, this type of topic is treated as if it were only a technical, legal or factual issue and the very important effects of people’s attitudes are ignored. This commentary deals with some of the softer, people issues. Hence, it is unapologetically subjective and very much an opinion piece by this author.

Profitability limits the number of oral drug targets
IP considerations have always been a core value of
IP and subtle productivity effects

• Intellectual property considerations decrease research productivity in subtle and unanticipated ways.

• Chemical probe exchange between Pharma and academia is hindered by academic IP interests.

• These are perceived as a subtle nuisance by the academic researcher.
Academic biology - chemistry disconnect

- Economically speculative targets lie in the academic domain
- The medicinal chemistry to explore these in a drug discovery sense lies in Pharma
- Cooperation between the two is hindered by very different academic and Pharma views on chemical quality.
Beautiful chemistry
Horrible chemistry

These look good to biologists

Remove these types of compounds from any assays

Conference on Small Molecule Science, San Jose CA, July 28
Academic biology enthusiasm versus drug discovery reality

100 million distinct compounds are synthesized and subjected to selection for binding to the N-terminal SH3 domain of the proto-oncogene Crk.

“The evolutionary approach has the potential to drastically simplify and accelerate small-mol. discovery.”

Evolving public private cooperation

Wikipedia talk:WikiProject Chemistry/CAS validation

From Wikipedia, the free encyclopedia
  - Wikipedia talk:WikiProject Chemistry

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4 Stereo Issues on Structures
5 Inorganics

CAS Discourages Using SciFinder for curating 3rd party databases (e.g. Wikipedia)

New announcement from CAS

CAS, a division of the American Chemical Society, is pleased to announce that it will contribute to the Wikipedia project. CAS will work with Wikipedia to help provide accurate CAS Registry Numbers® for current substances listed in Wikiprojects-Chemicals section of the Wikipedia Chemistry Portal that are of widespread general public interest.
Academic drug discovery efforts

• University of Dundee, Scotland
  — treatment of African sleeping sickness
• Medical Research Council Technology UK
  — health of the UK population
• Catholic University of Leuven, Belgium
  — CD3 (center for drug discovery and development)
Needed for academic drug discovery

ABOUT SEEDING DRUG DISCOVERY
For further information about the application process please contact the Wellcome Trust: techtransfer@wellcome.ac.uk.
Analytical opportunities

In 2004 at the Society for Biomolecular Sciences meeting 10% of attendees were academics. In 2008 at the SBS meeting 35% were academics.
Precompetitive initiatives

• Cooperation among pharma for activities viewed as clearly precompetitive
  – safety biomarkers
  – imaging technologies

• Cooperation among pharma for activities viewed as proprietary / IP sensitive?
    Arti K. Rai, Duke University Law School
Share chemistry without IP effect?

Share? Maybe!
It depends on context

InChIKey for Ivermectin

SPBDXSGPUHCETR-VHJJIIYNUBB
Richness in chemistry databases

• Cooperation between proprietary and publically accessible data sources
• New batch mode chemistry search options
• New linking of structures to calculated and experimental data
• Late breaking press release July 23, 2008
Open Access ChEMBL Databases

• Free access to large scale drug discovery chemogenomics data
  – Five year grant from Wellcome Trust to the European Bioinformatics Institute
  – www.ebi.ac.uk

• StARlite – Medicinal chemistry
  – ~430,000 unique compounds

• CandiStore – Clinical development candidates

• DrugStore – Launched drugs

• SARfari – integration platform for gene family chemogenomics and 3-D structural data
  – Kinases
  – Rhodopsin-like GPCRs
New chemistry batch abilities

SubScape™ ... Available to SciFinder Subscribers

SubScape is a new substance visualization tool available to subscribers who are using SciFinder 2007. SubScape allows you to easily visualize substances and manage substance answer sets retrieved in SciFinder to speed the discovery process.

With SubScape, you can:

- Identify novel substances which are structurally similar for the purposes of lead discovery
- Explore secondary uses for existing substances
- Research potential adverse effects for a drug
- Investigate competitive intelligence related to all of the substances listed in a patent

CAS Subscape™ allows one to process a SciFinder answer set of 20,000 compounds and map these against any CAS field.
New options for name search

Registry Number: 70288-36-7

No Structure Diagram Available

Formula: Unspecified

CA Index Name: Ivermectin

Other Names: 22,23-Dihydroavermectin B1; Cardomec; Cardstek 30; Cevamec; Equimec; Equimec Paste; Eqvalan; Heartgard; Heartgard 30; Hyvermectin, Iverc; Ivermectin; Ivomec; Ivermectin; Ketamine; Ketaminate; L640471; Mek 933; Mectizan; Noamectin; Oramec; Pandex; Phoanectin; Stromectol; Uvevec; Verm; Zmecterin

CAS SciFinder did not give a structure for Ivermectin

ChemSpider is a free access service providing a structure centric community for chemists. Providing access to millions of chemical structures and integration to a multitude of other online services ChemSpider is the richest single source of structure-based chemistry information.
New structure capture options

Ivermectin name search in Chemspider, then link directly to PubChem

Structure, data from PubChem and can then link to Medline
## Analytically useful properties

**Names and Synonyms**
- Validated by Experts, Validated by Users, Non-Validated, Removed by Users, Redirected by Users, Redirect Approved by Experts
- IVERMECTIN [Wiki]
- Ivermectin B1a

**Predicted Properties**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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<tbody>
<tr>
<td>LogP:</td>
<td>ACD/LogP: 6.61 XLogP: 2.80</td>
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<tr>
<td>ACD/LogD (pH 5.5):</td>
<td>6.61</td>
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<tr>
<td>ACD/BCF (pH 5.5):</td>
<td>62318.94</td>
</tr>
<tr>
<td>ACD/KOC (pH 5.5):</td>
<td>94095.72</td>
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<tr>
<td>#H bond acceptors:</td>
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<tr>
<td>#Freely Rotating Bonds:</td>
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<tr>
<td>Index of Refraction:</td>
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<tr>
<td>Molar Volume:</td>
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<td>Surface Tension:</td>
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<td>Flash Point:</td>
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<tr>
<td>Boiling Point:</td>
<td>940.4 °C at 760 mmHg</td>
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<tr>
<td># of Rule of 5 Violations:</td>
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<tr>
<td>ACD/LogD (pH 7.4):</td>
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<td>ACD/KOC (pH 7.4):</td>
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<td>Polar Surface Area:</td>
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<td>Molar Refractivity:</td>
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<td>Polarizability:</td>
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<td>Density:</td>
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<tr>
<td>Enthalpy of Vaporization:</td>
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<td>Vapour Pressure:</td>
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# Natural Products 1990-2000

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<th>CAS</th>
<th>Name</th>
<th>Indication/Use</th>
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<td></td>
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- **MWT < 350**
- **MWT 350-500**
- **MWT > 500**
- **Polymers**

Conference on Small Molecule Science, San Jose CA, July 28
Conclusions

- Academia, public sector, pharma
  - rapidly changing and dynamic scenario
- Academic drug discovery
  - growth and new opportunities for analytical
- Greater chemistry database synergies
- Better database batch mode capability
- Intellectual property
  - a nuisance sometimes, but also a positive change facilitator in unexpected ways