# DRAGON DATABASE OF GENES ASSOCIATED WITH PROSTATE CANCER (DDPC)

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# **RELEVEANCE OF DATA SHARING!**

Fragmented data on prostate cancer (PC) embedded in published biomedical literature

And the need to provide formatted data with biological relevance for generation of potential hypothesis

Our Prostate Cancer Knowledgebase can assist biologist to circumvent the large amount of energy and time spent in analyzing pertinent biological problems involving PC

### **HOME PAGE**

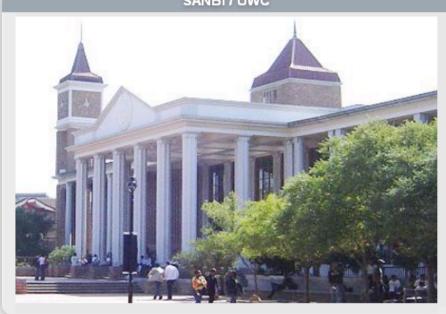


#### Dragon Database of Genes Implicated in Prostate Cancer

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#### SANBI / UWC



#### DDPC

Expert reviewed information summary about the genes implicated in prostate cancer, including comprehensive information about every specific gene.

A centralized resource for researchers to support functional characterization and analysis of molecular processes related to prostate cancer.

#### Please cite

DDPC: Dragon Database of Genes associated with Prostate Cancer

Monique Maqungo; Mandeep Kaur; Samuel K. Kwofie; Aleksandar Radovanovic; Ulf Schaefer; Sebastian Schmeier; Ekow Oppon; Alan Christoffels; Vladimir B. Bajic

Nucleic Acids Research 2010; doi: 10.1093/nar /qkq849

Start exploring...

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Acessibility: <a href="http://apps.sanbi.ac.za/ddpc/">http://apps.sanbi.ac.za/ddpc/</a> or <a href="http://cbrc.kaust.edu.sa/ddpc/">http://cbrc.kaust.edu.sa/ddpc/</a>

Nucleic Acid Research, Maqungo et al., 2010

# DRAGON DATABASE OF GENES ASSOCIATED WITH PC What is DDPC? (DDPC)

• An integrated knowledge database that has been developed to provide researchers with a multitude of information related to PC and PC-related genes, with the aim to support research of PC at a molecular level

# Why DDPC was created?

• To provide students, researchers and medical practitioners with enriched information on genes involved in PC

# What are the benefits of using DDPC?

• DDPC provides gene-associated data such as protein annotation, molecular pathways, ontologies and transcription regulation

# What is unique about DDPC?

- To the best of our knowledge there is no single comprehensive, web based resource that has integrated data solely on genes experimentally verified to be involved in PC
- It contains information on pre-compiled literature based text-mining report, transcription factor binding sites, drug and drug targets, and molecular pathways

#### **DESCRIPTION OF DDPC**

# Architecture is based on three-layer structure

- Presentation layer online graphical user interface developed using DHTML and JavaScript
- Logic layer comprises server side PHP and Perl modules
- Data layer MySQL data layer (relational database)

# **Data Mining**

- Perl script extracted data from Entrez Gene
- Retrieved 973 genes using query strings 'PC-related terms' and human(orgn)
- We manually curated the literature experimental evidence such as western blot, RT-PCR, immunohistochemistry, tissue microarray etc.
- 704 genes were verified to associated with PC
- Additional information PSA level, Gleason score
- Biological database such as GeneCards, HUGO, Entrez Gene

# **DrugBank data**

- List of drugs with potential effect on PC
- Absorption, distribution, metabolism, excretion and toxicity (ADMET) descriptors, metabolizing enzymes, drug targets, coordinate files for proteins and small drug molecules
- Links to other drug database RxList, KEGG drug and compound,
   PharmGKB and PubChem compound and substance

