xPharm

A Pharmacological Reference Work for Life Scientists

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Title: Product Sales Manager, Life Sciences
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xPharm

The new authoritative reference work for Medicinal Pharmacology and Life Science

- 2300 Agents
- 600 Targets
- 450 Disorders
- 180 Principles

>500 expert editors around the world continuously contribute to populating and updating database

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Emerging demand

- Demand for
  - High quality and focused information
  - provided in an usable language
  - though an easily accessed resource,
  - organized in a simple, well thought through manner,
  - stored in highly functional repository
  - and connected to deep supporting material.

Authoritative

- All content has been created by world leading authorities in pharmacology
- Executive Editors
  - Sam J. Enna
  - David B. Bylund
- Associate Editors
  - Hanns Mohler (Targets)
  - Gary O. Rankin and Israel Hanin (Agents)
  - Frank J. Dowd (Disorders)
  - Lynn Wecker (Principles)

Editors and contributors

David Bylund Ph.D.: current president of the American Society for Pharmacology and Experimental Therapeutics (ASPET); Chair of Pharmacology at University of Nebraska Medical Center, Omaha; listed by ISI as one of the world's most highly cited scientists

S.J. Enna Ph.D.: past president of ASPET, Professor of Pharmacology, University of Kansas Medical Center, Kansas City; Executive Editor-in-Chief of scholarly journals: "Pharmacology & Therapeutics" and "Biochemical Pharmacology"

Hanns Mohler, Ph.D. Director of the Institution of Pharmacology and Toxicology, Swiss Federal Institute of Technology, U. Zurich. Member of the European Academy of Sciences; previously Vice Director of research at Hoffman-LaRoche. Winner of multiple scientific awards in neuroscience. Listed by ISI as one of the world's most highly cited scientists

Roderick Flower, Ph.D. Director of the William Harvey Research Institute, London; President of the British Pharmacological Society

Joseph Beavo, Ph.D. University of Washington, Seattle; Member of the prestigious National Academy of Sciences

Target End-users

- Pharmacologists
- Geneticists
- Molecular Biologists
- Biochemists
- Cell Biologists/Neuroscientists
- Immunologists
- Physiologists/Toxicologists
- Toxicologists
- Medicinal Chemists

Relevant

- Authored by top scientists currently working in the field
- Records are written solely for xPharm by researchers
  - >500 contributors
  - Representing over 20 nations
  - Working in academic, government, and corporate institutions.
  - Data updated constantly by the primary researchers

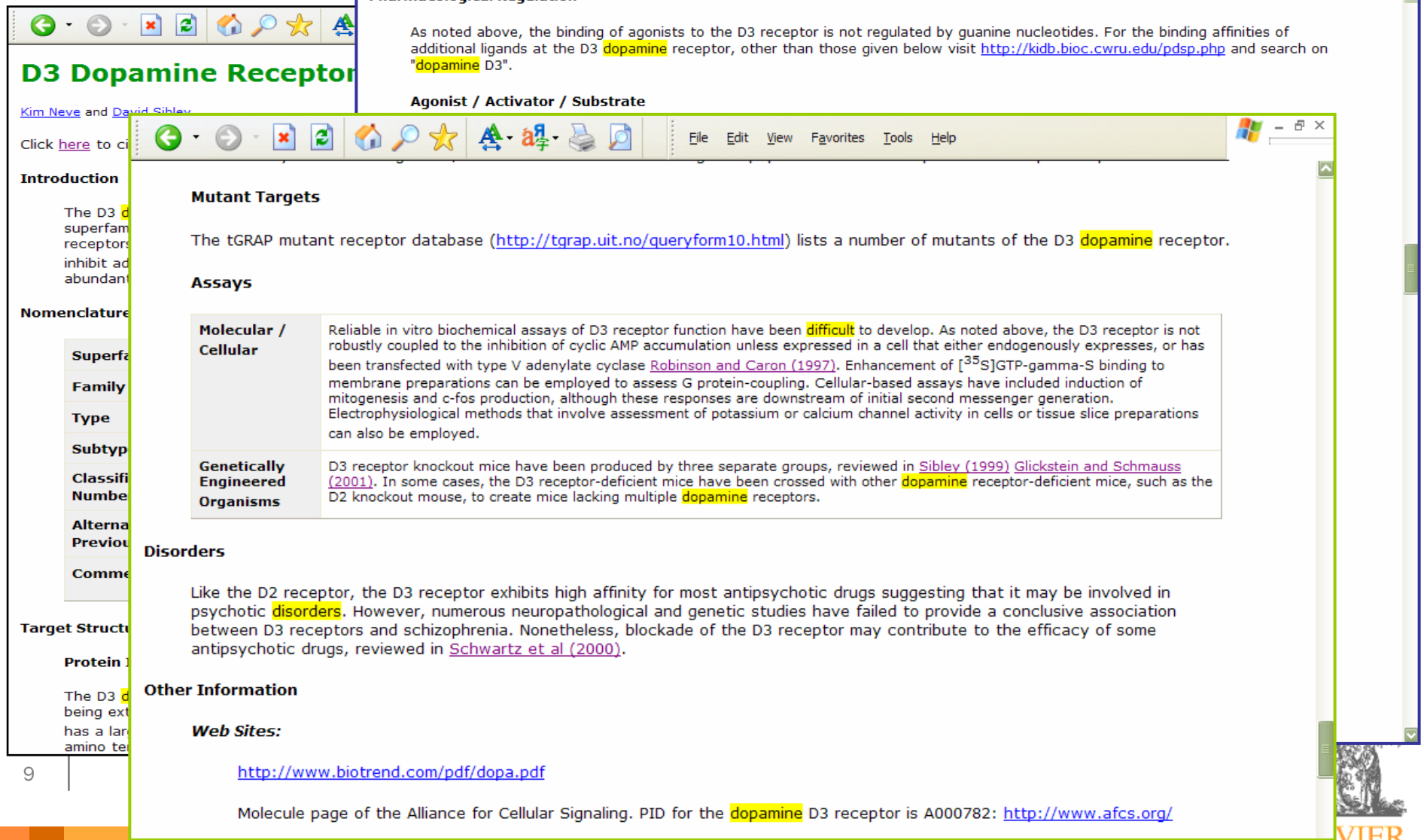
Detailed

“The drug research paradigm has moved from a compound looking for an effect to targets looking for a compound”

