Use of NDF-RT in PharmGKB

Diane E. Oliver, MD, PhD
Stanford University

May 21, 2003

Outline

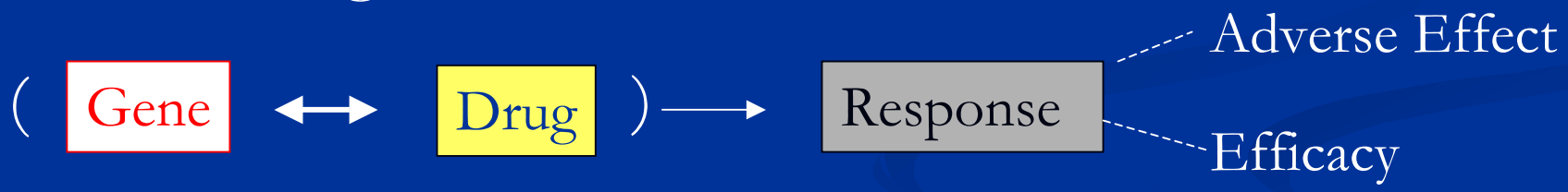
- Overview of PharmGKB
- Selection of drug terminology
- NDF-RT content and structure
- PharmGKB user interface
- Conclusion

Outline

- Overview of PharmGKB
- Selection of drug terminology
- NDF-RT content and structure
- PharmGKB user interface
- Conclusion

PharmGKB:
A Pharmagenetics Knowledge Base

- Pharmacogenetics = the science of how genes influence an individual's response to drugs
- Gene–drug association



- <u>Adverse Effect</u>

  6-mercaptopurine + TPMT
  - Fatal bone marrow suppression

- <u>Efficacy</u>

  Codeine + CYP2D6
  - No effect on pain

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve;jsessionid=855AED39CD6D045141F60A931FBCF51C?id=home.welcome Go Links

PharmGKB

The Pharmacogenetics and Pharmacogenomics Knowledge Base

Search PharmGKB: go

Home | Search | Submit | Resources | Help | Research Network | About Us

Welcome | Projects | Events | Overview | Newsletter | Advisory | Policies | Sign In | Register

Search the PharmGKB:

Search PharmGKB

(eg. "TPMT" or "codeine" or "leukemia")

PharmGKB is an integrated resource about how variation in human genes leads to variation in our response to drugs. Genomic data, molecular and cellular phenotype data, and clinical phenotype data are accepted from the scientific community at large. These data are then organized and the relationships between genes and drugs are then categorized into the following categories:

phenotype
- [CO] Clinical Outcome
- [PD] Pharmacodynamics & Drug Responses
- [PK] Pharmacokinetics
- [FA] Molecular & Cellular Functional Assays

- [Gn] Genotype

Categories of Pharmacogenetic Knowledge

In Memoriam:
Ira Herskowitz
(1946-2003)

A devoted and talented colleague and champion of pharmacogenetics.

Look For:
- All Genes
- Genes with Primary Data
- Genes with Variant Data
- All Drugs
- Drugs with Primary Data
- All Diseases
- All Pathways
- Submissions By Project
- Users with Submissions

Feedback | Sitemap | Privacy Policy | Usage Conditions | Sign In

The Pharmacogenetics Research Network and Knowledge Base is financially supported by grants from NIGMS, NHLBI, NHGRI, NIEHS, NCI, and NLM within the National Institutes of Health (NIH), U.S. Department of Health Human Services (HHS).

http://www.pharmgkb.org/do/serve?id=pharmgkb.team Internet

Outline

- Overview of PharmGKB
- Selection of drug terminology
- NDF-RT content and structure
- PharmGKB user interface
- Conclusion

Selection of Drug Terminology

- Selection criteria
  - Low cost
  - Few proprietary constraints (Web-based)
  - Generic names and trade names
  - Classification structure
- Goals
  - To link drug to gene
  - To index experimental datasets
  - To index pharmacogenetics articles

Drug Terminologies Considered

- NDC
- VA-NDF
- Multum
- Gold Standard Multimedia Clinical Pharmacology
- Micromedex
- FirstDataBank
- Facts and Comparisons
- NDF-RT

NDF-RT:
National Drug File – Reference Terminology

- Features Used
  - Generic names
  - Trade names
  - Ingredients
  - Mechanism of action
  - Physiologic effects
  - Conditions treated
- Features Not Used
  - Dose forms
  - Strength
  - Manufacturer
  - Package size
  - Package type
  - UMLS CUI
  - MeSH definition

Outline

- Overview of PharmGKB
- Selection of drug terminology
- NDF-RT content and structure
- PharmGKB user interface
- Conclusion

C:\Documents and Settings\oliver\DESKTOP\Apelon\Copy of apelontail500.xml - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address C:\Documents and Settings\oliver\DESKTOP\Apelon\Copy of apelontail500.xml Go Links


```xml
<?xml version="1.0" ?>
- <terminology ref_by="name" if_exists_action="replace">
  - <namespaceDef>
      <name>NDF</name>
    </namespaceDef>
  - <kindDef reference="false">
      <name>DRUG_KIND</name>
      <namespace>NDF</namespace>
    </kindDef>
  - <kindDef reference="false">
      <name>INGREDIENT_KIND</name>
      <namespace>NDF</namespace>
    </kindDef>
  - <kindDef reference="false">
      <name>FUNCTION_KIND</name>
      <namespace>NDF</namespace>
    </kindDef>
  - <kindDef reference="false">
      <name>PHARMACOKINETICS_KIND</name>
      <namespace>NDF</namespace>
    </kindDef>
  - <kindDef reference="false">
      <name>DISEASE_KIND</name>
      <namespace>NDF</namespace>
    </kindDef>
  - <kindDef reference="false">
      <name>HL7_DOSE_FORM_KIND</name>
      <namespace>NDF</namespace>
    </kindDef>
  - <roleDef>
```


