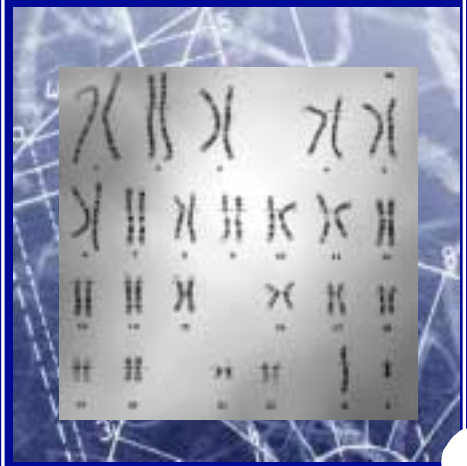


Application integration: Providing coherent drug discovery solutions

LION

Mitch Miller, Manish Sud, LION bioscience,

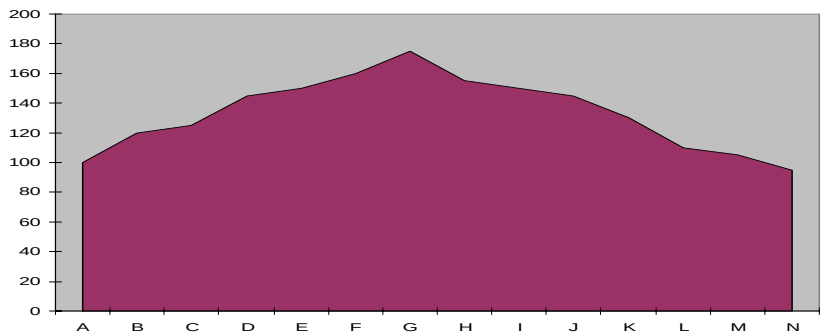
American Chemical Society 22 August 2002

Overview

- Introduction: exploring ‘application integration’
- Our integration platform
- Compound prioritization — one example
- Information traversal — another example

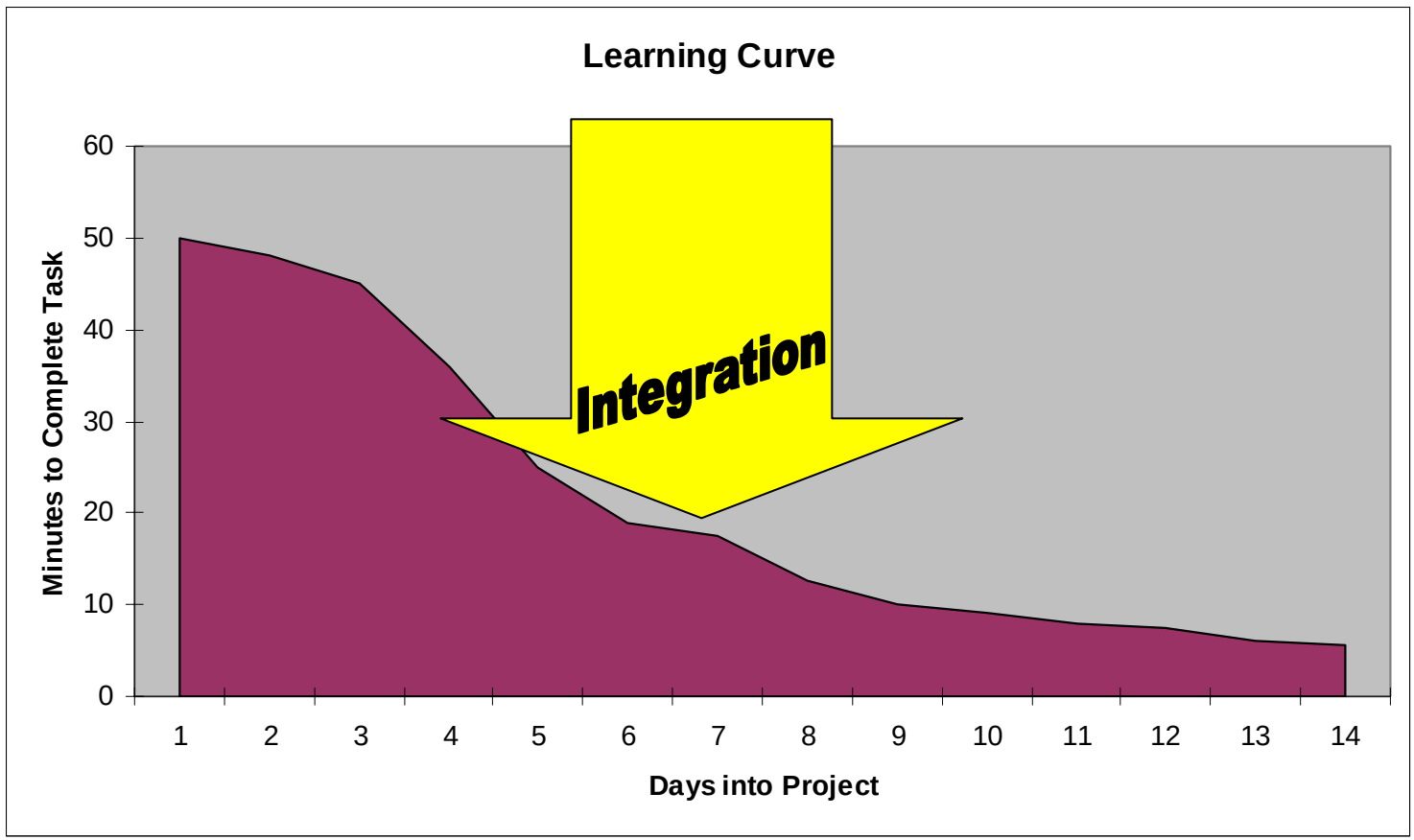
Introduction

- Application Integration
  - Great idea!
  - What does it mean?
- ‘The act or process of integrating’
  - ‘To make into a whole by bringing all parts together; unify’
- Mathematical
  - ‘A number computed by a limiting process in which the domain of a function, often an interval or planar region, is divided into arbitrarily small units, the value of the function at a point in each unit is multiplied by the linear or areal measurement of that unit, and all such products are summed. ‘
  - The area under a curve!



Which curve?

- The area under the information-access *learning* curve!
  - Learning curves go down, according to Gary Anthes in ComputerWorld, July 2, 2001
  - We want to *reduce* the area under the learning curve



An alternative definition?

Application integration:

A situation in which different applications share data and user interface elements, allowing the user to move quickly and efficiently between tasks and *work more productively*.

What are we integrating?

- Vertical applications:
  - Chemical database searching
  - Compound selection
  - Compound analysis
- Horizontal integration:
  - Assay data browsing and searching
  - Relationship browsing

Introducing LION DiscoveryCenter

- Integration framework for compound discovery
  - Supports all the applications listed
- Guiding principal: ‘Show me everything we know about **X**’
  - uniting information about drug-discovery topics
  - variety of sources — public and private
  - provide access to specialist tools
  - capture knowledge of individual scientists
  - jump to related Xs
- Bioinformatics products released last year
- Chemistry: from vision in April to functioning prototype
  - release scheduled for early 2003

Architecture –– From a Scientist's Point of View

- Summary sheet — key to '*show me everything*'
  - variety of information on a single topic in a single screen
  - described by XML -- easy to extend and customize
  - addressed by URL -- can be transmitted
- Session paradigm:
  - search -> browse -> drill down to summary sheets -> traverse
- 'Favorites' provide pointers to individual summary sheets
  - find out what's happening to the entities you're interested in
- Links between different types of data
  - build on natural relationships between items

Architecture –– From a Scientist's Point of View 2

- Annotations capture user knowledge
  - pertain to specific sections or to entire entities
  - shared or private
- Follow-up searching integrated into content display
- Fully-functional Java client
  - includes IceStorm browser to render Web content
  - domain-specific viewers for scientific content
- Component-based — easy to extend

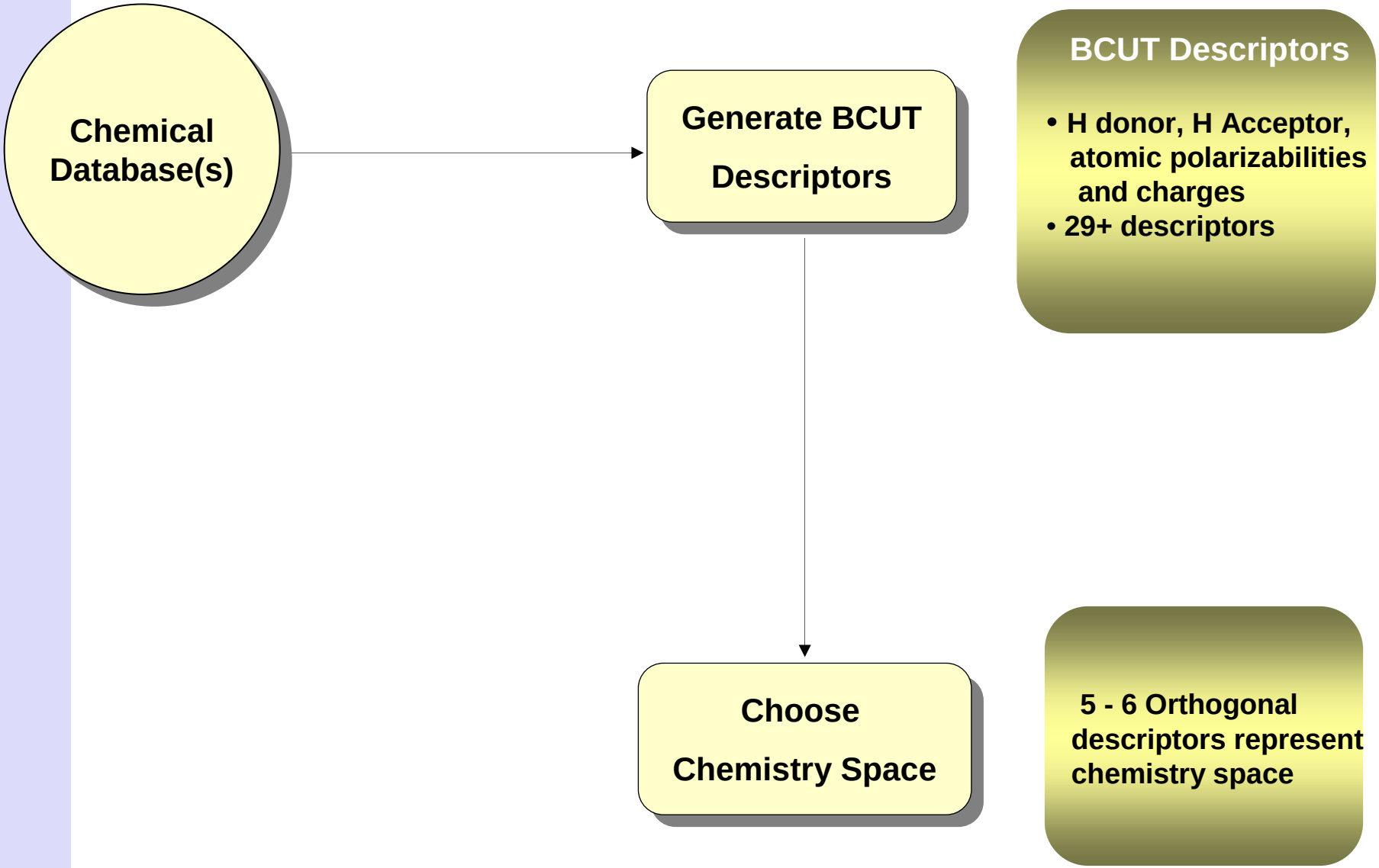
Change in Session Paradigm for Chemistry