Dr. Jurgen Drews, Modern Drug Discovery, April 2004

- xPharm displays more detailed information about pharmacologically relevant targets
  - Classification, alternate names
  - Structural information for humans and all relevant animal models
  - Control of expression, protein partners, physiological role
  - Disease associations
  - Pharmacological regulation
  - This information is not available in any other single source

Detailed



D3 Dopamine Receptor

Kim Neve and David Sibley

Click here to ci

Introduction

The D3 d
superfam
receptors
inhibit ad
abundant

Nomenclature

Superfa
Family
Type
Subtyp
Classifi Numbe
Alterna Previou
Comme

Target Structu

Protein

The D3 d
being ext
has a lar
amino te

Pharmacological Regulation

As noted above, the binding of agonists to the D3 receptor is not regulated by guanine nucleotides. For the binding affinities of additional ligands at the D3 dopamine receptor, other than those given below visit http://kidb.bioc.cwru.edu/pdsp.php and search on "dopamine D3".

Agonist / Activator / Substrate

Mutant Targets

The tGRAP mutant receptor database (http://tgrap.uit.no/queryform10.html) lists a number of mutants of the D3 dopamine receptor.

Assays

Molecular / Cellular	Reliable in vitro biochemical assays of D3 receptor function have been difficult to develop. As noted above, the D3 receptor is not robustly coupled to the inhibition of cyclic AMP accumulation unless expressed in a cell that either endogenously expresses, or has been transfected with type V adenylate cyclase Robinson and Caron (1997). Enhancement of [^{35}S]GTP-gamma-S binding to membrane preparations can be employed to assess G protein-coupling. Cellular-based assays have included induction of mitogenesis and c-fos production, although these responses are downstream of initial second messenger generation. Electrophysiological methods that involve assessment of potassium or calcium channel activity in cells or tissue slice preparations can also be employed.
Genetically Engineered Organisms	D3 receptor knockout mice have been produced by three separate groups, reviewed in Sibley (1999) Glickstein and Schmauss (2001). In some cases, the D3 receptor-deficient mice have been crossed with other dopamine receptor-deficient mice, such as the D2 knockout mouse, to create mice lacking multiple dopamine receptors.

Disorders

Like the D2 receptor, the D3 receptor exhibits high affinity for most antipsychotic drugs suggesting that it may be involved in psychotic disorders. However, numerous neuropathological and genetic studies have failed to provide a conclusive association between D3 receptors and schizophrenia. Nonetheless, blockade of the D3 receptor may contribute to the efficacy of some antipsychotic drugs, reviewed in Schwartz et al (2000).

Other Information

Web Sites:

http://www.biotrend.com/pdf/dopa.pdf

Molecule page of the Alliance for Cellular Signaling. PID for the dopamine D3 receptor is A000782: http://www.afcs.org/

Useful

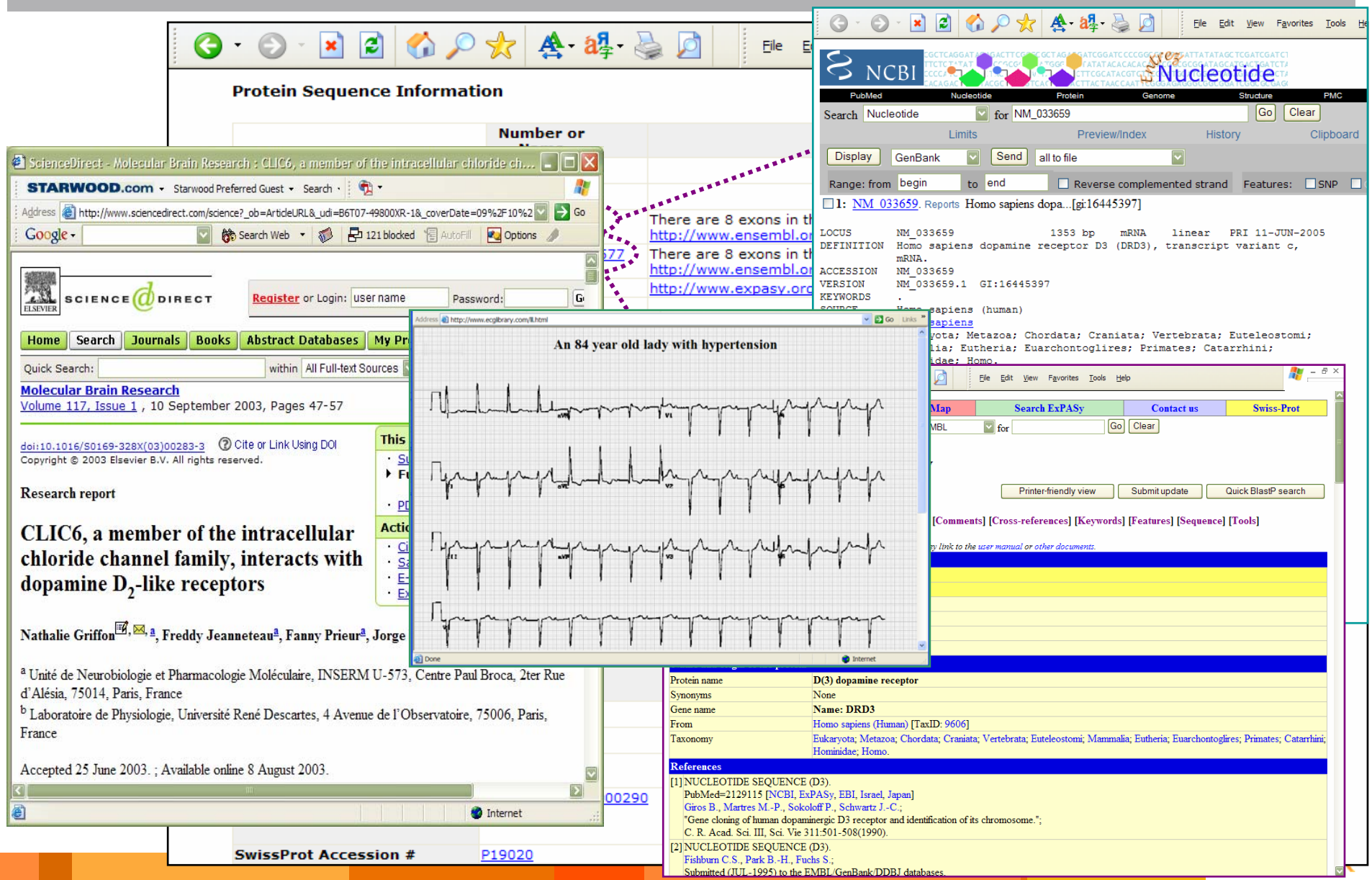
- Information on Disorders is organized for bench scientists to aid grant applications and business proposals
  - Classifications according to WHO and CDC where appropriate
  - Epidemiology: who gets the disease, the size of this population.
  - Consequences, pathophysiology: what happens if the disease is not treated
  - Standard and experimental therapies: what is known about pharmacological intervention and the mechanisms of therapeutics
  - Animal models: for basic study and toxicological tests
  - Sources of funding

