

# DiscoveryGate® in a university lab

## Find the information you need

With the DiscoveryGate® content service now available on Mac OS X, this powerful resource is accessible to a vast and growing community of academic, corporate and government researchers.

This "At the Bench" presents two illustrative search scenarios<sup>1</sup> set in an imaginary organic chemistry lab run by a fictitious Professor Erlenmeyer. Paula Petri is a graduate student with research and teaching responsibilities in Erlenmeyer's lab. Larry Liebig is an eager undergraduate recently assigned to the lab.

Although Paula is primarily focused on finishing her thesis, she knows that she's also expected to assist the undergraduates. Larry chose

Prof. Erlenmeyer's lab because of its reputation as an excellent learning environment, but he admits to feeling a little nervous during his first week at school with so much to learn.

Prof. Erlenmeyer knows that modern information technologies and the Internet have made it easier for scientists to access information. Erlenmeyer wants all his students to become familiar with the factual databases and reference works that support ongoing research in his lab.

The question is how to minimize noise from the flood of information available today, so that researchers can find pertinent data quickly and efficiently. Erlenmeyer believes that DiscoveryGate, with its campus-wide access model, is the solution to this challenge.

### Scenario 1: Searching analytical data

*Prof. Erlenmeyer:* Larry, your compound is a key intermediate. Have you compared the properties with those for reported compounds?

*Larry Liebig:* I've been too busy running an experiment to do a literature search. I'll check Chemical Abstracts during lunch.

*Prof. Erlenmeyer:* CA is good, but it's a simple molecule. See what you can find in Beilstein.

*Paula Petri:* Great idea. Larry, you can use DiscoveryGate to check the Beilstein Database<sup>2</sup>. You can compare your measured values with the reported physical properties data recorded there. Did you complete your analysis last night?

*Larry Liebig:* I got boiling point, NMR and IR spectra but haven't done UV yet.

*Paula Petri:* Let's check Beilstein for your spectral data. Bring your lab notebook.

*Larry Liebig:* I didn't know that I could run a structure search in Beilstein. Look, I found my compound (see Fig. 1). I also found a boiling point under low pressure that's close to my measured value (see Fig. 2). I'm also seeing solvents and other conditions that are useful...as well as literature links. Maybe I can find the proton NMR in a paper.

<sup>1</sup> Search scenarios based on material in an article written by Hirofumi Hashima, Ph.D. (Elsevier MDL Japan) and previously published in *Pharmaceutical Library Bulletin*, 2005, Vol. 5 (No.2), pgs.152-159. This journal is published by the Japan Pharmaceutical Library Association.

<sup>2</sup> Available under separate license from MDL Information Systems GmbH.

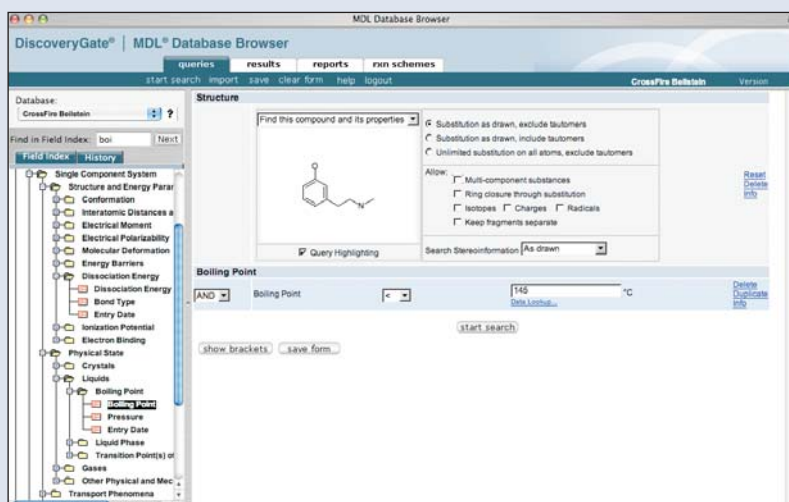


Figure 1: The chemical structure search query. Exact match and substructure search are both available.

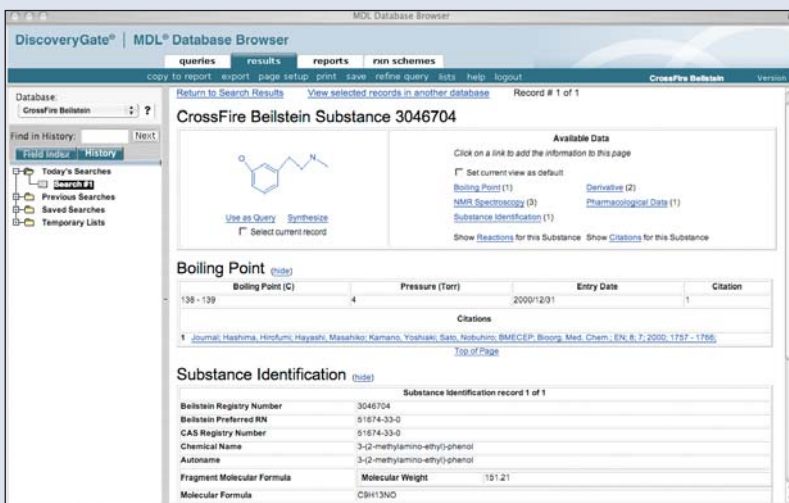


Figure 2: Sample boiling point record in the Beilstein Database

Figure 3: Sample NMR spectroscopy record in the Beilstein Database. Various details are shown. Chemical shift can be found in a cited journal via ScienceDirect.