- Search -> browse -> analyze -> drill down to summary sheets -> traverse
  - Use computational services to enhance data from databases
  - Possibly load set of compounds from disk file to initiate analysis
- LDC has compute services API to facilitate hooking in computational tools to better understand our compounds
- Examine one case in point:
  - Compound Prioritization

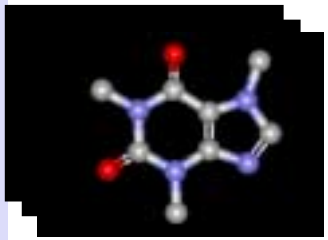
Compound Prioritization: An Overview

- An application currently in use at LION, predating LDC
- A means of assigning a score to a compound
  - how useful will this compound be for us?
- Based on existing models for biological activity and ADME
  - Biological activity models use Receptor Relevant ChemSpaces, generated using DiverseSolutions from R. S. Pearlman and K. M. Smith, University of Texas, distributed by Tripos
  - Predictive ADME using in-house models

Receptor-Relevant Chemspaces
Part I: Database Chemspace



Receptor-Relevant Chemspaces
Part II: Receptor-specific refinement



Known Ligands

Generate BCUT Descriptors

Only the chemistry space BCUT descriptors

Develop Receptor-Relevant Chemistry Space

Subset of chemspace BCUT descriptors relevant for a specific receptor

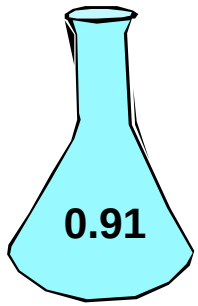
Receptor-Relevant Chemspaces at LION

- We have generated Receptor-Relevant Chemspaces for about 18 different receptors
- Used to estimate receptor specificity
  - suggest when a compound is similar to known ligands for our receptors
  - Is a proposed compound for one receptor likely to interact with others?
- Compound Prioritization user can select:
  - whether compounds should be *inside* or *outside* each of the various RRCs
  - cutoff for RRC
  - weighting

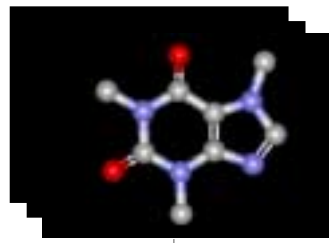
LION Predictive ADME Models

- We predict a variety of ADME parameters:
  - Caco-2 cell permeability (P_{eff})
  - %Fractional dose in portal vein (FDP)
  - Blood-brain barrier penetration (BBB)
  - CYP2D6
  - CYP3A4
- Similar to iDEA product

LION Structure-Based ADMET Predictions: Methodology



Assay Data



Structure Data

Data Quantitization

Molecular Descriptor Calculation/Selection

Machine Learning/ Pattern Recognition

Methods

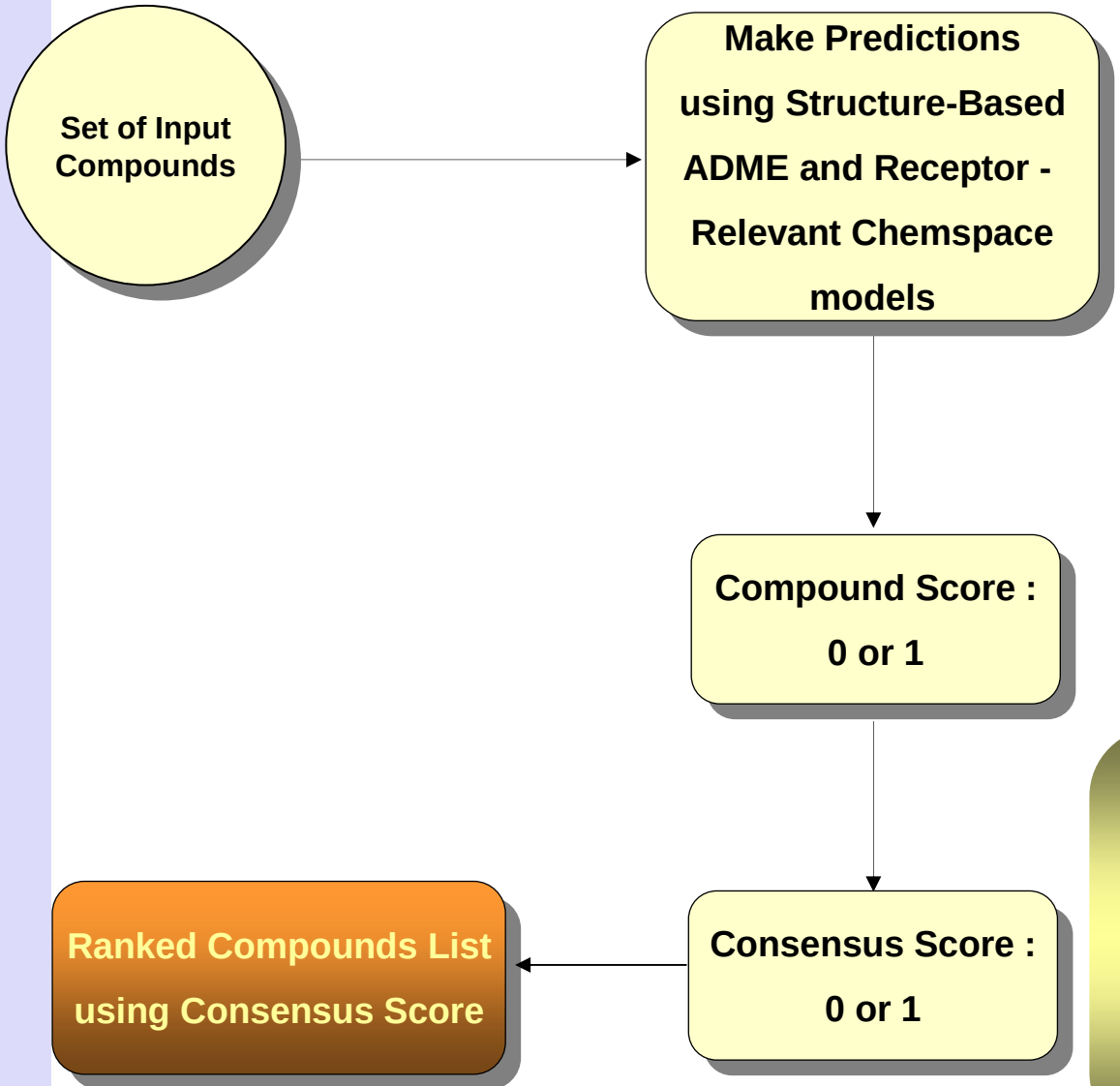
- PCA
- PLS
- PLS DA
- Neural Networks
- GA
- SA

Descriptors

1D: MW etc
2D: b_single etc

Activity Model

Compound Prioritization Schematic



Structure-Based Models

ADME: Caco-2 Peff, %FDP, BBB
CYP2D6, CYP3A4
Selectivity: Receptor-Relevant Chemspace models

Example: Caco-2 Peff

Acceptable: High or Medium
Unacceptable: Low
Weight: 2.0

Scoring

O : Fail criterion

1: Pass Criterion

Consensus Scoring

Consensus Score:

sum over N models(score*weight)/
sum over N models(maxscore*weight)

where score = 1 or 0 and
maxscore = 1

Previous Compound Prioritization Workflow

- Perform search in ISIS/Base
- Export SD file
- Start web application
- Load SD file
- Specify parameters
- View results

Making Visions Work.

i-discovery

Home | Prioritize | iDEA | Similarity | Diversity | Descriptors | QSAR | ChemDB | Resources | Feedback

rioritization

mpounds Prioritization: File, ESketcher or Sketcher ut

ssessment

mpounds Assessment: File, ESketcher or Sketcher ut

AR Analysis

R Table Prioritization & sessment: File input

Compounds Prioritization

Input Type: SD

Input File: F:\Projects\Sonoma\acs_mddr3.sdf Browse...

Available Models: select all

☑ Caco-2 Peff	Criterion:	High or Medium		Weight:	1.0
☑ %FDp	Criterion:	High or Medium		Weight:	1.0
☑ BBB Penetration	Criterion:	No		Weight:	1.0
☑ CYP2D6 Activity	Criterion:	No		Weight:	3.0
☑ CYP3A4 Activity	Criterion:	No		Weight:	3.0
☑ ERRa Chemspace	Criterion:	>=	Distance: 1.5	Weight:	1.0
☑ ERa Chemspace	Criterion:	>=	Distance: 1.5	Weight:	1.0

Making Visions Work.

i-discovery

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AR Analysis

R Table Prioritization & sessment: File input

☑ RXRa Chemspace	Criterion:	>=	Distance:	1.5	Weight:	1.0
☑ RXRb Chemspace	Criterion:	>=	Distance:	1.5	Weight:	1.0
☑ RXRg Chemspace	Criterion:	>=	Distance:	1.5	Weight:	1.0
☑ TR Chemspace	Criterion:	>=	Distance:	1.5	Weight:	1.0
☑ VDR Chemspace	Criterion:	>=	Distance:	1.5	Weight:	1.0

Compound Name Field: EXTREG (optional)

E-Mail Address: mmiller@netgenics.com

Prioritize | Defaults | Help

Note: The computation process encompasses three primary steps: transfer of data from browser to server, structure-based model calculations, and prioritization. Based on types of model(s) you plan to use for prioritization, it can take anywhere from few minutes to few hours! Specify your e-mail address to receive job completion notification by mail.

rioritization

mpounds Prioritization: File, ESketcher or Sketcher ut

ssessment

mpounds Assessment: File, ESketcher or Sketcher ut

AR Analysis

R Table Prioritization & sessment: File input

Compounds Prioritization Results

Compounds Prioritization calculation succeeded.

Results:

To download the results file, click the right mouse button on the download link and select Save Target/Link As option.