Extensive

- More pharmacology content than any other online product
- More current and extensive than a print reference work
- Complementary database to bioactivity, drug pipeline and biomedical databases
- External links to:
  - Genetic database
  - Protein database
  - Literature
  - Vendors and funding sources

Extensive & Comprehensive

xPharm



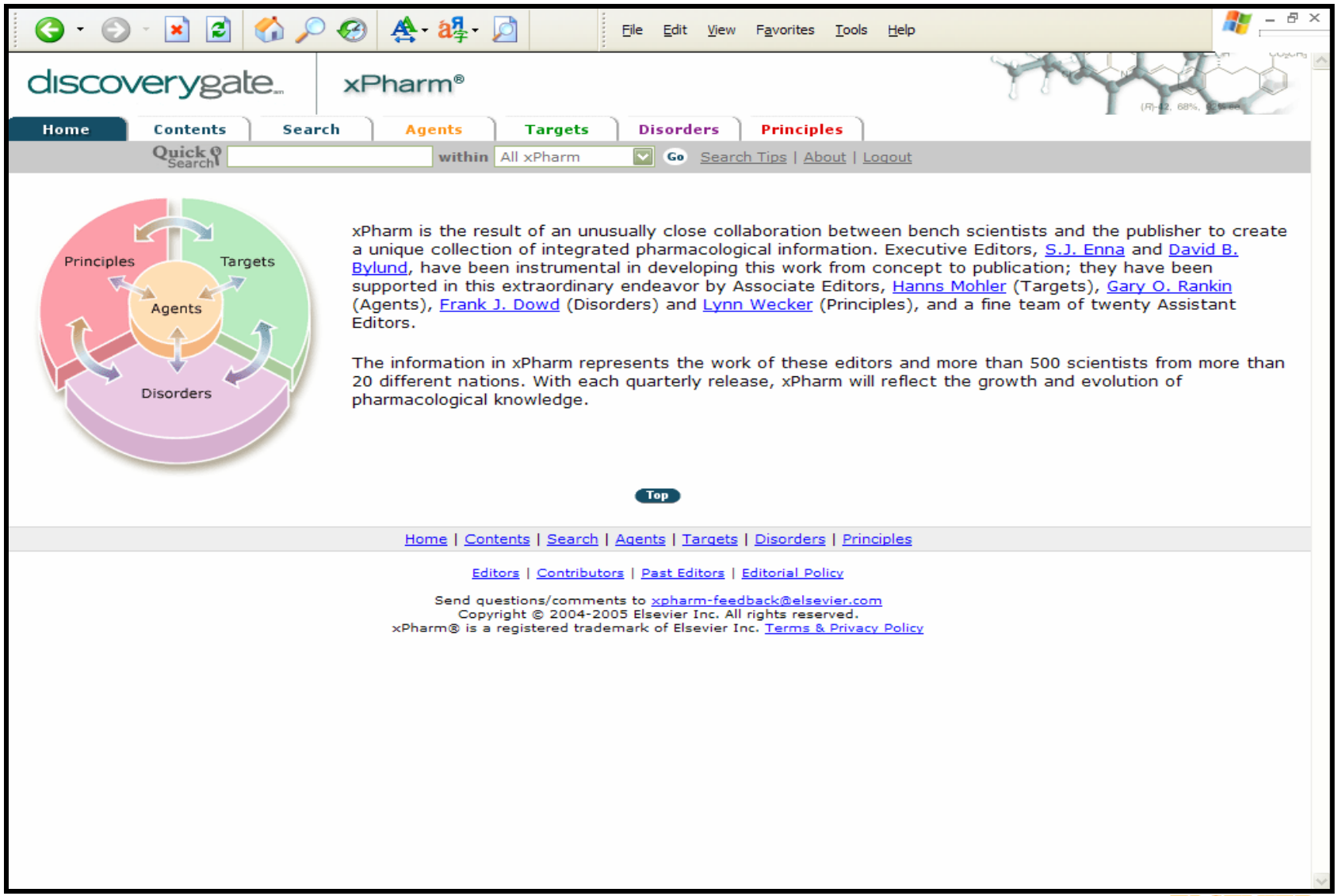
A Growing Resource

- Existing records are updated quarterly
- Breaking news can be added immediately
- New records added continuously
  - Subject to editorial approval