Done My Computer

C:\Documents and Settings\oliver\DESKTOP\Apelon\Copy of apelontail500.xml - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address C:\Documents and Settings\oliver\DESKTOP\Apelon\Copy of apelontail500.xml Go Links


```
  </conceptDef>
- <conceptDef>
    <name>FUROSEMIDE 20MG TAB [NDC: 52544030010]</name>
    <namespace>NDF</namespace>
    <primitive />
    <kind>DRUG_KIND</kind>
  - <definingConcepts>
      <concept>FUROSEMIDE 20MG TAB</concept>
    </definingConcepts>
    <definingRoles />
  - <properties>
    - <property>
        <name>NDC</name>
        <value>52544030010</value>
      </property>
    - <property>
        <name>NDF_Trade_Name</name>
        <value>FUROSEMIDE</value>
      </property>
    - <property>
        <name>PackageSize</name>
        <value>1000</value>
      </property>
    - <property>
        <name>PackageType</name>
        <value>BOTTLE</value>
      </property>
    - <property>
        <name>Manufacturer</name>
        <value>WATSON LABS INC</value>
      </property>
```


Done My Computer

Browse KB - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites Media

Address http://www.pharmgkb.org/kb/browse.jsp?kb=Drug+Vocabulary Go Links

Currently browsing:

Drug Vocabulary

- :THING (2)
  - :SYSTEM-CLASS (5)
  - Apelon_NDF (7)
    - Active Ingredients (12)
    - Cellular or Molecular Interactions (4)
    - Clinical Kinetics (4)
    - Diseases or Manifestations (21)
    - Pharmaceutical Preparations (32)
    - Physiologic Effects (12)
    - Proposed HL7 Drug Dose Forms (1)

Search

azathioprine

Search

Internet

Browse KB - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites Media

Address http://www.pharmgkb.org/kb/browse.jsp?kb=Drug+Vocabulary Go Links

Currently browsing:

Drug Vocabulary

- :THING (2)
  - :SYSTEM-CLASS (5)
  - Apelon_NDF (7)
    - Active Ingredients (12)
    - Cellular or Molecular Interactions (4)
    - Clinical Kinetics (4)
    - Diseases or Manifestations (21)
    - Pharmaceutical Preparations (32)
    - Physiologic Effects (12)
    - Proposed HL7 Drug Dose Forms (1)

Search

azathioprine

Search

New Search results

6-Mercaptopurine

Azathioprine

[IM600] IMMUNE SUPPRESSANTS

AZATHIOPRINE PREPARATION

AZATHIOPRINE 100

AZATHIOPRINE 100MG/VIL INJ

AZATHIOPRINE 100MG/VIL INJ

AZATHIOPRINE 100MG/VIL INJ [NDC: 00081059800]
AZATHIOPRINE 100MG/VIL INJ [NDC: 00081059871]
AZATHIOPRINE 100MG/VIL INJ [NDC: 00173059871]
AZATHIOPRINE 100MG/VIL INJ [NDC: 55390060020]

AZATHIOPRINE 50 MG

AZATHIOPRINE 50MG TAB

AZATHIOPRINE 50MG TAB

Internet

Browse KB - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites Media

Address http://www.pharmgkb.org/kb/browse.jsp?kb=Drug+Vocabulary Go Links

Currently browsing:

Drug Vocabulary

- :THING (2)
  - :SYSTEM-CLASS (5)
  - Apelon_NDF (7)
    - Active Ingredients (12)
    - Cellular or Molecular Interactio
    - Clinical Kinetics (4)
    - Diseases or Manifestations (21)
    - Pharmaceutical Preparations (32)
    - Physiologic Effects (12)
    - Proposed HL7 Drug Dose Forms (1)

Search

azathioprine

Search

Subclass of [IM600] IMMUNE SUPPRESSANTS:

AZATHIOPRINE PREPARATION

DrugVocabulary_17387

[New Instance] [Edit Class] [Find in Ontology]

Slot	Value
:DIRECT-SUBCLASSES	AZATHIOPRINE 50 MG AZATHIOPRINE 100
:DIRECT-SUPERCLASSES	[IM600] IMMUNE SUPPRESSANTS
:ROLE	Concrete
has_Ingredient	Azathioprine
has_MoA	Antimetabolites Antimetabolites, Antineoplastic
has_PE	Immunosuppressive Activity Musculoskeletal Activity
may_treat	Crohn Disease Inflammatory Bowel Diseases Colitis, Ulcerative Multiple Sclerosis Myasthenia Gravis

Jump to Selected Frame

Internet

Browse KB - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites Media

Address http://www.pharmgkb.org/kb/browse.jsp?kb=Drug+Vocabulary Go Links

- [CV000] CARDIOVASCULAR MEDICA
- [DE000] DERMATOLOGICAL AGENTS
- [DX000] DIAGNOSTIC AGENTS (4)
- [GA000] GASTROINTESTINAL MEDI
- [GU000] GENITOURINARY MEDICAT
- [HS000] HORMONES / SYNTHETICS
- [IM000] IMMUNOLOGICAL AGENTS
  - [IM100] VACCINES (21)
  - [IM200] TOXOIDS (2)
  - [IM300] ANTIVENINS/ANTITOXI
  - [IM400] IMMUNE SERUMS
  - [IM500] IMMUNOGLOBULINS (6)
  - [IM600] IMMUNE SUPPRESSANTS
    - AZATHIOPRINE PREPARATION
      - AZATHIOPRINE 100 (1)
      - AZATHIOPRINE 50 MG (1)
    - BASILIXIMAB PREPARATION (