View:

- Compounds Models Criteria Distribution

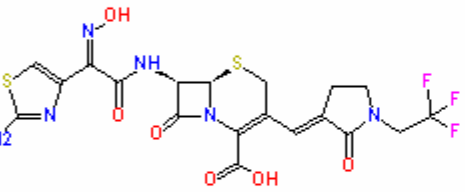
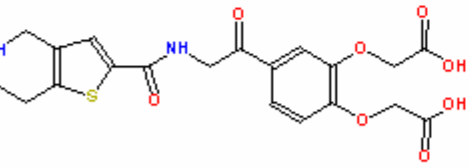
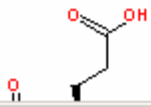
- Compounds Prioritization Results
- Compounds Prioritization Results with Structures

- Compounds Prioritization Results with Background Highlighting
- Compounds Prioritization Results with Structures and Background Highlighting

- Compounds Prioritization Results with Text Highlighting
- Compounds Prioritization Results with Structures and Text Highlighting

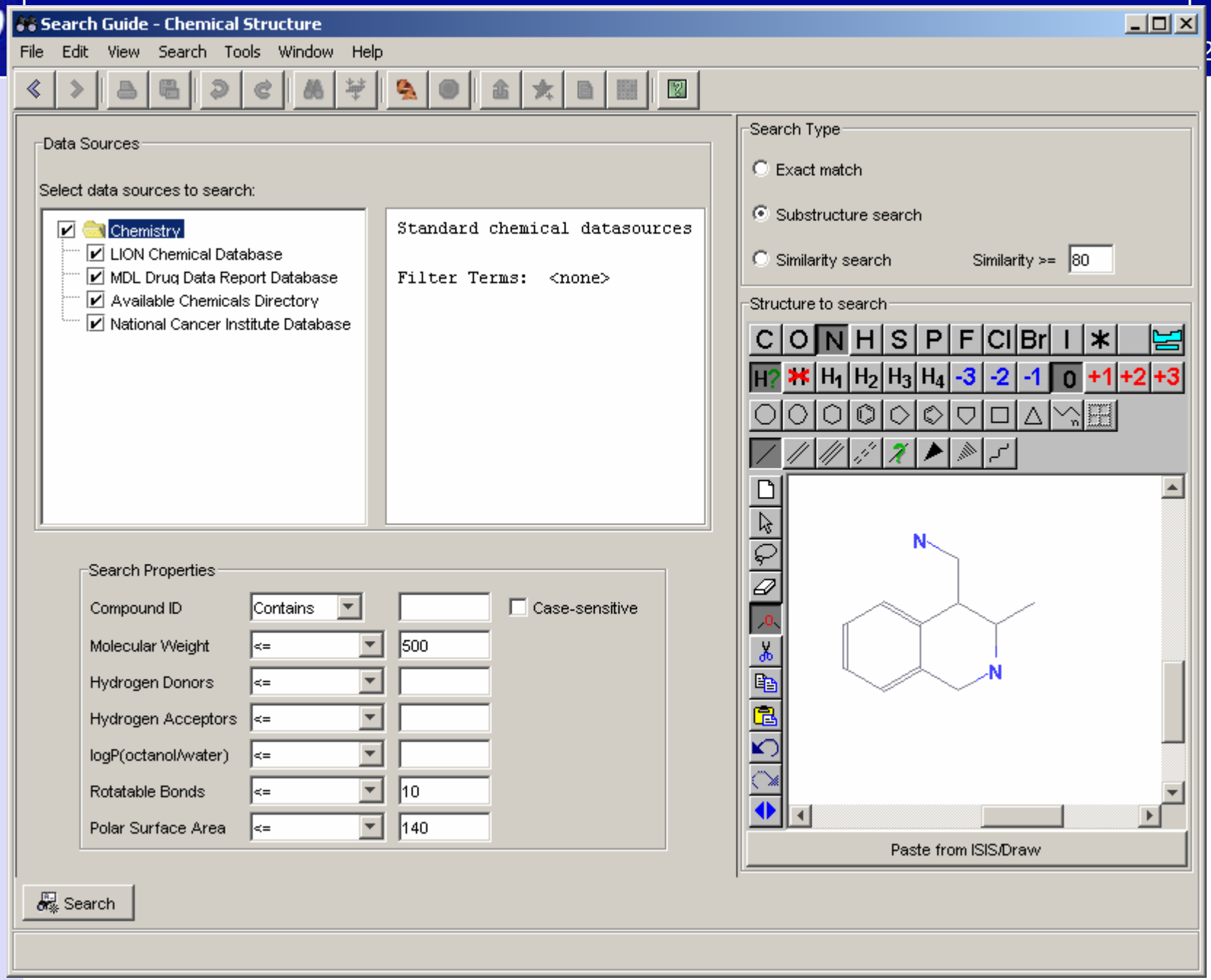
- Caco-2 Peff Predictions
- Caco-2 Peff Predictions with Structures
- %FDp Predictions
- %FDp Predictions with Structures
- BBB Penetration Predictions
- BBB Penetration Predictions with Structures
- CYP2D6 Activity Predictions
- CYP2D6 Activity Predictions with Structures

Compounds Prioritization Results

Structure	MOLNAME	Rank Score	Caco-2 Peff (High or Medium)	%FDp (High or Medium)	BBB Penetration (No)	CYP2D6 Activity (No)	CYP3A4 Activity (No)	ERRa Distance (>= 1.5)	ERa Distance (>= 1.5)	FXR Distance (>= 1.5)	GR Distance (>= 1.5)	LX Dista (>=
	RO-25-6833	0.926	Low	Low	No	No	No	10.082	6.464	2.918	7.587	4.0
	ME-3277	0.926	Low	Medium	No	No	No	9.285	3.819	1.037	7.851	3.3
	LOMETREXOL	0.778	Low	High	No	No	Yes	6.374	3.419	2.389	8.768	3.5

Compound Prioritization in LDC

- Perform search in LDC Search Guide
- Browse results
- Select ‘Compound Prioritization’ from application menu
- Fill in parameters
- Add results to form


Search Guide - Chemical Structure
File Edit View Search Tools Window Help
Data Sources
Select data sources to search:
Chemistry
LION Chemical Database
MDL Drug Data Report Database
Available Chemicals Directory
National Cancer Institute Database
Standard chemical datasources
Filter Terms: <none>
Search Type
Exact match
Substructure search
Similarity search
Similarity >= 80
Structure to search
C O N H S P F Cl Br I *
H? * H1 H2 H3 H4 -3 -2 -1 0 +1 +2 +3
N
N
Paste from ISIS/Draw
Search Properties
Compound ID Contains Case-sensitive
Molecular Weight <= 500
Hydrogen Donors <=
Hydrogen Acceptors <=
logP(octanol/water) <=
Rotatable Bonds <= 10
Polar Surface Area <= 140
Search

Search Guide - Chemical Structure: Substructure search

File Edit View Search Tools Window Help Compute Services Filter Export

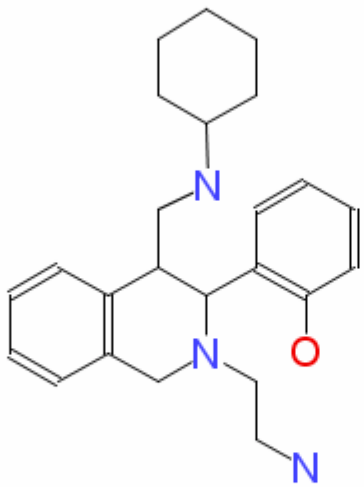
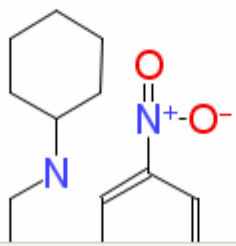
Compound Prioritization
Molconn-Z
MOE

Address: dctp://kewel.sd.lionbioscience.com/NetG ...h=SearchGuide&SEARCH_TYPE%3DSubstructureSearch&AUTO_START%3DY&CRITER

Search terms: Substructure search

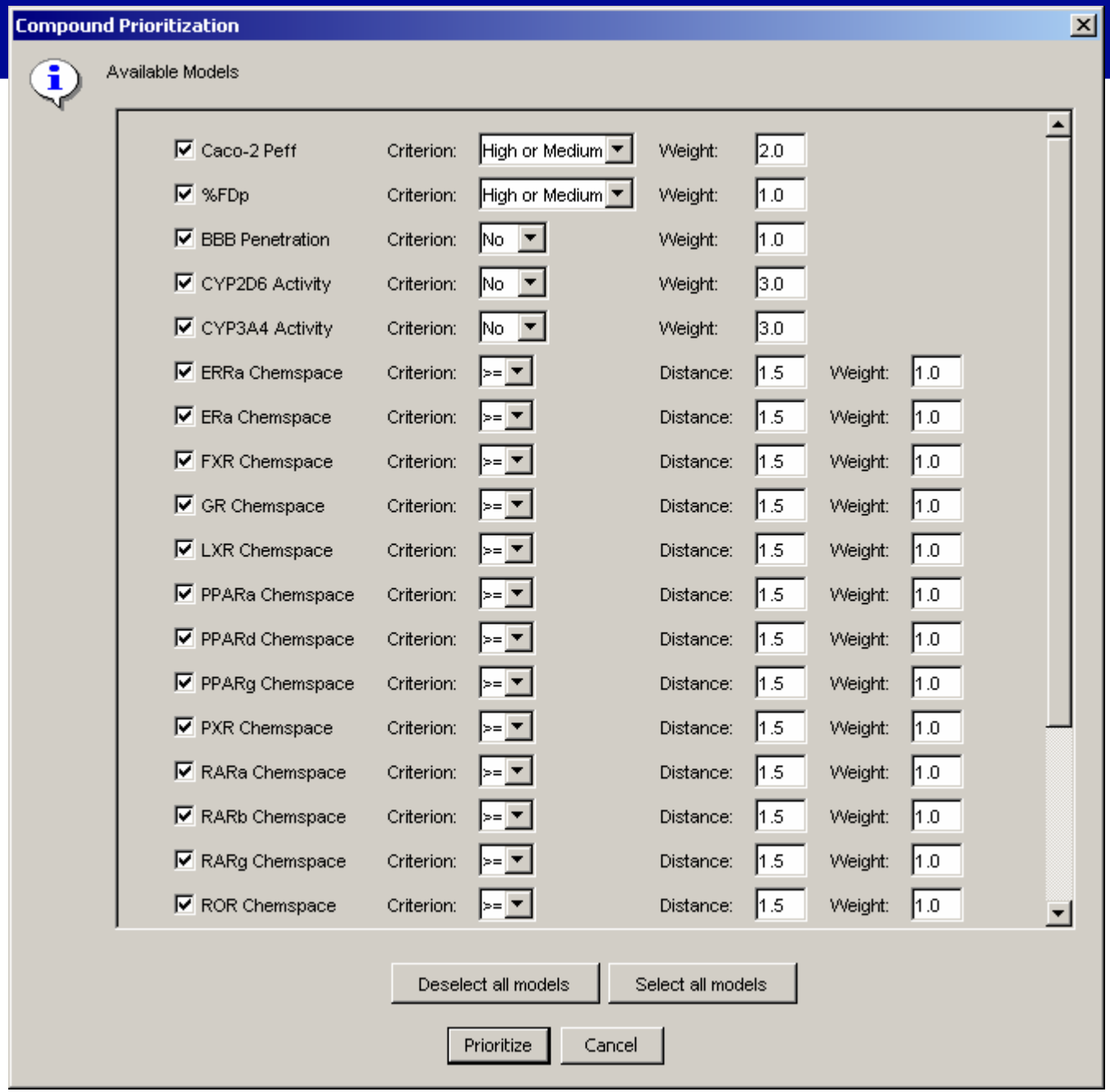
Chemical Results 1 to 29:

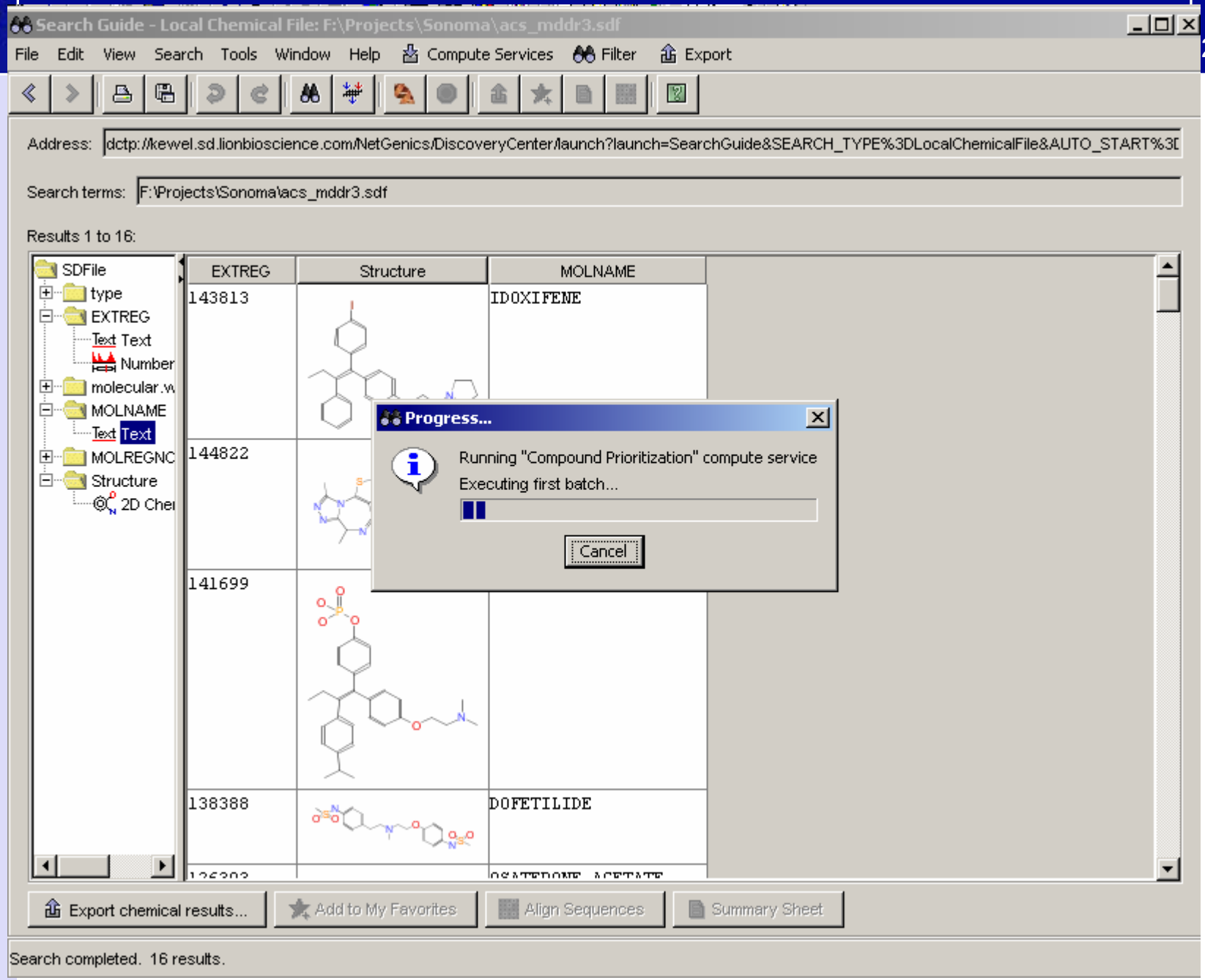
Query
- URN
- Structure
- Compound id
- Hydrogen acceptors
- Hydrogen donors
- Id
- Logp(octanol/water)
- Mol2d
- Molecular Formula
- Molecular Weight
- Polar surface area
- Registration Date
- Rotatable bonds

Row	Structure	Molecular Weight	Molecular Formula	ID	
1		379.5450	$C_{24}H_{33}N_3O$	TR0240500002	urn:x :LION :TR02
			$C_{24}H_{31}ClN_4O_2$	TR0240500013	urn:x :LION :TR02

Export chemical results... Add to My Favorites Align Sequences Summary Sheet

Search completed. 29 results.


Compound Prioritization
Available Models
Caco-2 Peff Criterion: High or Medium Weight: 2.0
%FDp Criterion: High or Medium Weight: 1.0
BBB Penetration Criterion: No Weight: 1.0
CYP2D6 Activity Criterion: No Weight: 3.0
CYP3A4 Activity Criterion: No Weight: 3.0
ERRa Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
ERa Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
FXR Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
GR Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
LXR Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
PPARa Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
PPARd Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
PPARg Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
PXR Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
RARa Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
RARb Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
RARg Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
ROR Chemspace Criterion: >= Distance: 1.5 Weight: 1.0
Deselect all models
Select all models
Prioritize
Cancel


Search Guide - Local Chemical File: F:\Projects\Sonoma\acs_mddr3.sdf
File Edit View Search Tools Window Help Compute Services Filter Export
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Search terms: F:\Projects\Sonoma\acs_mddr3.sdf
Results 1 to 16:
SDFile
type
EXTREG
Text Text
Number
molecular.w
MOLNAME
Text Text
MOLREGNC
Structure
2D Chei
EXTREG
Structure
MOLNAME
143813
IDOXIFENE
144822
141699
138388
DOFETILIDE
Progress...
Running "Compound Prioritization" compute service
Executing first batch...
Cancel
Export chemical results...
Add to My Favorites
Align Sequences
Summary Sheet
Search completed. 16 results.

Search Guide - Chemical Structure: Substructure search

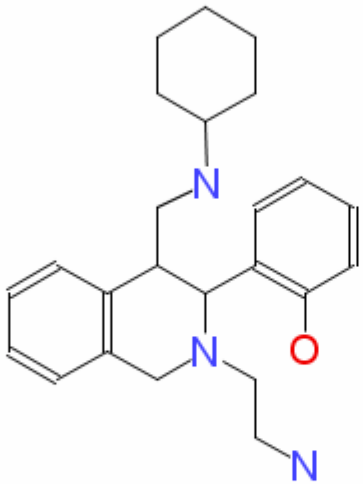
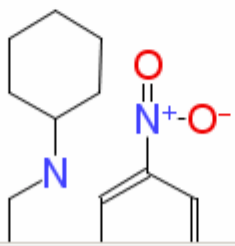
File Edit View Search Tools Window Help Compute Services Filter Export

Address: dctp://kewel.sd.lionbioscience.com/NetGenics/DiscoveryCenter/launch?launch=SearchGuide&SEARCH_TYPE%3DSubstructureSearch&AUTO_START%3DY&CRITER

Search terms: Substructure search

Chemical Results 1 to 29:

- Query
  - URN
  - Structure
  - Compound id
  - Hydrogen acceptors
  - Hydrogen donors
  - Id
  - Logp(octanol/water)
  - Mol2d
  - Molecular Formula
  - Molecular Weight
  - Polar surface area
  - Registration Date
  - Rotatable bonds
  - Compound Prioritization

Row	Structure	Molecular Weight	Molecular Formula	ID	
1		379.5450	$C_{24}H_{33}N_3O$	TR0240500002	urr :LI :TF
			$C_{24}H_{31}ClN_4O_2$	TR0240500013	urr :LI :TF

Export chemical results... Add to My Favorites Align Sequences Summary Sheet

Search completed. 29 results.

Search Guide - Chemical Structure: Substructure search

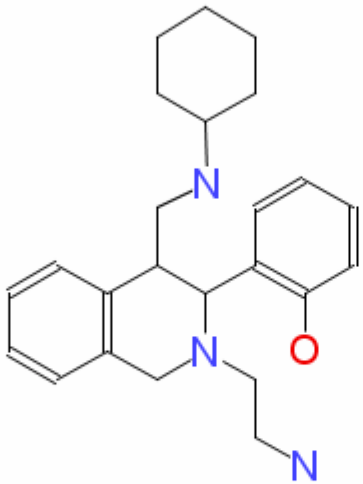
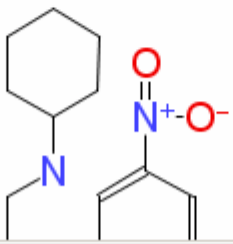
File Edit View Search Tools Window Help Compute Services Filter Export

Address: dctp://kewel.sd.lionbioscience.com/NetGenics/DiscoveryCenter/launch?launch=SearchGuide&SEARCH_TYPE%3DSubstructureSearch&AUTO_START%3DY&CRITER

Search terms: Substructure search

Chemical Results 1 to 29:

- Compound Prioritization
  - Mol Id
  - Rank Score
    - Text Text
    - Number
  - Caco-2 Peff(High or M
  - %FDp(High or Medium)
  - BBB Penetration(Yes)
  - CYP2D6 Activity(No)
  - CYP3A4 Activity(No)
  - ERRa Distance(>= 1.5)
  - ERa Distance(>= 1.5)
  - FXR Distance(>= 1.5)
  - GR Distance(>= 1.5)
  - LXR Distance(>= 1.5)
  - PPARa Distance(>= 1.5
  - PPARd Distance(>= 1.5
  - PPARg Distance(>= 1.5
  - PXR Distance(>= 1.5)
  - RARa Distance(>= 1.5)
  - RARb Distance(>= 1.5)
  - RARg Distance(>= 1.5)
  - ROR Distance(>= 1.5)
  - RXRa Distance(>= 1.5)
  - RXRb Distance(>= 1.5)

Row	Structure	Molecular Weight	Molecular Formula	ID
1		379.5450	$C_{24}H_{33}N_3O$	TR0240500002
2			$C_{24}H_{31}ClN_4O_2$	TR0240500013

Export chemical results... Add to My Favorites Align Sequences Summary Sheet

Search completed. 29 results.