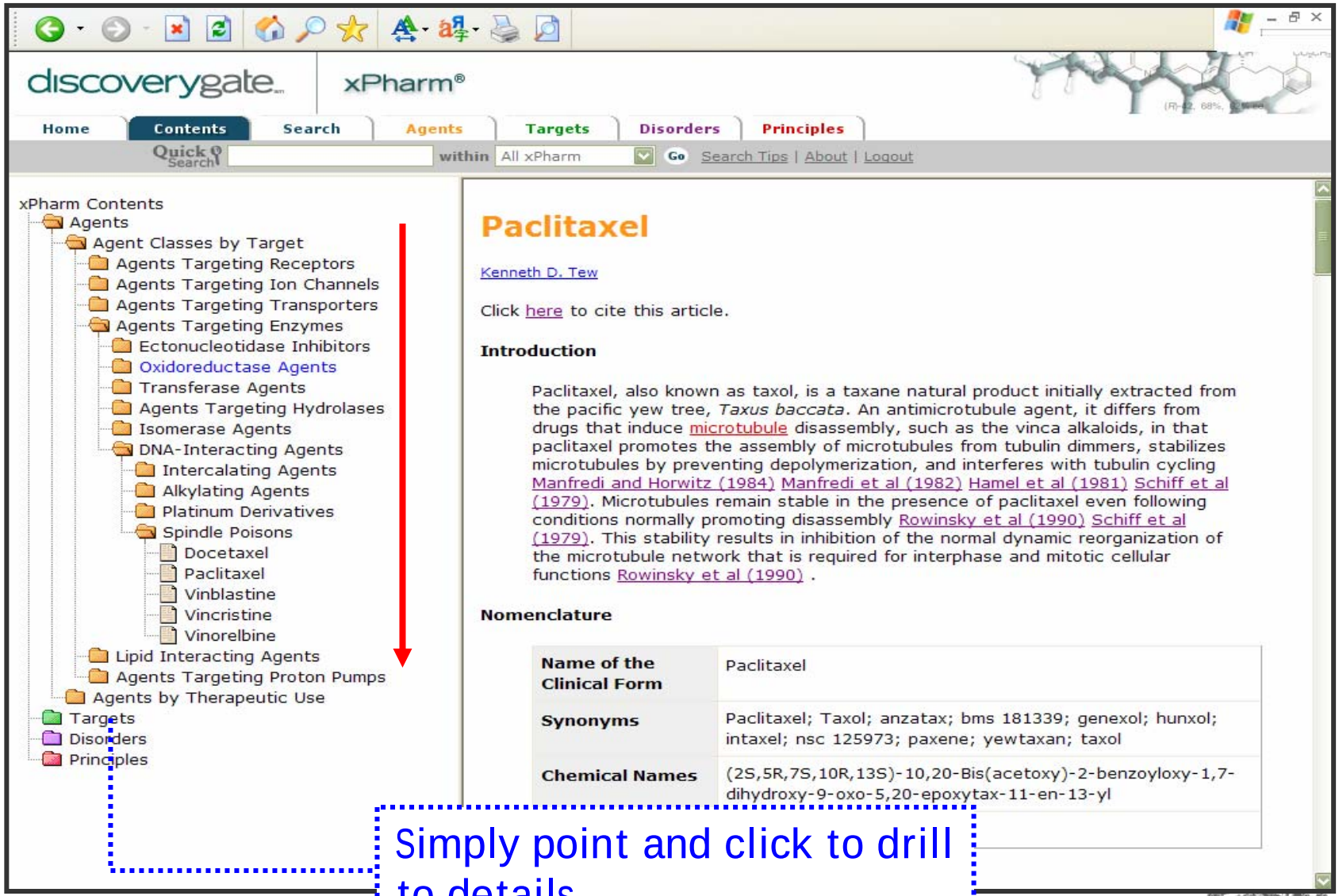
Easy to use

- Home Page access easy for non specialists. “Browsing of the table of Table of Contents was easy to use” – User
- Support for basic and advanced queries
- Answers pharmacology questions with focused results. (not found in journal articles, e.g. those on PubMed, or in current database offerings)
- Discover common pharmacological elements from disparate records.