Search

Search

Subclass of [IM600] IMMUNE SUPPRESSANTS:

AZATHIOPRINE PREPARATION

DrugVocabulary_17387 [New Instance] [Edit Class] [Find in Ontology]

Slot	Value
:DIRECT-SUBCLASSES	AZATHIOPRINE 50 MG AZATHIOPRINE 100
:DIRECT-SUPERCLASSES	[IM600] IMMUNE SUPPRESSANTS
:ROLE	Concrete
has_Ingredient	Azathioprine
has_MoA	Antimetabolites Antimetabolites, Antineoplastic
has_PE	Immunosuppressive Activity Musculoskeletal Activity
may_treat	Crohn Disease Inflammatory Bowel Diseases Colitis, Ulcerative Multiple Sclerosis Myasthenia Gravis

Jump to Selected Frame

Show all slots for AZATHIOPRINE PREPARATION

View AZATHIOPRINE PREPARATION Internet

Additional Trade Names

FDA Orange Book

PROCAINAMIDE HYDROCHLORIDE~Capsule; Oral~PRONESTYL~APOTHECON~250MG~007335~001~AB~Approved prior to Jan 1, 1982~No~RX

DICYCLOMINE HYDROCHLORIDE~Capsule; Oral~BENTYL~AVENTIS PHARMS~10MG~007409~003~AB~OCT 15, 1984~Yes~RX

NOREPINEPHRINE BITARTRATE~Injectable; Injection~LEVOPHED~ABBOTT~EQ 1MG BASE/ML~007513~001~~Approved prior to Jan 1, 1982~Yes~RX

METHIMAZOLE~Tablet; Oral~TAPAZOLE~LILLY~5MG~007517~002~AB~Approved prior to Jan 1, 1982~No~RX

ASPIRIN~Tablet, Extended Release; Oral~8-HOUR BAYER ~BAYER~650MG~016030~001~~Approved prior to Jan 1, 1982~No~DISCN

HYDROCORTISONE~Tablet; Oral~CORTEF~PHARMACIA AND UPJOHN~10MG~008697~001~BP~Appro

WARFARIN SODIUM~Tablet; Oral~COUMADIN~BRISTOL MYERS SQUIBB~10MG~009218~005~AB~Approved prior to Jan 1, 1982~Yes~RXved prior to Jan 1, 1982~Yes~RX

Outline

- Overview of PharmGKB
- Selection of drug terminology
- NDF-RT content and structure
- PharmGKB user interface
- Conclusion

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve;jsessionid=855AED39CD6D045141F60A931FBCF51C?id=home.welcome Go Links

PharmGKB

The Pharmacogenetics and Pharmacogenomics Knowledge Base

Search PharmGKB: go

Home | Search | Submit | Resources | Help | Research Network | About Us

Welcome | Projects | Events | Overview | Newsletter | Advisory | Policies | Sign In | Register

Search the PharmGKB:

Search PharmGKB

(eg. "TPMT" or "codeine" or "leukemia")

PharmGKB is an integrated resource about how variation in human genes leads to variation in our response to drugs. Genomic data, molecular and cellular phenotype data, and clinical phenotype data are accepted from the scientific community at large. These data are then organized and the relationships between genes and drugs are then categorized into the following categories:

phenotype
- [CO] Clinical Outcome
- [PD] Pharmacodynamics & Drug Responses
- [PK] Pharmacokinetics
- [FA] Molecular & Cellular Functional Assays

- [Gn] Genotype

Categories of Pharmacogenetic Knowledge

In Memoriam:
Ira Herskowitz
(1946-2003)

A devoted and talented colleague and champion of pharmacogenetics.

Look For:
- All Genes
- Genes with Primary Data
- Genes with Variant Data
- All Drugs
- Drugs with Primary Data
- All Diseases
- All Pathways
- Submissions By Project
- Users with Submissions

Feedback | Sitemap | Privacy Policy | Usage Conditions | Sign In

The Pharmacogenetics Research Network and Knowledge Base is financially supported by grants from NIGMS, NHLBI, NHGRI, NIEHS, NCI, and NLM within the National Institutes of Health (NIH), U.S. Department of Health Human Services (HHS).

Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve?id=submit.relationship Go Links

PharmGKB

The Pharmacogenetics and Pharmacogenomics Knowledge Base

Search PharmGKB: go

Home | Search | Submit | Resources | Help | Research Network | About Us

Submit Data | Submit Feedback

Submit Relationship Between a Gene, Drug, and/or Disease

Gene: [Look Up Gene]

Drug: [Look Up Drug]

Disease: [Look Up Disease]

Categories of Pharmacological Knowledge:
- ☐ Clinical Outcome
- ☐ Pharmacodynamics & Drug Response
- ☐ Pharmacokinetics
- ☐ Molecular & Cellular Functional Assays
- ☐ Genotype

Degree of Confidence: Select Degree of Confidence

Type of Evidence: Select Type of Evidence

Evidence: [Search PubMed]

Evidence Location:
- ☐ Title
- ☐ Abstract
- ☐ Body

Keywords:
(separated by commas)

Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve;jsessionid=855AED39CD6D045141F60A931FBCF51C?id=home.welcome Go Links

PharmGKB

The Pharmacogenetics and Pharmacogenomics Knowledge Base

Search PharmGKB: go

Home | Search | Submit | Resources | Help | Research Network | About Us

Welcome | Projects | Events | Overview | Newsletter | Advisory | Policies | Sign In | Register