Search Guide - Chemical Structure: Substructure search

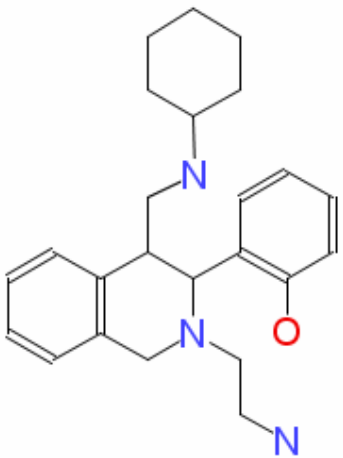
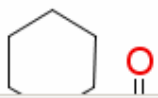
File Edit View Search Tools Window Help Compute Services Filter Export

Address: dctp://kewel.sd.lionbioscience.com/NetGenics/DiscoveryCenter/launch?launch=SearchGuide&SEARCH_TYPE%3DSubstructureSearch&AUTO_START%3DY&CRITERIA%3Dabcdef&PROPEF

Search terms: Substructure search

Chemical Results 1 to 29:

- Compound Prioritization
  - Mol Id
  - Rank Score
    - Text Text
    - Number
  - Caco-2 Peff(High or M
  - %FDp(High or Medium)
  - BBB Penetration(Yes)
  - CYP2D6 Activity(No)
  - CYP3A4 Activity(No)
  - ERRa Distance(>= 1.5)
  - ERa Distance(>= 1.5)
  - FXR Distance(>= 1.5)
  - GR Distance(>= 1.5)
  - LXR Distance(>= 1.5)
  - PPARa Distance(>= 1.5
  - PPARd Distance(>= 1.5
  - PPARg Distance(>= 1.5
  - PXR Distance(>= 1.5)
  - RARa Distance(>= 1.5)
  - RARb Distance(>= 1.5)
  - RARg Distance(>= 1.5)
  - ROR Distance(>= 1.5)
  - RXRa Distance(>= 1.5)
  - RXRb Distance(>= 1.5)

Row	Structure	Molecular Weight	Molecular Formula	ID	Rank Score
1		379.5450	$C_{24}H_{33}N_3O$	TR0240500002	0.556
			$C_{24}H_{31}ClN_4O_2$	TR0240500013	

Export chemical results... Add to My Favorites Align Sequences Summary Sheet

Search completed. 29 results.

Search Guide - Chemical Structure: Substructure search

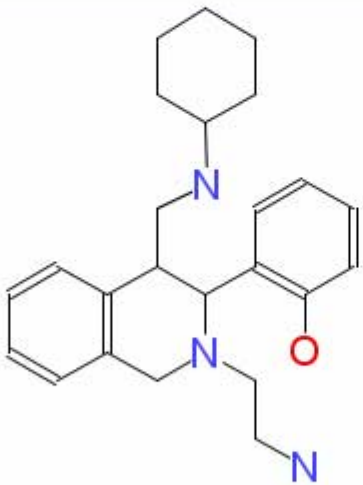
File Edit View Search Tools Window Help Compute Services Filter Export

Address: dctp://kewel.sd.lionbioscience.com/NetGenics/DiscoveryCenter/launch?launch=SearchGuide&SEARCH_TYPE%3DSubstructureSearch&AUTO_START%3DY&CRITERIA%3Dabcdef&PR

Search terms: Substructure search

Chemical Results 1 to 29:

- Compound Prioritization
  - Mol Id
  - Rank Score
    - Text Text
    - Number
  - Caco-2 Peff(High or M
  - %FDp(High or Medium)
  - BBB Penetration(Yes)
  - CYP2D6 Activity(No)
  - CYP3A4 Activity(No)
  - ERRa Distance(>= 1.5)
  - ERa Distance(>= 1.5)
  - FXR Distance(>= 1.5)
  - GR Distance(>= 1.5)
  - LXR Distance(>= 1.5)
  - PPARa Distance(>= 1.5
  - PPARd Distance(>= 1.5
  - PPARg Distance(>= 1.5
  - PXR Distance(>= 1.5)
  - RARa Distance(>= 1.5)
  - RARb Distance(>= 1.5)
  - RARg Distance(>= 1.5)
  - ROR Distance(>= 1.5)
  - RXRa Distance(>= 1.5)
  - RXRb Distance(>= 1.5)

Row	Structure	Molecular Weight	Molecular Formula	ID	Rank Score
1		379.5450	$C_{24}H_{33}N_3O$	TR0240500002	0.556
			$C_{24}H_{31}ClN_4O_2$	TR0240500013	

urn:x-
:LION
:TR02

Ascending
Descending

Edit
Numeric Sort
View Result Detai
Tools

Export chemical results... Add to My Favorites Align Sequences Summary Sheet

Search completed. 29 results.

Search Guide - Chemical Structure: Substructure search

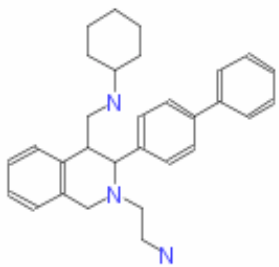
File Edit View Search Tools Window Help Compute Services Filter Export

Address: dctp://kewel.sd.lionbioscience.com/NetGenics/DiscoveryCenter/launch?launch=SearchGuide&SEARCH_TYPE%3DSubstructureSearch&AUTO_START%3DY&

Search terms: Substructure search

Chemical Results 1 to 29:

- Compound Prioritizat
  - Mol Id
  - Rank Score
    - Text Text
    - Number
  - Caco-2 Peff(Hig
  - %FDp(High or M
  - BBB Penetratio
  - CYP2D6 Activit
  - CYP3A4 Activit
  - ERRa Distance(
  - ERa Distance(>
  - FXR Distance(>
  - GR Distance(>=
  - LXR Distance(>
  - PPARa Distanc
  - PPARd Distanc
  - PPARg Distanc
  - PXR Distance(>
  - RARa Distance
  - RARb Distance
  - RARg Distance
  - ROR Distance(>
  - RXRa Distance
  - RXRb Distance

Row	Structure	Molecular Weight	Molecular Formula	Rank Score	
1		406.6140	$C_{26}H_{38}N_4$	0.929	TR024050005
2		439.6430	$C_{30}H_{37}N_3$	0.929	TR024050006
			$C_{26}H_{\cdots}N_{\cdots}O$		TR024290000

Export chemical results... Add to My Favorites Align Sequences Summary Sheet

Search completed. 29 results.

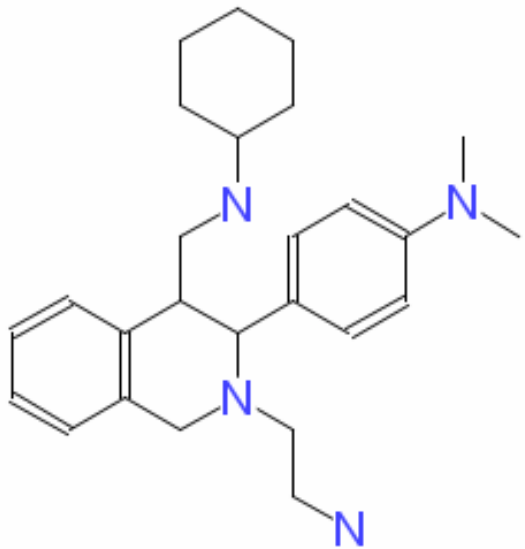
Small Molecule Summary Sheet for LION Chemical Database: TR0240500055

File Edit View Notes Tools Window Help

Address: enter/launch?launch=SummarySheet&urn%3Ax-compound%3ALIONCHEMDB-2D%3ATR0240500055

- Small Molecule
  - Structure and ID
    - 2D Structure
    - 3D Structure
    - Basic Info
  - Batches
    - Batches
  - Similar Molecules
    - MDDR Db
    - ACD Db
    - NCI Db
    - LION Db
  - Molecular Descriptors
    - Drug-Likeness
    - Molconn-Z (subset)
    - MOE (subset)
  - Predicted Bio. Props.
    - Predicted ADMET
  - Assays
    - Bio. Assay Results
  - Nomenclature
    - Compound Names
  - Ordering
    - ChemNavigator
  - Status of Activities
    - Investigators
    - All Notes

2D Structure



Integrating Different Entities by Relationship

- Starting from one compound of interest, we can proceed in many directions:
  - Find other, similar compounds
  - Find assays of interest

Small Molecule Summary Sheet for LION Chemical Database: TR0240500055

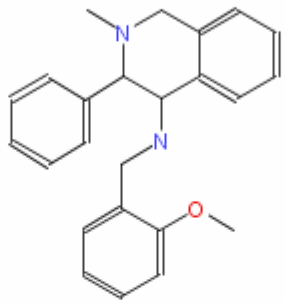
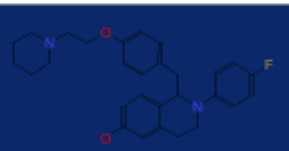
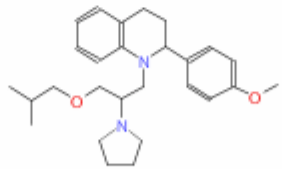
File Edit View Notes Tools Window Help

Address: enter/launch?launch=SummarySheet&urn%3Ax-compound%3ALIONCHEMDB-2D%3ATR0240500055

- Small Molecule
  - Structure and ID
    - 2D Structure
    - 3D Structure
    - Basic Info
  - Batches
    - Batches
  - Similar Molecules
    - MDDR Db
    - ACD Db
    - NCI Db
    - LION Db
  - Molecular Descriptors
    - Drug-Likeness
    - Molconn-Z (subset)
    - MOE (subset)
  - Predicted Bio. Props.
    - Predicted ADMET
  - Assays
    - Bio. Assay Results
  - Nomenclature
    - Compound Names
  - Ordering
    - ChemNavigator
  - Status of Activities
    - Investigators
    - All Notes

MDDR Db

Similar Structures from MDDR 1 to 41:

Row	Compound ID	2D Structure	Sim. Coeff.	Mol. Wt.	Mol. Fmla.
1	190292		69.98	358.4880	C24 H26 N2 O
2	295061		65.60	460.5897	C29 H33 F N2 O2
3	168806		63.59	422.6092	C27 H38 N2 O2
	163304		63.42	329.4849	C20 H31 N3 O

Export... Summary Sheet

Open Summary Sheet

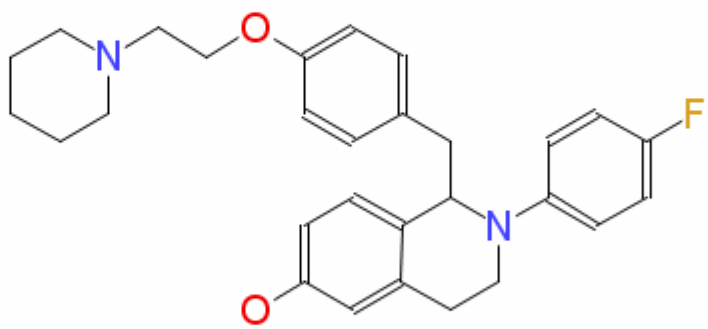
Small Molecule Summary Sheet for MDL Drug Data Report Database: 295061