www.xPharm.com

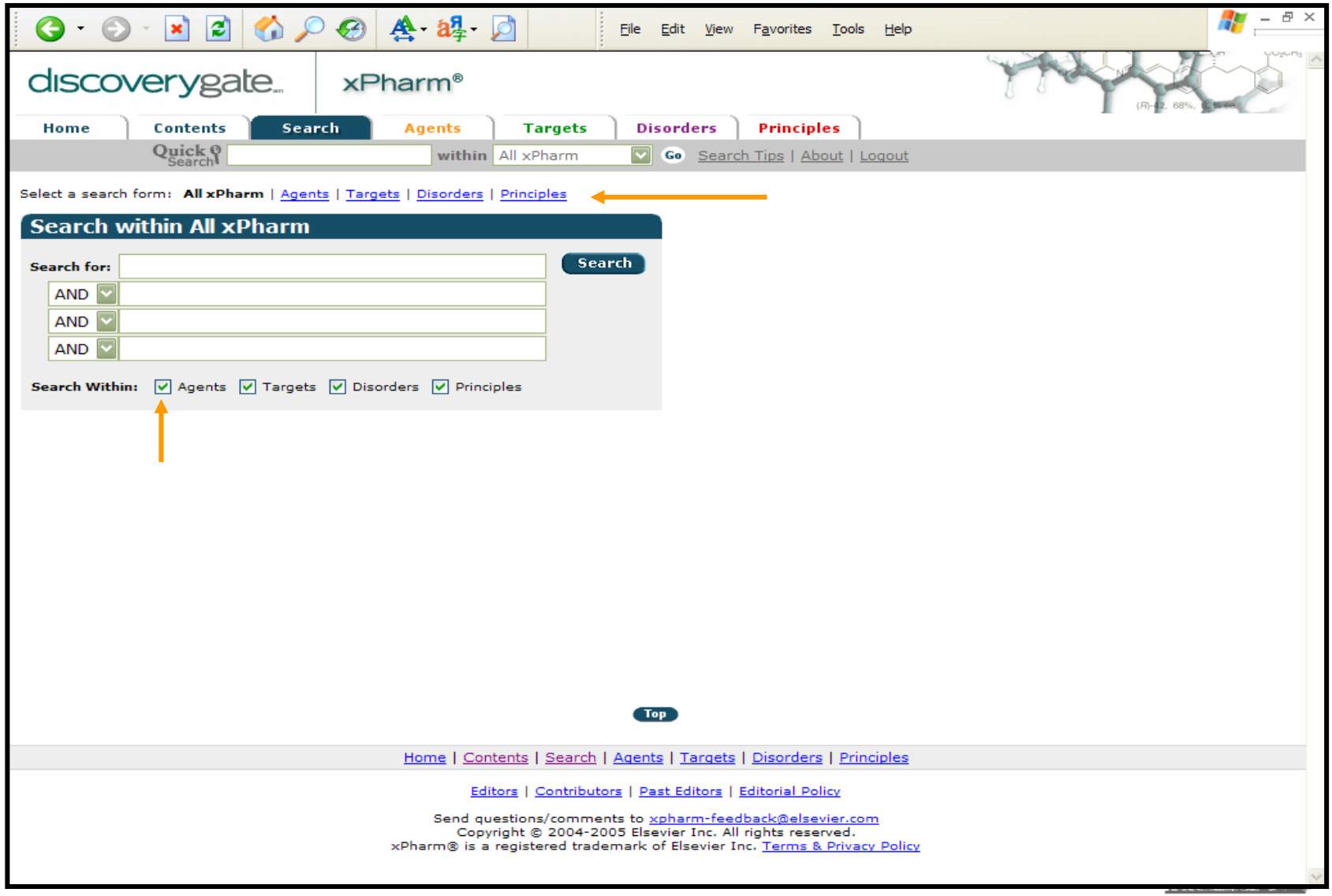


Easy to browse ToC

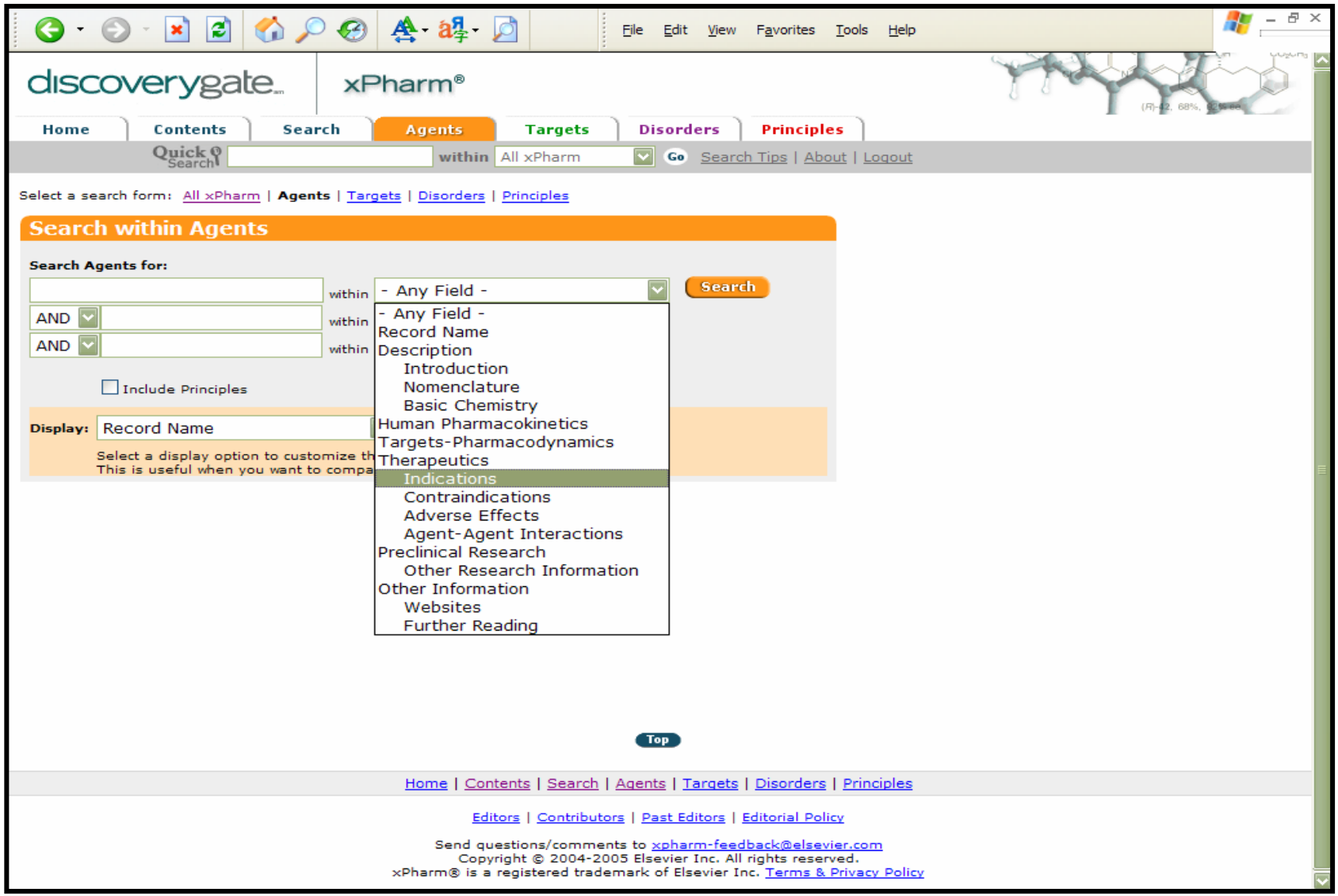


Simply point and click to drill to details.