Search the PharmGKB:

Search PharmGKB

(eg. "TPMT" or "codeine" or "leukemia")

PharmGKB is an integrated resource about how variation in human genes leads to variation in our response to drugs. Genomic data, molecular and cellular phenotype data, and clinical phenotype data are accepted from the scientific community at large. These data are then organized and the relationships between genes and drugs are then categorized into the following categories:

phenotype
- [CO] Clinical Outcome
- [PD] Pharmacodynamics & Drug Responses
- [PK] Pharmacokinetics
- [FA] Molecular & Cellular Functional Assays

- [Gn] Genotype

Categories of Pharmacogenetic Knowledge

In Memoriam:
Ira Herskowitz
(1946-2003)

A devoted and talented colleague and champion of pharmacogenetics.

Look For:
- All Genes
- Genes with Primary Data
- Genes with Variant Data
- All Drugs
- Drugs with Primary Data
- All Diseases
- All Pathways
- Submissions By Project
- Users with Submissions

Feedback | Sitemap | Privacy Policy | Usage Conditions | Sign In

The Pharmacogenetics Research Network and Knowledge Base is financially supported by grants from NIGMS, NHLBI, NHGRI, NIEHS, NCI, and NLM within the National Institutes of Health (NIH), U.S. Department of Health Human Services (HHS).

Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve?id=browse.drugs Go Links

PharmGKB

The Pharmacogenetics and Pharmacogenomics Knowledge Base

Search PharmGKB: go

Home | Search | Submit | Resources | Help | Research Network | About Us

Search | Browse | dbSNP Surveillance

Browse All Drugs By Name

A 696 B 255 C 529 D 279 E 159 F 164 G 133 H 134 I 203 J 4 K 19 L 144 M 316
N 116 O 108 P 485 Q 18 R 91 S 327 T 271 U 19 V 83 W 28 X 10 Y 7 Z 32

- abacavir
- abacavir sulfate
- abciximab
- absorption base
- acacia
- acacia powder
- acarbose
- accu-chek comfort curve (glucose) hi/lo control soln
- accu-chek comfort curve (glucose) hi/med/lo control soln
- accu-chek comfort curve-h (glucose) hi/lo control soln
- accu-chek instant plus (cholesterol) test strip
- ace inhibitors
- acebutolol
- acebutolol hydrochloride
- acemannan
- acenocoumarol
- acetamide mea

Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve;jsessionid=855AED39CD6D045141F60A931FBCF51C?id=home.welcome Go Links

PharmGKB

The Pharmacogenetics and Pharmacogenomics Knowledge Base

Search PharmGKB: go

Home | Search | Submit | Resources | Help | Research Network | About Us

Welcome | Projects | Events | Overview | Newsletter | Advisory | Policies | Sign In | Register

Search the PharmGKB:

Search PharmGKB

(eg. "TPMT" or "codeine" or "leukemia")

PharmGKB is an integrated resource about how variation in human genes leads to variation in our response to drugs. Genomic data, molecular and cellular phenotype data, and clinical phenotype data are accepted from the scientific community at large. These data are then organized and the relationships between genes and drugs are then categorized into the following categories:

phenotype
- [CO] Clinical Outcome
- [PD] Pharmacodynamics & Drug Responses
- [PK] Pharmacokinetics
- [FA] Molecular & Cellular Functional Assays

- [Gn] Genotype

Categories of Pharmacogenetic Knowledge

In Memoriam:
Ira Herskowitz
(1946-2003)

A devoted and talented colleague and champion of pharmacogenetics.

Look For:
- All Genes
- Genes with Primary Data
- Genes with Variant Data
- All Drugs
- Drugs with Primary Data
- All Diseases
- All Pathways
- Submissions By Project
- Users with Submissions

Feedback | Sitemap | Privacy Policy | Usage Conditions | Sign In

The Pharmacogenetics Research Network and Knowledge Base is financially supported by grants from NIGMS, NHLBI, NHGRI, NIEHS, NCI, and NLM within the National Institutes of Health (NIH), U.S. Department of Health Human Services (HHS).

Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve?id=browse.drugs.data Go Links

PharmGKB

The Pharmacogenetics and Pharmacogenomics Knowledge Base

Search PharmGKB: go

Home | Search | Submit | Resources | Help | Research Network | About Us

Search | Browse | dbSNP Surveillance

Browse Drugs With PharmGKB Data

- epirubicin
- etoposide
- flavopiridol
- mercaptopurine
- methotrexate
- midazolam
- nifedipine
- rifampin
- tamoxifen
- topoisomerase ii inhibitors
- troleandomycin
- xenobiotics

[Back to Top]

Feedback | Sitemap | Privacy Policy | Usage Conditions Sign In

The Pharmacogenetics Research Network and Knowledge Base is financially supported by grants from NIGMS, NHLBI, NHGRI, NIEHS, NCI, and NLM within the National Institutes of Health (NIH), U.S. Department of Health Human Services (HHS).

Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve?objId=PA449552&objCls=Drug Go Links

PharmGKB

The Pharmacogenetics and Pharmacogenomics Knowledge Base

Search PharmGKB: go

Home | Search | Submit | Resources | Help | Research Network | About Us

Search | Browse | dbSNP Surveillance

etoposide

Generic Names: None

Trade Names: Etoposide; Toposar; Vepesid

PharmGKB Accession ID: PA449552

Cross-References

Search PubMed

Search Medline Plus

PharmGKB Primary Data

Phenotype Data Sets: 1 phenotype data set submitted

Related Genes

Relationship View Details

Unknown

Related Diseases

Relationship View Details

Unknown

Details

Ingredients: Etoposide

Mechanism Of Action: Nucleic Acid Synthesis Inhibitors

http://www.pharmgkb.org/do/serve Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve?objId=PA449552&objCls=Drug Go Links

PharmGKB Primary Data

Phenotype Data Sets: 1 phenotype data set submitted

Search PubMed
Search Medline Plus

Related Genes

Relationship View Details

Unknown

Related Diseases

Relationship View Details

Unknown

Details

Ingredients:	Etoposide
Mechanism Of Action:	Nucleic Acid Synthesis Inhibitors
Pharmacological Effects:	Antineoplastic Activity, Phytogenic
Conditions Treated:	Head and Neck Neoplasms, Histiocytosis, Histiocytosis, Langerhans-Cell, Kidney Neoplasms, Neoplasms, Germ Cell and Embryonal, Pancreatic Neoplasms, Sarcoma, Kaposi, Uterine Neoplasms

Feedback | Sitemap | Privacy Policy | Usage Conditions Sign In

PGRN

The Pharmacogenetics Research Network and Knowledge Base is financially supported by grants from NIGMS, NHLBI, NHGRI, NIEHS, NCI, and NLM within the National Institutes of Health (NIH), U.S. Department of Health Human Services (HHS). PharmGKB is managed at Stanford University. This work is supported by the NIH/NIGMS Pharmacogenetics Research Network and Database (U01GM61374). ©2001-2003 PharmGKB.

Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve?objId=PA126753360&objCls=PhenotypeDataset Go Links

PharmGKB

The Pharmacogenetics and Pharmacogenomics Knowledge Base

Search PharmGKB: go

Home | Search | Submit | Resources | Help | Research Network | About Us

Search | Browse | dbSNP Surveillance

Phenotype Data Set PA126753360

Details

Genes: ABCB1, CYP3A4, CYP3A5, GSTP1, UGT1A1, VDR

Drugs: etoposide

Diseases: ALL (acute lymphoblastic leukemia)

Phenotype Data File: PA126753360

Group	PAAR-SJCRH (Pharmacogenetics of Anticancer Agents)
Investigator	Mary Relling, PharmD
Reference	NA
Description	Study of etoposide (vp16) and its metabolite, catechol. PK parameters are exactly as described in: Relling MV, Yanishevski Y, Nemec J, Evans WE, Boyett JM, Behm FG, Pui C-H. Etoposide and antimetabolite pharmacology in patients who develop secondary acute myeloid leukemia. Leukemia 12:346-352, 1998 (PMID: 9529129) and Panetta JC, Wilkinson M, Pui C-H, Relling MV. Limited and optimal sampling strategies for etoposide and etoposide catechol in children with leukemia. J Pharmacokinet Pharmacodyn 29:171-188, 2002. (PMID: 12361214)

Sample demographic information column headings are coloured grey, phenotypic information column headings

Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve?objId=PA126753360&objCls=PhenotypeDataset Go Links

Sample demographic information column headings are coloured grey, phenotypic information column headings are coloured green, genotypic information column headings are coloured yellow, background information column headings are coloured purple.

Column heading descriptions	
PharmGKB ID	Sample ID numbers in the PharmGKB. A search can be performed to find genotype information on samples using these ID numbers.
Vol vp16 (l/m^2)	Volume of distribution (Vc) for etoposide (vp16).
Kcp (1/hr)	Intercompartmental rate constant, central to peripheral.
Kpc (1/hr)	Intercompartmental rate constant, peripheral to central.
Ke total (1/hr)	Elimination rate constant.
K vp16 cat (1/hr)	Rate constant for conversion of etoposide (vp16) to catechol.
Ke cat (1/hr)	Elimination rate constant for catechol.
AUC vp16 (uM.hr/L)	Area under the curve for etoposide (vp16).
AUC cat (uM.hr/L)	Area under the curve for catechol.
Clearance vp16 (ml/min/m^2)	Clearance of etoposide (vp16).
vp/cat ratio	The ratio of etoposide (vp16) to catechol AUCs.
IV Duration time (hr)	Duration of the etoposide (vp16) IV infusion.
Dose rate (mg/hr)	Etoposide (vp16) unnormalized dose in mg/hour.
Dose (mg/m^2)	Dose of etoposide (vp16) (mg/m^2).
Time	Time point in therapy (Day 29 induction, week 19, and week 54 of continuation, see References+Dose rate (mg/hr) above for protocol details) at which measurements were taken.

Keywords: etoposide, catechol, pharmacokinetics, children, acute lymphoblastic leukemia

Disclaimer: Patients and doctors should NOT make treatment decisions based on the information in the PharmGKB as it is purely a research resource. Questions about the data should be directed to Mary Relling, PharmD.

Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve?objId=PA126753360&objCls=PhenotypeDataset Go Links

Keywords: etoposide, catechol, pharmacokinetics, children, acute lymphoblastic leukemia

Disclaimer: Patients and doctors should NOT make treatment decisions based on the information in the PharmGKB as it is purely a research resource. Questions about the data should be directed to Mary Relling, PharmD.

Download the original file.