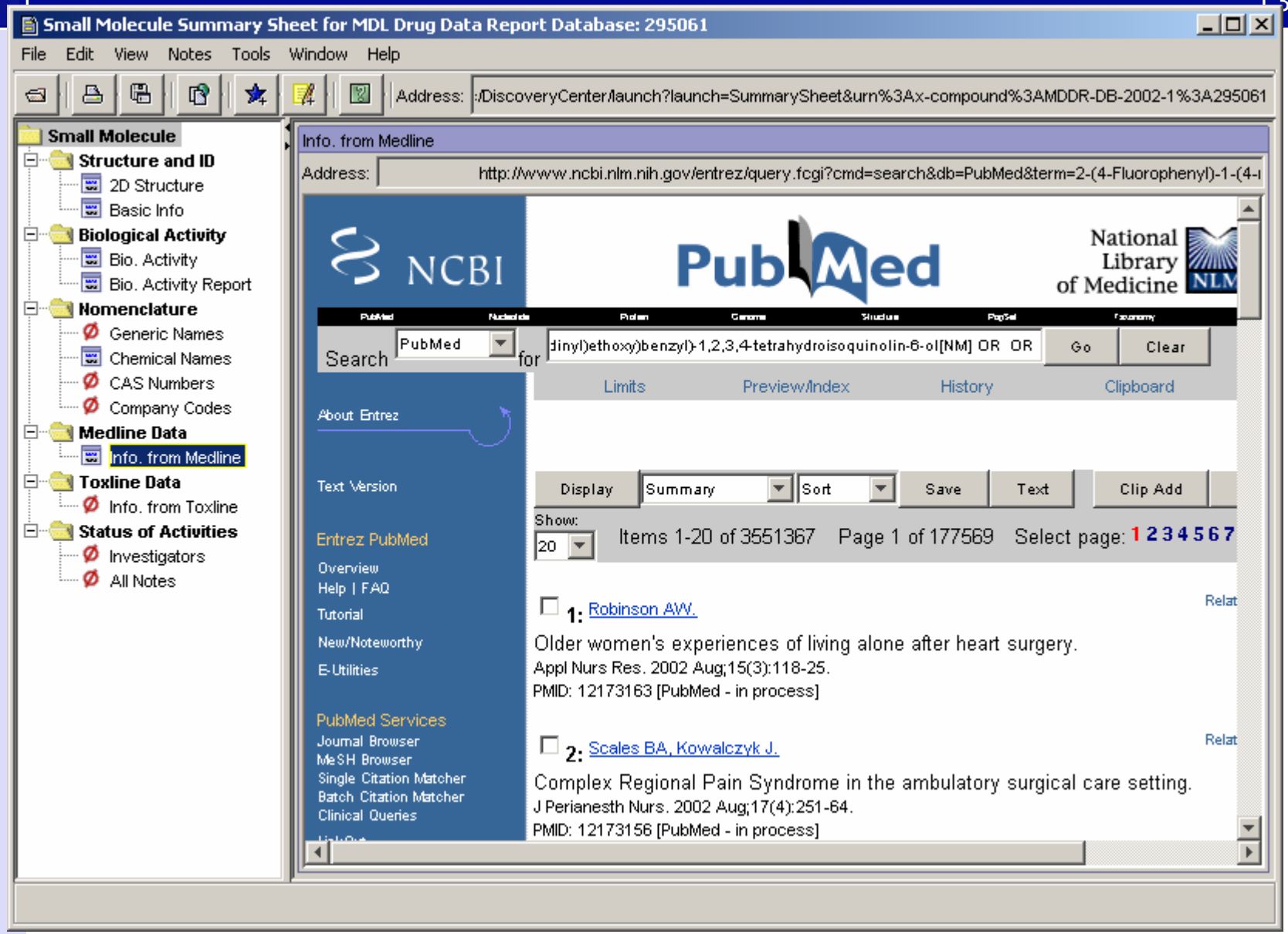
File Edit View Notes Tools Window Help

Address: :/DiscoveryCenter/launch?launch=SummarySheet&urn%3Ax-compound%3AMDDR-DB-2002-1%3A295061

- Small Molecule
  - Structure and ID
    - 2D Structure
    - Basic Info
  - Biological Activity
    - Bio. Activity
    - Bio. Activity Report
  - Nomenclature
    - Generic Names
    - Chemical Names
    - CAS Numbers
    - Company Codes
  - Medline Data
    - Info. from Medline
  - Toxline Data
    - Info. from Toxline
  - Status of Activities
    - Investigators
    - All Notes

2D Structure




Small Molecule Summary Sheet for MDL Drug Data Report Database: 295061
File Edit View Notes Tools Window Help
Address: :/DiscoveryCenter/launch?launch=SummarySheet&urn%3Ax-compound%3AMDDR-DB-2002-1%3A295061
Small Molecule
Structure and ID
2D Structure
Basic Info
Biological Activity
Bio. Activity
Bio. Activity Report
Nomenclature
Generic Names
Chemical Names
CAS Numbers
Company Codes
Medline Data
Info. from Medline
Toxline Data
Info. from Toxline
Status of Activities
Investigators
All Notes
Info. from Medline
Address: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=search&db=PubMed&term=2-(4-Fluorophenyl)-1-(4-
NCBI
PubMed
National Library of Medicine
Search PubMed for
Go
Clear
Limits
Preview/Index
History
Clipboard
About Entrez
Text Version
Entrez PubMed
Overview
Help | FAQ
Tutorial
New/Noteworthy
E-Utilities
PubMed Services
Journal Browser
MeSH Browser
Single Citation Matcher
Batch Citation Matcher
Clinical Queries
Display
Summary
Sort
Save
Text
Clip Add
Show:
20
Items 1-20 of 3551367
Page 1 of 177569
Select page: 1 2 3 4 5 6 7
1: Robinson AW.
Older women's experiences of living alone after heart surgery.
Appl Nurs Res. 2002 Aug;15(3):118-25.
PMID: 12173163 [PubMed - in process]
2: Scales BA, Kowalczyk J.
Complex Regional Pain Syndrome in the ambulatory surgical care setting.
J Perianesth Nurs. 2002 Aug;17(4):251-64.
PMID: 12173156 [PubMed - in process]

1: Appl Nurs Res 2002 Aug;15(3):118-25

Related Articles, Books, LinkOut

ELSEVIER SCIENCE
FULL-TEXT ARTICLE

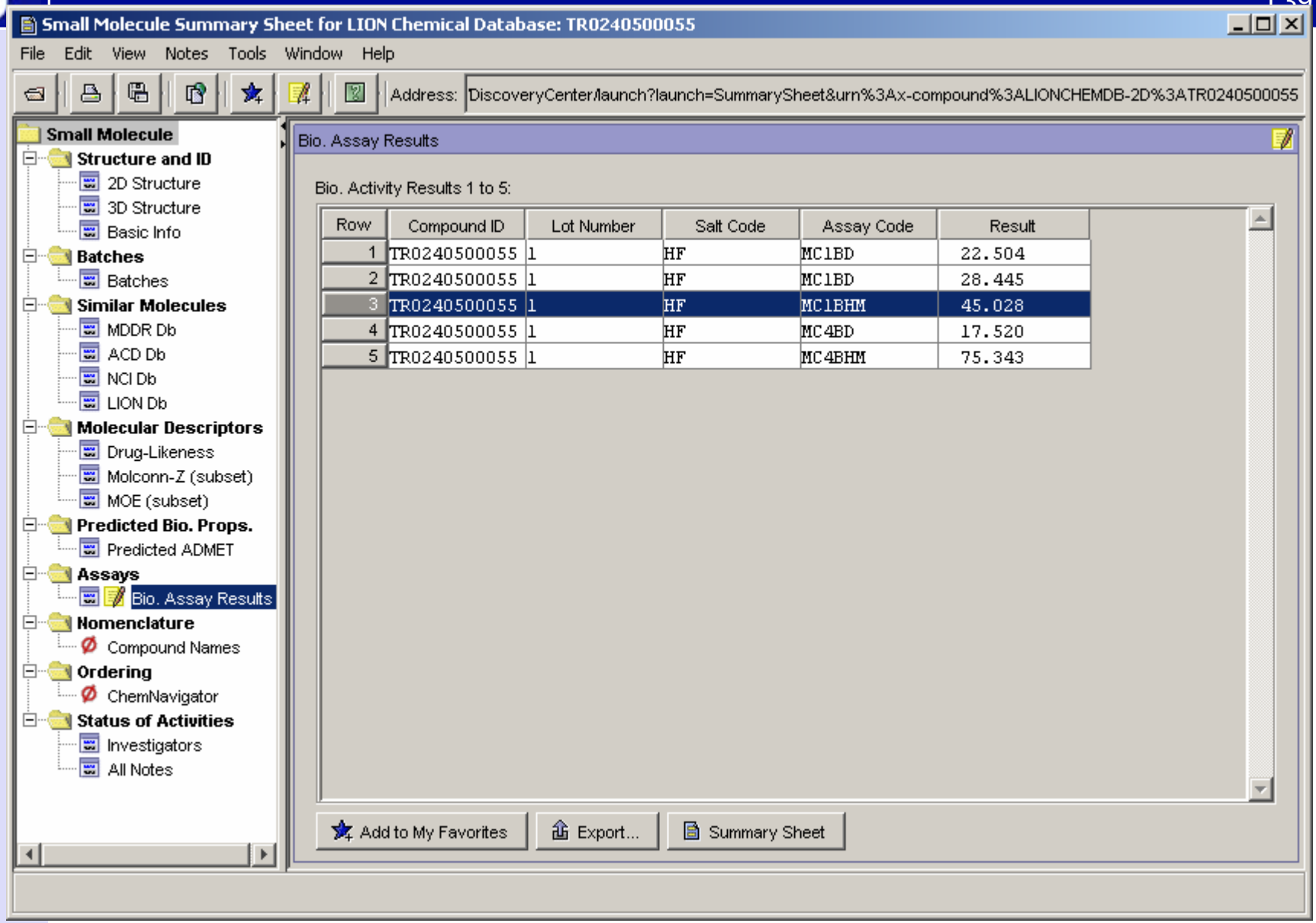
Older women's experiences of living alone after heart surgery.