Search all of xPharm



Search in selected Field Index



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BROWSE & SEARCH EXAMPLES

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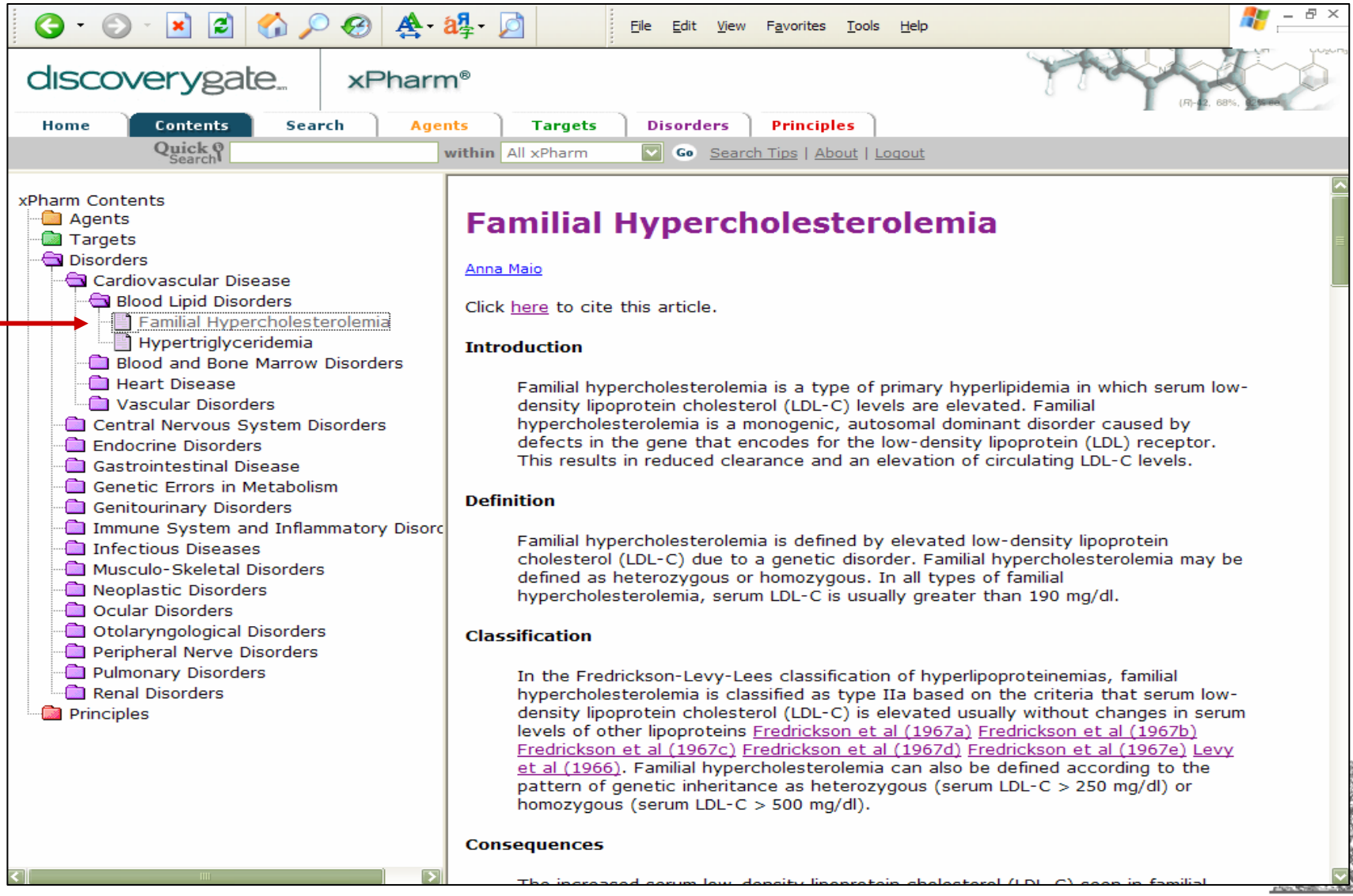
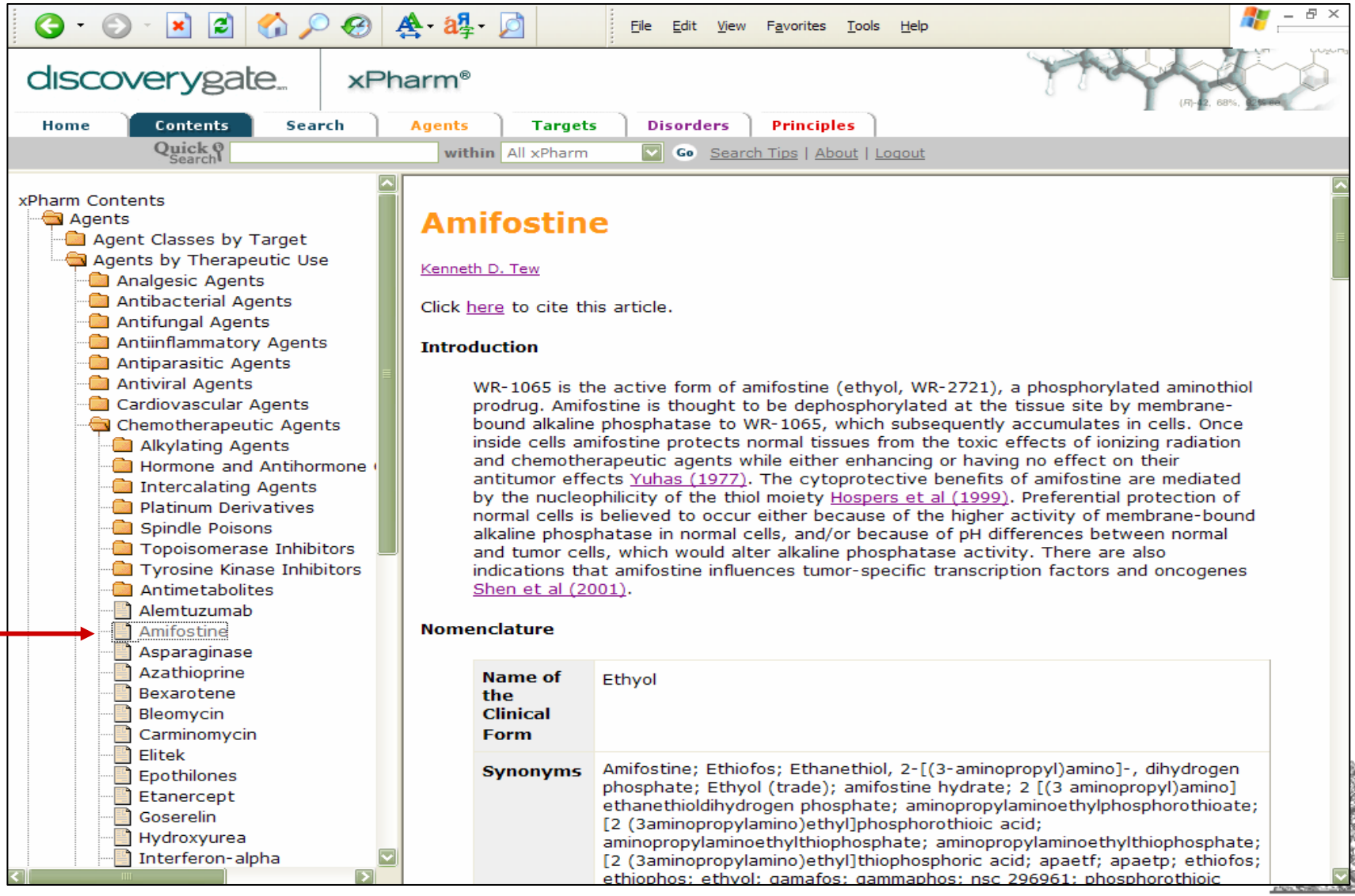
Browsing for Disorder – Familial Hypercholesterolemia



Browsing for Agent - Amifostine



SEARCH SCENARIO:

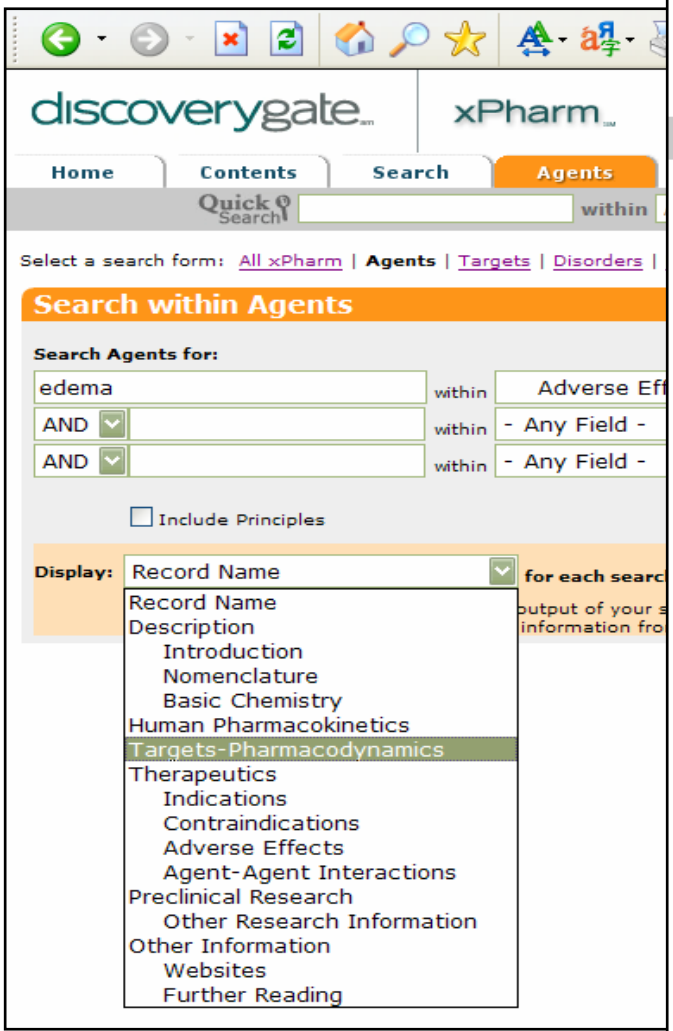
Example 1:

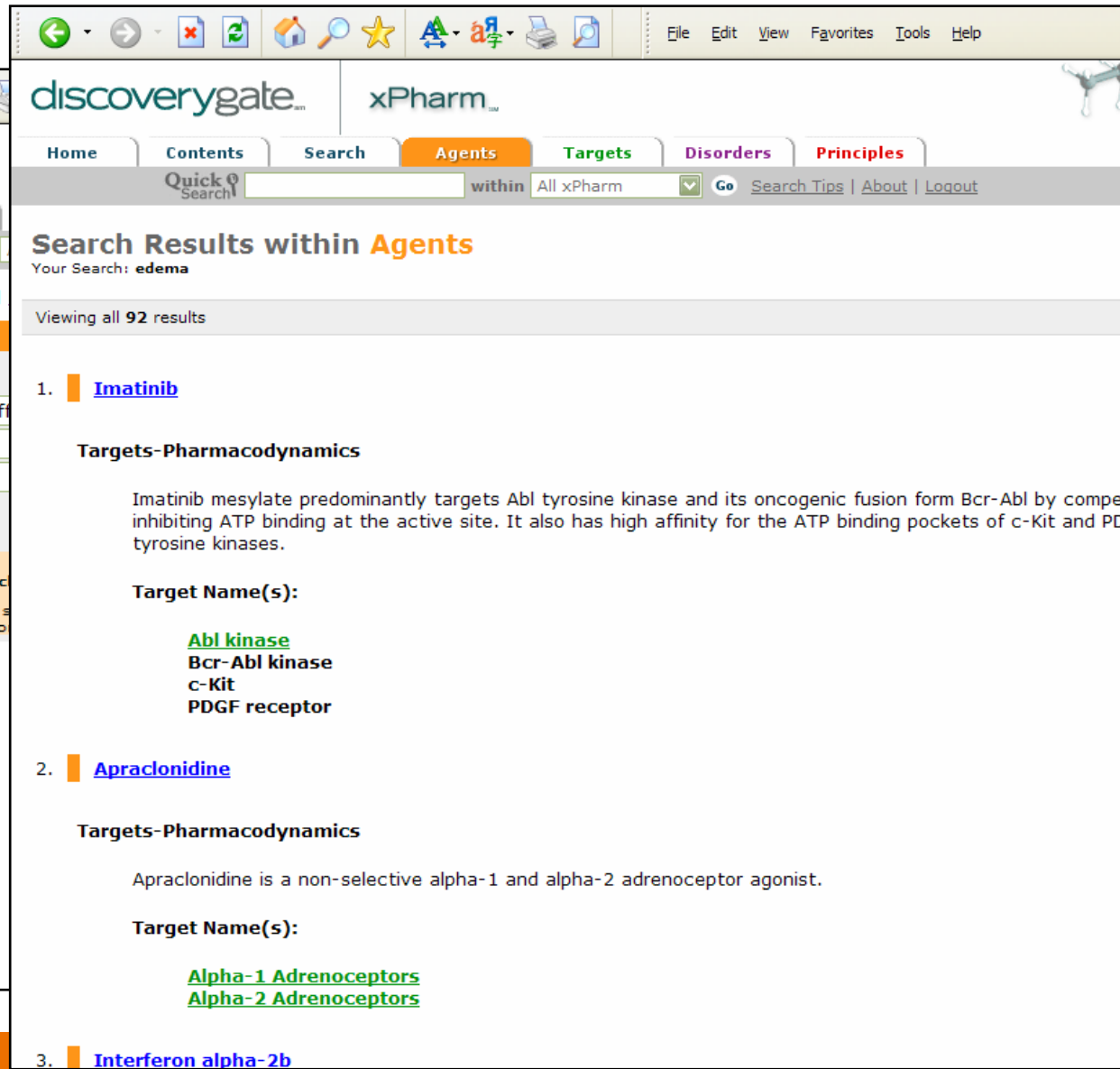
What agents give edema as a side effect?

Example 2:

What targets does Alzheimer's disease affect?