PharmGKB ID	Vol vp16 (l/m^2)	Kcp (1/hr)	Kpc (1/hr)	Ke total (1/hr)	K vp16 cat (1/hr)	Ke cat (1/hr)	AUC vp16 (uM.hr/L)	AUC cat (uM.hr/L)	Clearance vp16 (ml/min/m^2)	vp/cat ratio	IV Duration time (hr)	Doses rate (mg/hr)	Dose (mg/m^2)	Time
PA126745689	9.93	0.0206	0.0362	0.3177	0.0069	0.0939	159.17	11.61	52.58	0.0729	2.08	244.65	299.95	day 29
PA126745690	7.36	0.0933	0.0450	0.1105	0.0009	2.4739	573.75	0.22	13.55	0.0004	1.92	257.86	290.96	week 54
PA126745690	8.87	0.0214	0.0353	0.9162	0.1008	2.1917	66.60	3.06	135.41	0.0459	2.00	254.84	300.00	day 29
PA126745695	9.00	0.0393	0.0358	0.4154	0.0163	1.6072	137.43	1.39	62.29	0.0101	2.00	254.84	300.00	day 29
PA126745698	7.97	0.0306	0.0372	0.1634	0.0074	1.1703	386.67	2.43	21.70	0.0063	1.50	343.83	303.57	week 54
PA126745698	13.65	0.0190	0.0356	0.2569	0.0103	1.0341	144.03	1.43	58.46	0.0099	2.17	232.14	296.10	day 29
PA126745699	6.61	0.0201	0.0354	0.2850	0.0394	3.7867	269.06	2.80	31.42	0.0104	1.00	512.41	301.60	week 54
PA126745699	8.82	0.0478	0.0390	0.1761	0.0078	0.7108	318.88	3.50	25.89	0.0110	1.92	262.93	296.68	week 19
PA126745699	9.81	0.0187	0.0356	0.2073	0.0141	1.0172	244.74	3.39	33.90	0.0139	2.25	226.09	299.42	day 29
PA126745704	9.32	0.0550	0.0398	0.2078	0.0106	0.6821	260.00	4.04	32.29	0.0155	2.17	235.24	300.05	week 54
PA126745704	10.01	0.0088	0.0356	0.2769	0.0052	0.0787	180.33	11.78	46.19	0.0653	2.25	223.66	296.20	day 29

Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve?objId=PA646466&objCls=PharmacogeneticRelationship Go Links

PharmGKB

The Pharmacogenetics and Pharmacogenomics Knowledge Base

Search PharmGKB: go

Home | Search | Submit | Resources | Help | Research Network | About Us

Search | Browse | dbSNP Surveillance

Pharmacogenetic Relationship PA646466

Details

Genes: ABCB1

Drugs: prednisone

Diseases: -

Relationship: [CO] Clinical Outcome
[PD] Pharmacodynamics and Drug Response

Submitted By: Gilbert J Burckart

Confidence Level: Medium

Evidence: PubMed Article (*The MDR1 polymorphisms at exons 21 and 26 predict steroid weaning in pediatric heart transplant patients.*) by HongXia Zheng, Steven Webber, Adriana Zeevi, Erin Schuetz, Jiong Zhang, Jatinder Lamba, Pamela Bowman, Gilbert J Burckart

Abstract: Various polymorphisms of the MDR1 gene that encodes for P-glycoprotein (P-gp), a transmembrane pump, have been identified. A silent mutation C3435T in exon 26 and a G2677T mutation in exon 21 have been correlated with P-gp expression and function in humans. The objectives of this study were (a) to determine whether the MDR1 exon 21 and exon 26 polymorphisms were related to steroid weaning

Done Internet

Entrez-PubMed - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites Media

Address http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12175731&dopt=Abstract Go

NCBI

PubMed

National Library of Medicine NLM

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

Search PubMed for Go Clear

Limits Preview/Index History Clipboard Details

About Entrez

Text Version

Entrez PubMed
Overview
Help | FAQ
Tutorial
New/Noteworthy
E-Utilities

PubMed Services
Journals Database
MeSH Database
Single Citation Matcher
Batch Citation Matcher
Clinical Queries
LinkOut
Cubby

Related Resources
Order Documents
NLM Gateway
TOXNET
Consumer Health
Clinical Alerts
ClinicalTrials.gov
PubMed Central

Privacy Policy

Display Abstract Show: 20 Sort Send to Text

1: Hum Immunol 2002 Sep;63(9):765-70

Related Articles, Links

ELSEVIER SCIENCE
FULL-TEXT ARTICLE

The MDR1 polymorphisms at exons 21 and 26 predict steroid weaning in pediatric heart transplant patients.

Zheng H, Webber S, Zeevi A, Schuetz E, Zhang J, Lamba J, Bowman P, Burckart GJ.

Schools of Pharmacy and Medicine, University of Pittsburgh, Pittsburgh, PA 15261, USA.

Various polymorphisms of the MDR1 gene that encodes for P-glycoprotein (P-gp), a transmembrane pump, have been identified. A silent mutation C3435T in exon 26 and a G2677T mutation in exon 21 have been correlated with P-gp expression and function in humans. The objectives of this study were (a) to determine whether the MDR1 exon 21 and exon 26 polymorphisms were related to steroid weaning in a pediatric heart transplant (HTx) population, and (b) to determine whether an association exist between the MDR1 exon 21 and exon 26 polymorphisms in these patients. Sixty-nine pediatric HTx patients were studied. MDR1 genotyping was determined by polymerase chain reaction amplification, sequencing the DNA, and sequence evaluation using Polyphred software (University of Washington) to identify genotypes. The steroid dose at 1 year post-transplantation was recorded. For steroid weaning at one year post-HTx for MDR1 C3435T, 12 of 18 (67%) patients in the CC genotype were still on prednisone, whereas only 18 of 47 (38%) of the CT/TT group were still receiving prednisone ($p = 0.04$). Similar results were observed for the MDR1 G2677T genotyping and steroid weaning. Forty-three of 46 patients (93.5%) who have MDR1 C3435T allele also have a mutant G2677T allele ($p < 0.001$). We conclude that (a) a significantly larger number of MDR1 3435 CC HTx patients remain on steroids at 1 year after transplantation, and (b) the MDR1 C3435T genotype is associated with the G2677 genotype in pediatric HTx patients.