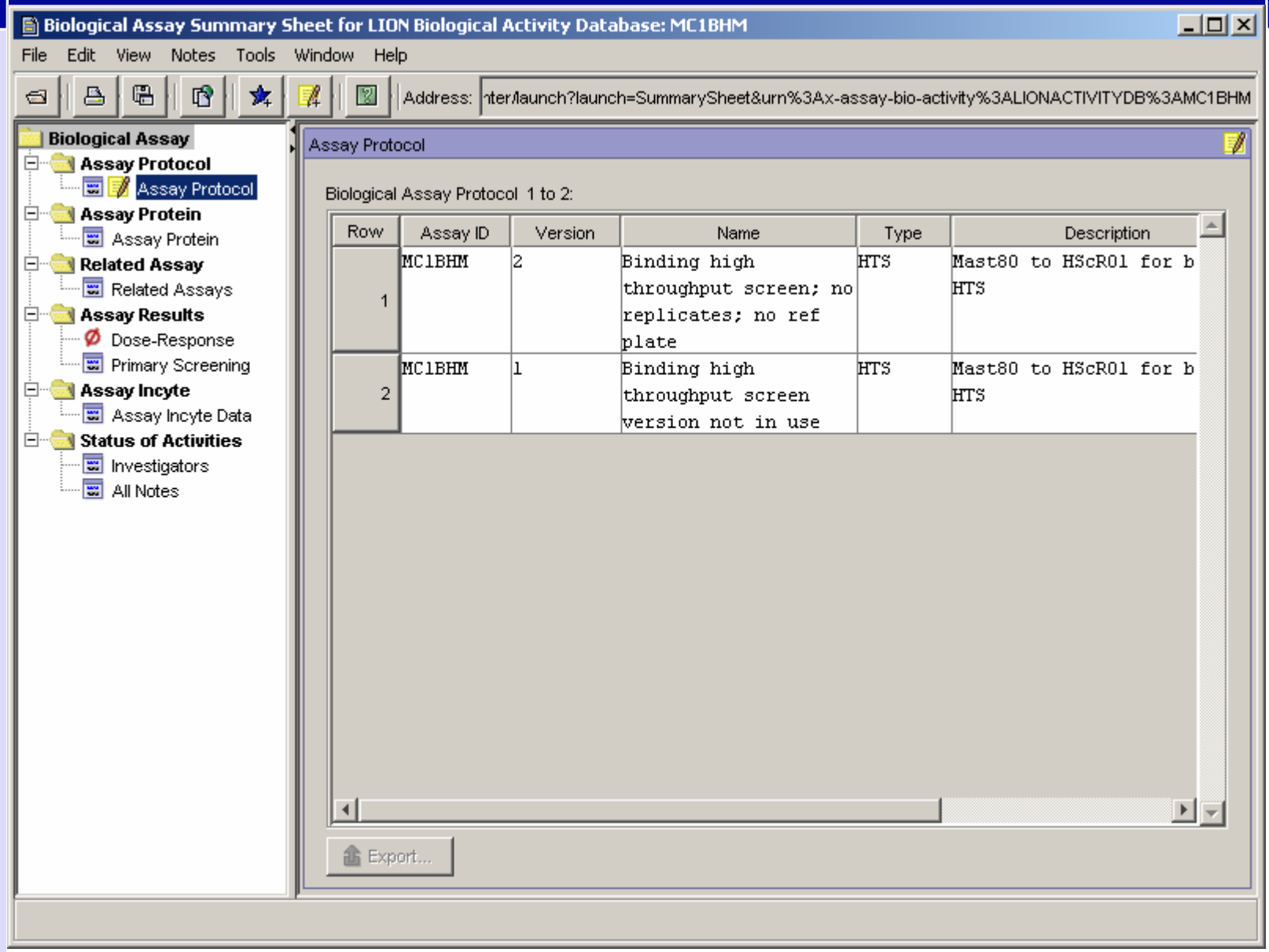
Robinson AW.

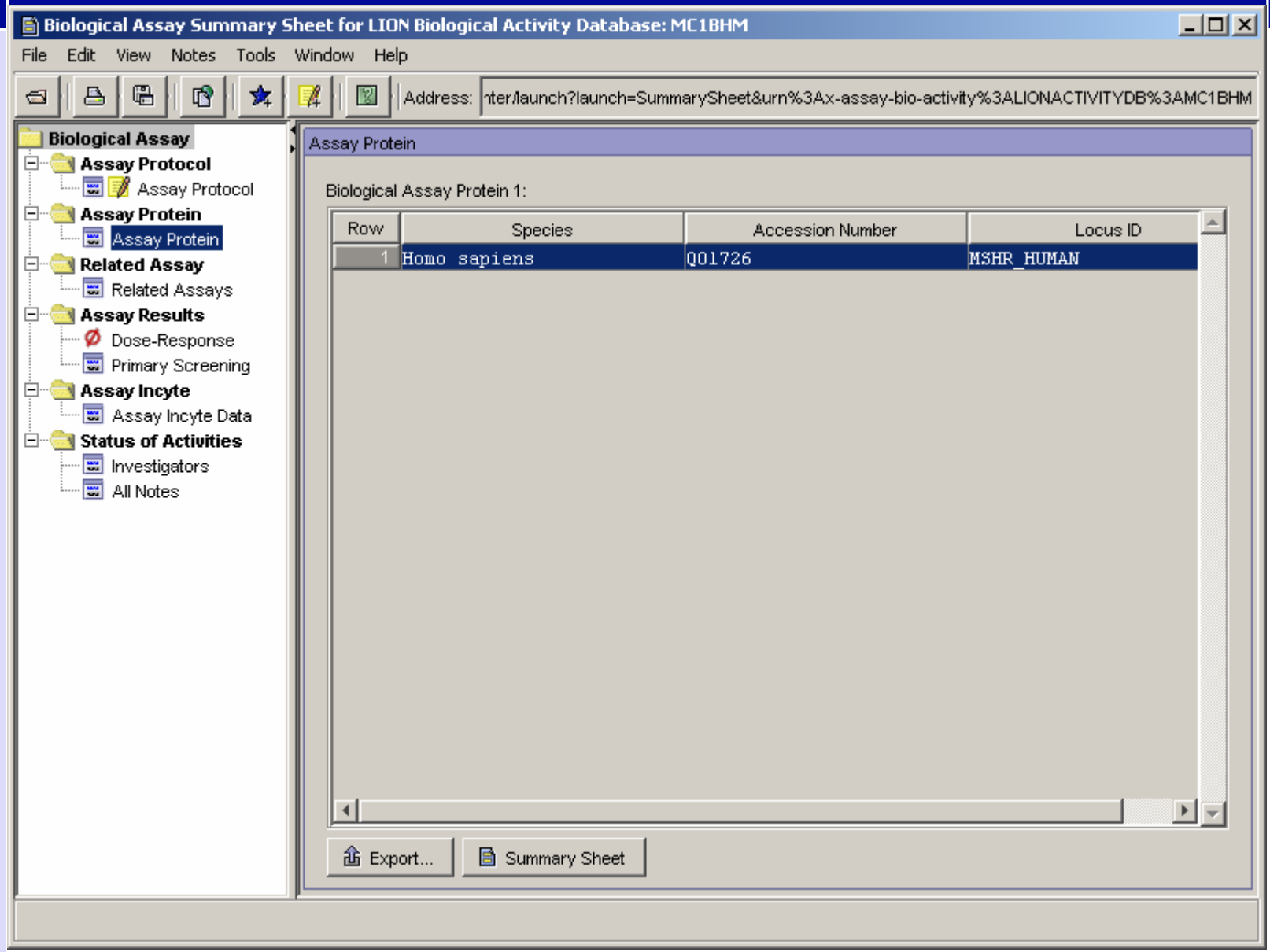
Anne White Robinson, RN, DNS, College of Nursing and Allied Health Professions, University of Louisiana at Lafayette, Lafayette, LA.

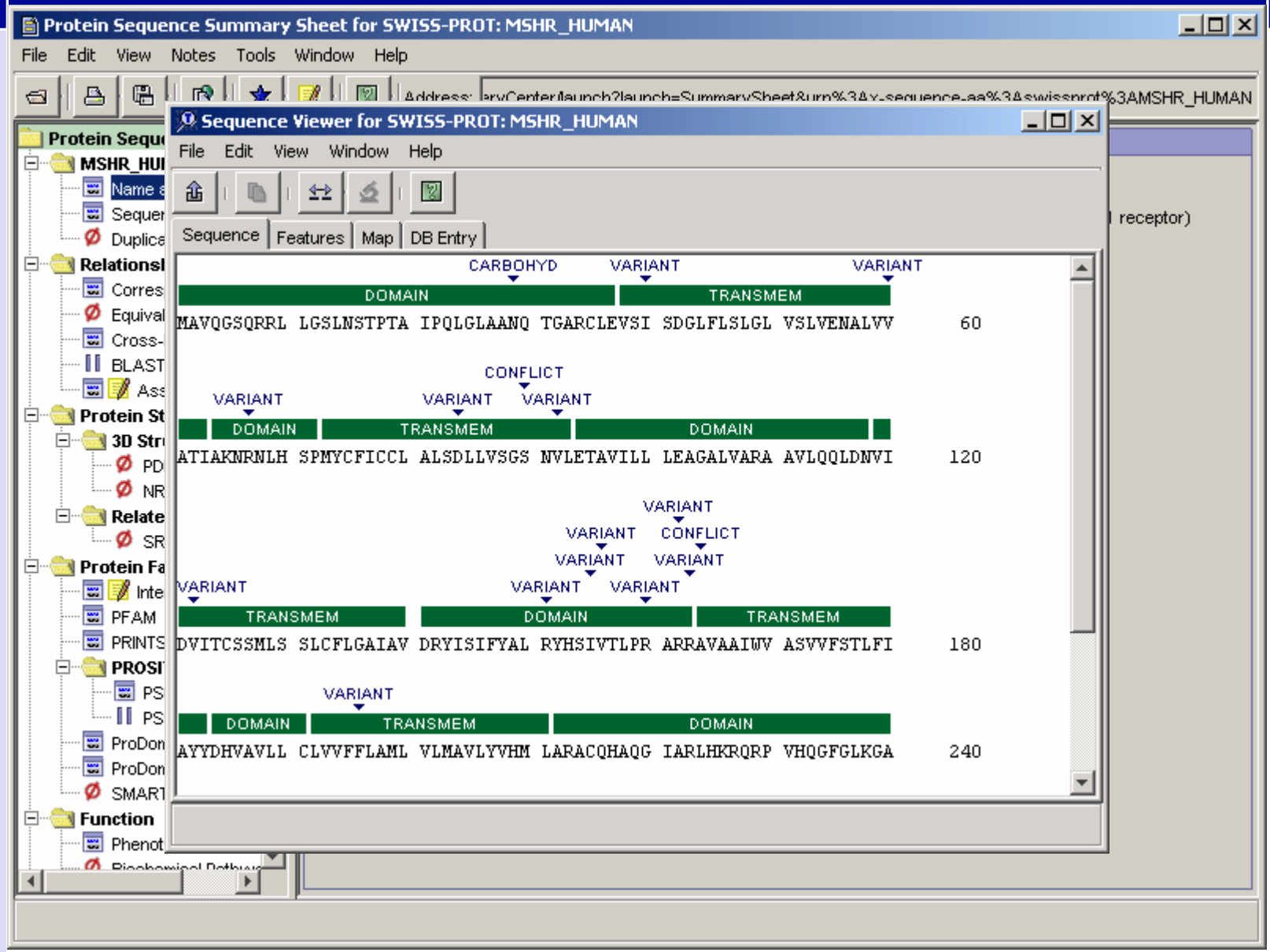
An increasing number of women who have coronary artery disease have undergone heart surgery and are living alone. This qualitative descriptive study identified four primary themes that constituted essential structures of the post-recovery experience for 12 older women living alone after coronary artery bypass surgery. Themes included (1) survival relief, experienced as awe and gratitude; (2) going on, described as an obligation; (3) living within a contracted world, structured by a sense of vulnerability; and (4) regained independence, characterized by affirmation of self-worth and personal freedom. Post-recovery meant restoring the identity the women had known before surgery together with actualizing the value of self-reliance.