Figure 4: A sample query in the Beilstein Database for isoflavonoid derivatives with apoptosis-related activities

Figure 5: A sample query in the MDL® Compound Index for isoflavonoids including pharmacological data and the Lipinski "Rule of five"

*Paula Petri:* Here's a journal that's available electronically. You can review it right here at the workstation (see Fig. 3). Go to the experimental section, and you'll find the proton NMR chemical shifts. Is the solvent in the paper the same as yours?

*Larry Liebig:* I know chemical shifts depend on solvents. The solvents are the same. The chemical shifts match too. Ok, I'll go ahead and compare the other analytical results. Thanks, Paula.

*Prof. Erlenmeyer:* This is looking good. We're finding the analytical data we need easily and efficiently using the factual databases in DiscoveryGate.

## Scenario 2: Accessing a wide range of information

*Prof. Erlenmeyer:* Paula, your synthesized natural product shows interesting apoptosis induction activity. Take a look at other compounds with the same scaffold and see if similar activity is reported. If you find interesting results in any of the databases, we should synthesize some derivatives.

*Paula Petri:* Hmm...apoptosis induction. I probably won't find much about that in pharmacological databases like MDL® Comprehensive Medicinal Chemistry and MDL® Drug Data Report. I could search PubMed, but you can't do structure searches there.

*Larry Liebig:* It looks as if the Beilstein Database abstracts biological activity data from papers since 1980. We could check there (see Fig. 4).

*Paula Petri:* Yes, I'm finding a few compounds in Beilstein, along with brief experimental summaries. These compounds show various biological activities. I'm seeing anti-inflammatory and enzyme inhibition activities in addition to apoptosis. We should let Professor Erlenmeyer know about them. Good work, Larry.

*Larry Liebig:* The drop-down pick list in DiscoveryGate makes it easy to select the databases to include in a search, and the "Also-Found-In" links show related records in different databases. Let's formulate a query containing a substructure and combine it with "pharmacological data exists."

*Paula Petri:* To assess drug-likeness, we should add Lipinski's "Rule of Five" to the query, so we can sort the results with that value too (see Fig. 5).

Larry Liebig: I got way too many hits when I searched for apoptosis on the Internet.

Paula Petri: Why not look at the xPharm® database of pharmacological information on DiscoveryGate? It's organized around Agents, Targets, Disorders and Principles. Open xPharm in DiscoveryGate and see what you can find for apoptosis under "Principles."

Larry Liebig: Good call. I see several chapters here that touch on apoptosis. Some of them contain useful diagrams (see Fig. 6). I'll put these together and present them at our next seminar.

Prof. Erlenmeyer: In today's R&D environment, the barriers between scientific disciplines are rapidly falling away. Our knowledge base needs to draw from a wide range of subject areas. A tool like DiscoveryGate is invaluable in helping us find the information we need quickly. With DiscoveryGate, we can search over 20 chemistry and pharmacology databases simultaneously. We can also link to patents, journals, major reference works and our own internal data repositories—here in the lab, in the university library or wherever we have an Internet connection.

In addition to the classical signal transduction pathways, two others have been implicated in the generation of neoplasia: the DNA damage repair and sensing response (4), and **apoptosis**, or programmed cell death (see Fig. 3). **Apoptosis** should not be confused with necrosis, the lysis of cells and release of cell contents into the environment causing inflammation. **Apoptosis** is a highly regulated physiological process essential for correct development and **maintenance of homeostasis** (5).

Fig. 3. Diagram describing **apoptosis**, or programmed cell death.

**Enzymes** that recognize and repair damage to DNA, indicated by the star in the diagram, play a crucial role in preventing the accumulation of mutations that lead to neoplasia (4). For example, a genetic predisposition to **skin cancer** in patients with Xeroderma pigmentosum, an inherited autosomal recessive disorder, is associated with increased sensitivity to ultraviolet-induced mutagenesis, and thus, to skin cancer. Sensitivity appears to be due to a deficiency in the removal of thymine dimers that are induced by ultraviolet light and therefore to efficiently correct DNA damage resulting from exposure to the sun. If DNA damage cannot be corrected, normal cells have a mechanism to prevent further proliferation by directing them toward programmed cell death or **apoptosis** (5). The p53 protein is a critical element in this death pathway. It interacts with other proteins, including those resident on the mitochondria, to promote death of the damaged cells. If p53, a tumor suppressor, is mutated, the cell death program is not initiated and a cell with damaged DNA continues to grow and divide. Two other proteins in the apoptotic pathway are Bax, a pro-apoptotic

Figure 6: Diagram illustrating the mechanism of apoptosis in xPharm

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