PMID: 12175731 [PubMed - indexed for MEDLINE]

Internet

Outline

- Overview of PharmGKB
- Selection of drug terminology
- NDF-RT content and structure
- PharmGKB user interface
- Conclusion

Conclusion

- NDF-RT satisfies our requirements
- Additional trade names from Orange Book
- Inheritance hierarchy of concepts with roles and properties
  - Need tool to view (Protégé)
  - Also converted to relational tables
- Will upgrade to new versions

Thank you.

oliver@smi.stanford.edu

Acknowledgements: The Pharmacogenetics Research Network and Knowledge Base is financially supported by grants from NIGMS, NHLBI, NHGRI, NIEHS, NCI, and NLM within the National Institutes of Health (NIH).

NDF-RT in PharmGKB
Two Versions

- File 1: Initial version
  - 85 MB
- File 2: Updated version
  - 95 MB
  - New additions:
    - Codes
    - Ids
    - Search names
    - More classification information

Concept Def

<name>ASPIRIN 325MG TAB [NDC: 00839676409] </name>


```
<conceptDef>
 name>ASPIRIN 325MG TAB [NDC: 00839676409]</name>
<namespace>NDF</namespace>
<primitive/>
<kind>DRUG_KIND</kind>
<definingConcepts>
<concept>ASPIRIN 325MG TAB</concept>
</definingConcepts>
<definingRoles>
</definingRoles>
<properties>
<property>
 <name>NDC</name>
 <value>00839676409</value>
</property>
<property>
 <name>NDF_Trade_Name</name>
 <value>ASPIRIN 325MG TABLET</value>
</property>
<property>
 <name>PackageSize</name>
 <value>250</value>
</property>
<property>
 <name>PackageType</name>
 <value>BOTTLE</value>
</property>
<property>
 <name>Manufacturer</name>
 <value>H L MOORE DRUG</value>
</property>
</properties>
</conceptDef>
```


FILE 1

<namespace>NDF</namespace>

<kind>DRUG_KIND</kind>

<concept>ASPIRIN 325MG TAB</concept>

<name>NDC</name>
<value>00839676409</value>

<name>NDF_Trade_Name</name>
<value>ASPIRIN 325MG TABLET</value>

<name>PackageSize</name>
<value>250</value>

<name>PackageType</name>
<value>BOTTLE</value>

<name>Manufacturer</name>
<value>H L MOORE DRUG</value>

```
<conceptDef>
<name>ASPIRIN 325MG TAB [NDC: 00839676409]</name>
<code>C133144</code>
<id>133145</id>
<namespace>0</namespace>
<primitive/>
<kind>3</kind>
<definingConcepts>
<concept>12797</concept>
</definingConcepts>
<definingRoles>
</definingRoles>
<properties>
<property>
<name>49</name>
<value>ASPIRIN 325MG TABLET</value>
</property>
<property>
<name>55</name>
<value>250</value>
</property>
<property>
<name>75</name>
<value>ASPIRIN 325MG TAB [NDC: 00839676409]</value>
</property>
<property>
<name>57</name>
<value>BOTTLE</value>
</property>
<property>
<name>53</name>
<value>H L MOORE DRUG</value>
</property>
<property>
<name>51</name>
<value>00839676409</value>
</property>
</properties>
</conceptDef>
```


FILE 2


```
<namespace>0</namespace>
<code>C133144</code>
<id>133145</id>
<kind>3</kind>
<name>49</name>
<value>ASPIRIN 325MG TABLET</value>
<name>55</name>
<value>250</value>
<name>57</name>
<value>BOTTLE</value>
<name>53</name>
<value>H L MOORE DRUG</value>
<name>51</name>
<value>00839676409</value>
```

Processing to Reveal Contents

1. Definitions
2. ID and name for decoding
3. Kinds
4. Cardinality

6 “Kind” Definitions

- DRUG_KIND
- INGREDIENT_KIND
- FUNCTION_KIND
- PHARMACOKINETICS_KIND
- DISEASE_KIND
- HL7_DOSE_FORM_KIND

6 "Role" Definitions

DRUG	may_treat	DISEASE
DRUG	has_Ingredient	INGREDIENT
DRUG	has_MoA *	FUNCTION
DRUG	has_PE *	FUNCTION
DRUG	has_PK *	PHARMACOKINETICS
DRUG	has_DoseForm	HL7_DOSE_FORM

Legend: *has_MoA = has Mechanism of Action
*has_PE = has Physiologic Effect
*has_PK = has Pharmacokinetics

25 "Property" Definitions

- NDF_Strength
- NDF_Units
- SNF_Strength
- SNF_Units
- SNF_SCDC
- NDF_Dose_Form
- NDF_ROA
- VA_Class
- VA_Class_Name
- NDF_Print_Name
- SNF_SCD
- NDF_Trade_Name
- NDC

- Manufacturer
- PackageSize
- PackageType
- MeSH_UI
- Synonym
- Included_MeSH_UIs
- UMLS_CUI
- MeSH_Definition
- Status
- Last_Revised
- Comment
- Search_Name

123,341 "Concept" Definitions (Examples)