PMID: 12173163 [PubMed - in process]


Small Molecule Summary Sheet for LION Chemical Database: TR0240500055
File Edit View Notes Tools Window Help
Address: DiscoveryCenter/launch?launch=SummarySheet&urn%3Ax-compound%3ALIONCHEMDB-2D%3ATR0240500055
Small Molecule
Structure and ID
2D Structure
3D Structure
Basic Info
Batches
Batches
Similar Molecules
MDDR Db
ACD Db
NCI Db
LION Db
Molecular Descriptors
Drug-Likeness
Molconn-Z (subset)
MOE (subset)
Predicted Bio. Props.
Predicted ADMET
Assays
Bio. Assay Results
Nomenclature
Compound Names
Ordering
ChemNavigator
Status of Activities
Investigators
All Notes
Bio. Assay Results
Bio. Activity Results 1 to 5:
Row | Compound ID | Lot Number | Salt Code | Assay Code | Result
1 | TR0240500055 | 1 | HF | MC1BD | 22.504
2 | TR0240500055 | 1 | HF | MC1BD | 28.445
3 | TR0240500055 | 1 | HF | MC1BHM | 45.028
4 | TR0240500055 | 1 | HF | MC4BD | 17.520
5 | TR0240500055 | 1 | HF | MC4BHM | 75.343
Add to My Favorites
Export...
Summary Sheet


Biological Assay Summary Sheet for LION Biological Activity Database: MC1BHM
File Edit View Notes Tools Window Help
Address: nter/launch?launch=SummarySheet&urn%3Ax-assay-bio-activity%3ALIONACTIVITYDB%3AMC1BHM
Biological Assay
Assay Protocol
Assay Protocol
Assay Protein
Assay Protein
Related Assay
Related Assays
Assay Results
Dose-Response
Primary Screening
Assay Incyte
Assay Incyte Data
Status of Activities
Investigators
All Notes
Assay Protocol
Biological Assay Protocol 1 to 2:
Row | Assay ID | Version | Name | Type | Description
1 | MC1BHM | 2 | Binding high throughput screen; no replicates; no ref plate | HTS | Mast80 to HScR01 for b HTS
2 | MC1BHM | 1 | Binding high throughput screen version not in use | HTS | Mast80 to HScR01 for b HTS
Export...


Biological Assay Summary Sheet for LION Biological Activity Database: MC1BHM
File Edit View Notes Tools Window Help
Address: nter/launch?launch=SummarySheet&urn%3Ax-assay-bio-activity%3ALIONACTIVITYDB%3AMC1BHM
Biological Assay
Assay Protocol
Assay Protocol
Assay Protein
Assay Protein
Related Assay
Related Assays
Assay Results
Dose-Response
Primary Screening
Assay Incyte
Assay Incyte Data
Status of Activities
Investigators
All Notes
Assay Protein
Biological Assay Protein 1:
Row
Species
Accession Number
Locus ID
1
Homo sapiens
Q01726
MSHR_HUMAN
Export...
Summary Sheet


Protein Sequence Summary Sheet for SWISS-PROT: MSHR_HUMAN
File Edit View Notes Tools Window Help
Sequence Viewer for SWISS-PROT: MSHR_HUMAN
File Edit View Window Help
Sequence Features Map DB Entry
CARBOHYD VARIANT VARIANT
DOMAIN TRANSMEM
MAVQGSQRRL LGSLNSTPTA IPQLGLAANQ TGARCLEVSI SDGLFLSLGL VSLVENALVV 60
CONFLICT
VARIANT VARIANT VARIANT
DOMAIN TRANSMEM DOMAIN
ATIAKNRNLH SPMYCFICCL ALSDLLVSGS NVLETAVILL LEAGALVARA AVLQQLDNVI 120
VARIANT
VARIANT CONFLICT
VARIANT VARIANT
VARIANT VARIANT VARIANT
TRANSMEM DOMAIN TRANSMEM
DVITCSSMLS SLCFLGAIAV DRYISIFYAL RYHSIVTLPR ARRAVAAIWV ASVVFSTLFI 180
VARIANT
DOMAIN TRANSMEM DOMAIN
AYYDHVAVLL CLVVFFLAML VLMAVLYVHM LARACQHAQG IARLHKRQRP VHQGFGLKGA 240
Protein Sequ
MSHR_HU
Name
Sequer
Duplica
Relationsl
Corres
Equival
Cross-
BLAST
Ass
Protein St
3D Str
PD
NR
Relate
SR
Protein Fa
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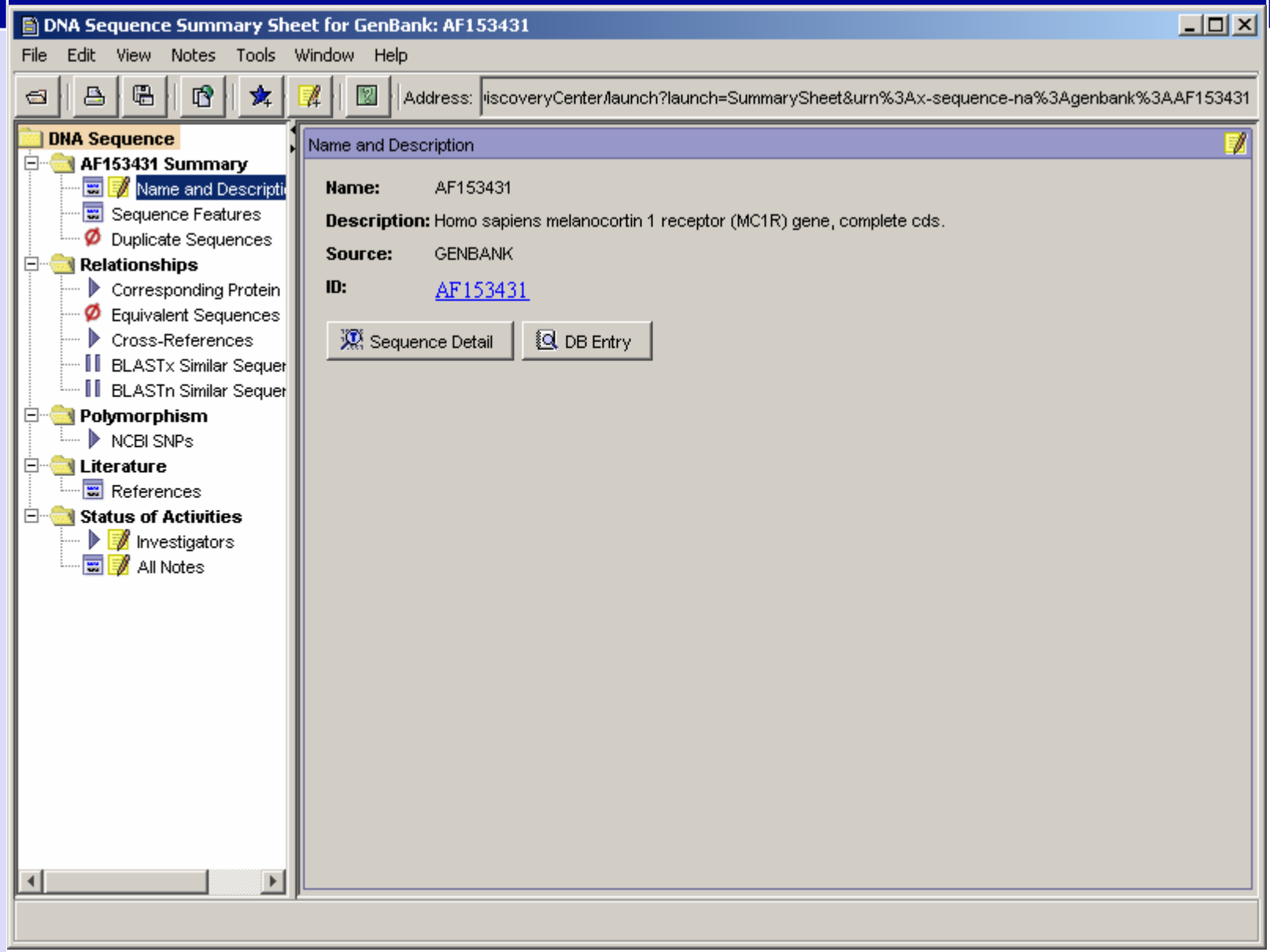
PRINTS
PROSI
PS
PS
ProDon
ProDon
SMART
Function
Phenot
receptor)


DNA Sequence Summary Sheet for GenBank: AF153431
File Edit View Notes Tools Window Help
Address: iscoveryCenter/launch?launch=SummarySheet&urn%3Ax-sequence-na%3Agenbank%3AAF153431
DNA Sequence
AF153431 Summary
Name and Descripti
Sequence Features
Duplicate Sequences
Relationships
Corresponding Protein
Equivalent Sequences
Cross-References
BLASTx Similar Sequer
BLASTn Similar Sequer
Polymorphism
NCBI SNPs
Literature
References
Status of Activities
Investigators
All Notes
Name and Description
Name: AF153431
Description: Homo sapiens melanocortin 1 receptor (MC1R) gene, complete cds.
Source: GENBANK
ID: AF153431
Sequence Detail
DB Entry

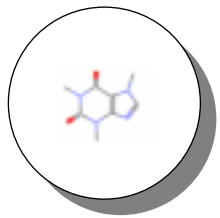
Conclusion

- Integration decreases the learning curve for a set of applications by providing a unified interface and allowing them to share information
- LION DiscoveryCenter provides integration
  - between chemical applications
  - between chemistry and related drug-design disciplines

Acknowledgements

- John Harby
- Ty Jacobs
- John Jaeger
- Lewis Jardine
- Chris Knauft
- Anatoli Krassavine
- Darryl Leòn
- Scott Markel
- Stephen Porter
- Adrian Smith
- Manish Sud
- IT Groups

Questions?



mitchell.miller@lionbioscience.com