Agents with edema S/E





SEARCH SCENARIO:

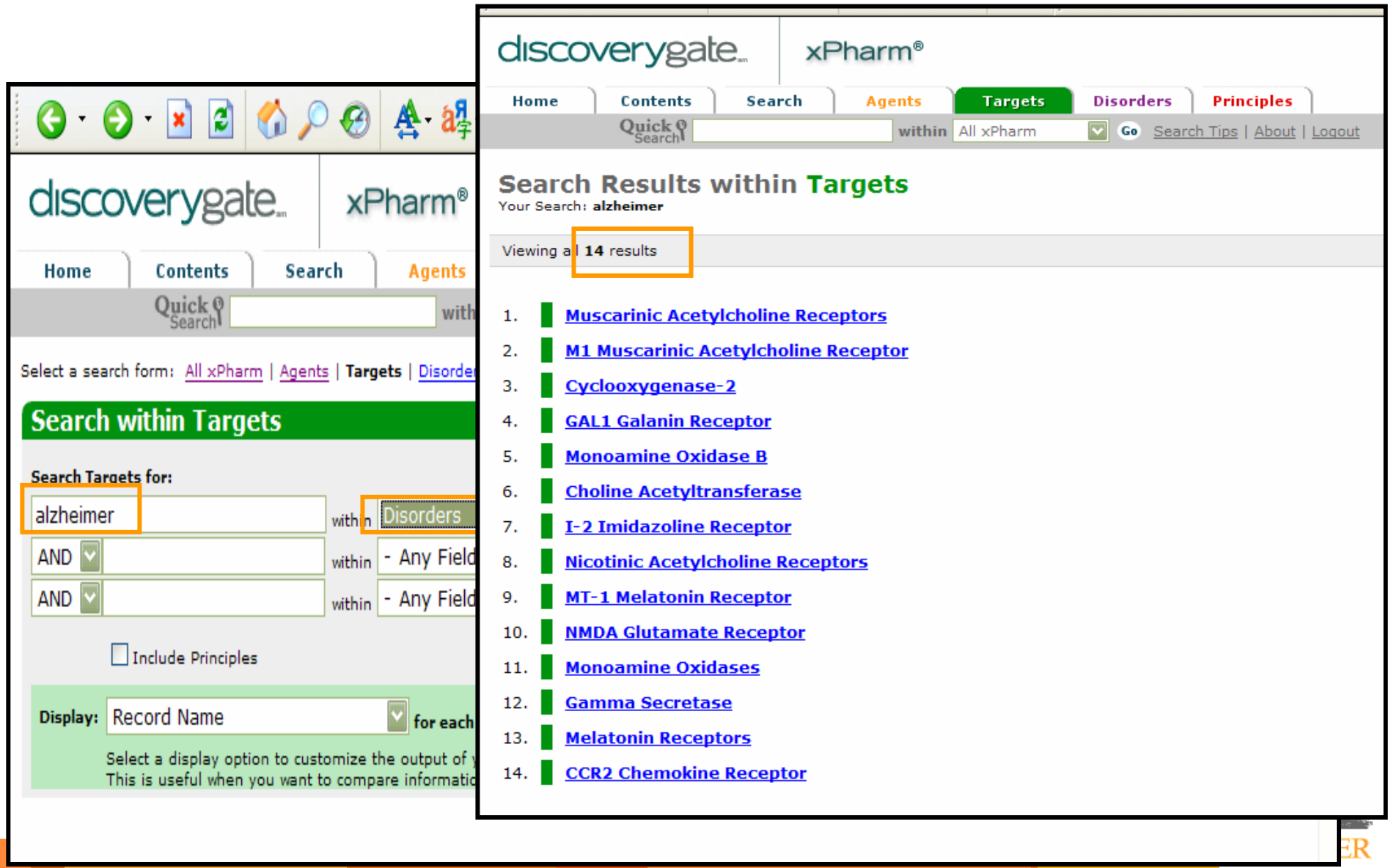
Example 1:

What agents give edema as a side effect?

Example 2:

What targets does Alzheimer's disease affect?

Targets related to Alzheimer's Disease



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ARTICLE EXAMPLES

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ARTICLES

- Paralens (panadol)
- xPharm editors
- Viral Replication
- Breast Cancer
- Monoamine oxidase

Summary

- xPharm is a growing resource, content is reviewed and updated frequently by recognized pharmacologists; and it is authoritative
- xPharm contains greater detail and more information on targets and disorders than any other single online resource
- The emphasis on experimental pharmacology (new agents, new targets)
- Easy to use- no training necessary
- xPharm is the ideal source to get answers to pharmacological questions
- Offers unlimited web-based access to users in an academic institution.

Thank you!

- Questions?
- Product Sales Manager: Doreen Tan
- Personal 14-day evaluation available at http://www.mdl.com
- Further questions, please visit http://www.mdl.com/products/knowledge/xpharm/index.jsp;
- or email D.Tan@elsevier.com

xPharm

COMMON QUESTIONS

Common questions on xPharm

- **Q:** Is xPharm only about approved drugs?
  A: No. xPharm's emphasis is on experimental drugs about which pharmacological activity is known. The detailed information that is provided is pre-clinical, and agents with known toxicity in whole animals may be included because of their experimental utility for life scientists. However, approved drugs are included where their pharmacology is representative of a whole class of compounds.

- **Q:** When will xPharm be complete?
  A: Never: this is a living database that will evolve with the growth of research in specific areas of target development and therapeutics. The xPharm database will be updated quarterly, with breaking news updated constantly.

Common questions on xPharm

- **Q:** Why are there only a couple of thousand agents in xPharm, and more than 100,000 in MDDR?
  A: xPharm is not intended as an exhaustive catalog of NCE's. One can select an agent in xPharm according to its biological properties and then search for all similar compounds in MDDR.

- **Q**: What is the difference between xPharm and MDDR?
  A: MDDR is a database designed for chemists. It has 132,000 compounds and for some of these, the molecular target(s) and the therapeutic use(s) are named. By contrast, xPharm is intended primarily for life scientists providing detailed information about molecular targets, and about the diseases they are related to with links to representative examples of agent classes. Thus, xPharm and MDDR provide complementary views of pharmacological information intended for different audiences.

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PRICING MODEL FOR
ACADEMICS & GOVERNMENT INSITUTIONS

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Pricing Model (A&G)

*Population Band**		*2005 Subscription US$*		
Lower limit	*Upper limit*	*DiscoveryGate*	*xPharm*	*Patent Chemistry Database*
1	50	27,657	8,018	8,627
51	250	34,213	10,023	10,783
251	500	39,961	12,528	13,479

* For academics, population band refers to the number of faculty members + post-doc students in the relevant life science disciplines. E.g.. Pharmacy dept for xPharm.

** For government institutions, population size takes into account the number of relevant life science FTEs, including contractors.