Diseases or Manifestations (DISEASE_KIND)
Infectious Diseases (DISEASE_KIND)
Absorption (PHARMACOKINETICS_KIND)
Cytochromes (PHARMACOKINETICS_KIND)
Immunological Activity (FUNCTION_KIND)
Analgesics, Opioid (FUNCTION_KIND)
ALBUMIN PREPARATION (DRUG_KIND)
ALBUMIN (INGREDIENT_KIND)
ORTHO-NOVUM 1/35 TAB,21 (DRUG_KIND)
ETHINYL ESTRADIOL (DRUG_KIND)
PREDNISONE 5MG TAB [NDC: 00615053621] (DRUG_KIND)
PREDNISONE 5MG TAB [NDC: 00677011701] (DRUG_KIND)

Processing to Reveal Contents

1. Definitions
2. ID and name for decoding
3. Kinds
4. Cardinality

Current time: Sun Apr 21 10:42:49 2002
Perl script: extractIDName.pl
Input file: apelon2.xml
Output file: outputIDName.txt

ID	NAME
3	DRUG_KIND
5	INGREDIENT_KIND
7	FUNCTION_KIND
9	PHARMACOKINETICS_KIND
11	DISEASE_KIND
13	HL7_DOSE_FORM_KIND
15	has_Ingredient
17	has_MoA
19	has_PE
21	has_PK
23	may_treat
25	has_DoseForm
27	NDF_Strength
29	NDF_Units
31	SNF_Strength

Processing to Reveal Contents

1. Definitions
2. ID and name for decoding
3. Kinds
4. Cardinality

Current time: Wed Apr 24 17:46:27 2002
Perl script: countEachKind.decode.pl
Input file: apelon2.xml
Output file: outputCountEachKind.decode.txt

There are 58 occurrences of PHARMACOKINETICS_KIND.
There are 3997 occurrences of DISEASE_KIND.
There are 113971 occurrences of DRUG_KIND.
There are 154 occurrences of HL7_DOSE_FORM_KIND.
There are 4759 occurrences of INGREDIENT_KIND.
There are 402 occurrences of FUNCTION_KIND.

Total number of concepts = 123341
Sum of occurrences of each kind = 123341

Processing to Reveal Contents

1. Definitions
2. ID and name for decoding
3. Kinds
4. Cardinality

Cardinalities of Roles

may_treat	10
has_Ingredient	4
has_MoA	4
has_PE	9
has_PK	0
has_DoseForm	1

Cardinalities of Properties (Part 1 of 2)

NDF_Strength	1
NDF_Units	1
SNF_Strength	2
SNF_SCDC	2
NDF_Dose_Form	4
NDF_ROA	11
VA_Class	6
VA_Class_Name	3
NDF_Print_Name	1
SNF_SCD	2
NDF_Trade_Name	3
NDC	2

Cardinalities of Properties (Part 2 of 2)

Manufacturer	2
PackageSize	2
PackageType	2
MeSH_UI	2
Synonym	3
Included_MeSH_UIs	1
UMLS_CUI	1
MeSH_Definition	2
Status	1
Last_Revised	0
Comment	0
Search_Name	?

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve?objId=PA267&objCls=Gene Go Links

PharmGKB

The Pharmacogenetics and Pharmacogenomics Knowledge Base

Search PharmGKB: go

Home | Search | Submit | Resources | Help | Research Network | About Us

Search | Browse | dbSNP Surveillance

ABCB1

ATP-binding cassette, sub-family B (MDR/TAP), member 1

Alternate Names: P glycoprotein 1/multiple drug resistance 1; P-glycoprotein-1/multiple drug resistance-1; multidrug resistance 1

Alternate Symbols: ABC20; GP170; MDR1; P-GP; PGY1

PharmGKB Primary Data

Phenotype Data Sets: 1 phenotype data set submitted

Reference Sequences: None submitted

Variant Positions: None submitted

Related Drugs	Relationship	View Details
arsenite	[PD] [Gn]	[View Details]
colchicine	[FA]	[View Details]
digoxin	[CO] [PD] [PK] [FA] [Gn]	[View Details]
efavirenz	[PK]	[View Details]
nortriptyline	[PD]	[View Details]

PharmGKB Accession ID: PA267

Cross-References

Ensembl ID: ABCB1

GenAtlas ID: ABCB1

GenBank ID: AF016535

GenBank ID: M14758

GeneCard ID: ABCB1

LocusLink ID: 5243

MutDB: ABCB1

Internet

PharmGKB: The Pharmacogenetics and Pharmacogenomics Knowledge Base - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites History

Address http://www.pharmgkb.org/do/serve?objId=PA267&objCls=Gene Go Links

Related Drugs	Relationship	View Details
arsenite	[PD] [Gn]	[View Details]
colchicine	[FA]	[View Details]
digoxin	[CO] [PD] [PK] [FA] [Gn]	[View Details]
efavirenz	[PK]	[View Details]
nortriptyline	[PD]	[View Details]
prednisone	[CO] [PD]	[View Details]
tacrolimus	[FA]	[View Details]
vincristine	[FA]	[View Details]
xenobiotics	[FA] [Gn]	[View Details]

Related Diseases	Relationship	View Details
HIV	[PK]	[View Details]
liver transplantation	[FA]	[View Details]
major depression	[PD]	[View Details]

Details

Cytogenetic Location: 7q21.1

OMIM Phenotype: Colchicine resistance

Product Name: ATP-binding cassette, sub-family B (MDR/TAP), member 1

GenBank ID: M14758

GeneCard ID: ABCB1

LocusLink ID: 5243

MutDB: ABCB1

OMIM Accession: 171050

Ref Seq NM Accession: NM_000927

Ref Seq NP Accession: NP_000918

SOURCE ID: ABCB1

UCSC Genome Browser ID: NM_000927

Internet