#### **DESCRIPTION OF DDPC**

# **Transcription Regulation**

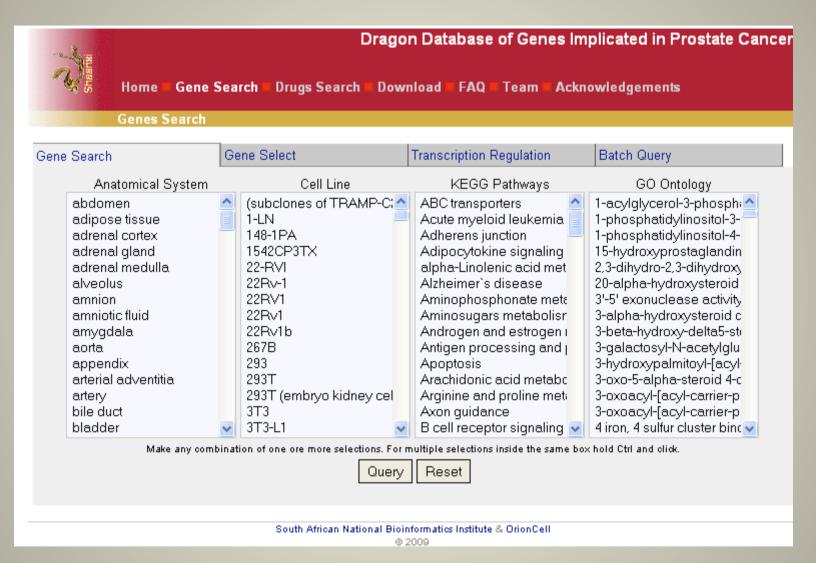
- DDPC provides information on regulatory potential of PC genes and associated regulatory networks
- Information on genes' promoters and putative transcription factor binding sites (TFBSs)
- Extracted 1766 promoters each covering region [-1000, +200] relative transcription start site of PC gene FANTOM 3 promoter set based on CAGE libraries
- Mammalian matrix models in TRANSFAC Professional ver. 11.4 used map TFBSs to both strands of each promoter
- To decrease the incidence of false-positive TFBSs predictions Match<sup>™</sup> program with a profile for score thresholds that aims to minimize false positives
- All mammalian transcription factors (TFs) known to be associated with TRANSFAC position weight matrices were used to obtain information on binding of TFs to promoters of PC genes
- A total 689 mammalian TFs with unique ID were extracted from TRANSFAC as associated with our TFBS
- Information on predicted TFBS, the associated TFs and genes they potentially control which can be mined in DDPC

# **DESCRIPTION OF DDPC**

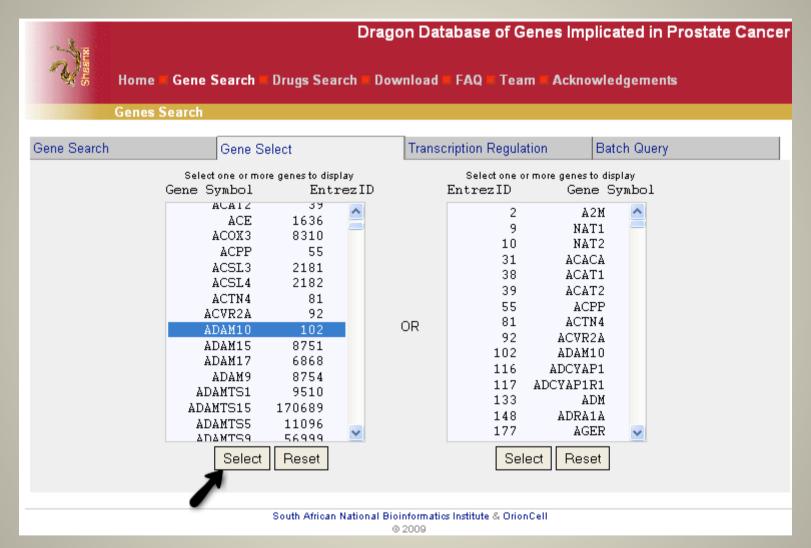
# **Text-mining Information**

- Pre-compiled list of text-mined information from PubMed records has been integrated into DDPC
- An overview on potential gene interactions/associations and pathways
- To generate a pre-compiled result, PubMed database was queried using PC keywords of each of the PC gene 'A26C3' OR 'POTE22' AND mammal AND 'cancer'
- List of 558 347 abstracts was obtained from PubMed and queried results were analyzed using Dragon Exploration System (DES)
- Text-mining dictionaries used by DES in this process were 'metabolites and enzymes', 'genes and proteins', and 'chemical with pharmacological effects'
- Text-mining results are shown as list of tables and graphical representations of interactive networks of genes of interest with other essential biological receptors and pathways

#### **GENE SEARCH**



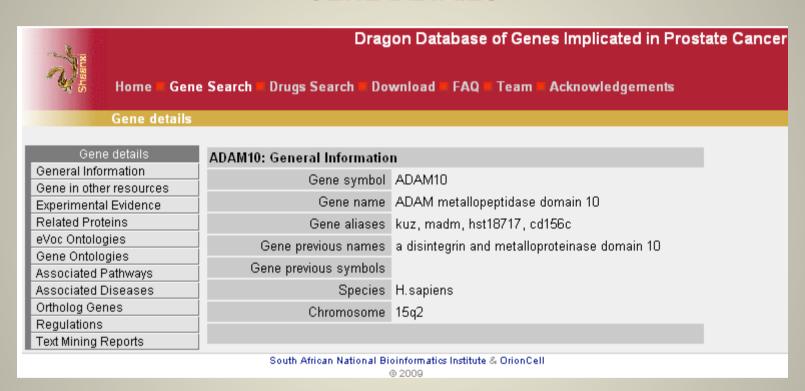
#### **GENE SELECT**



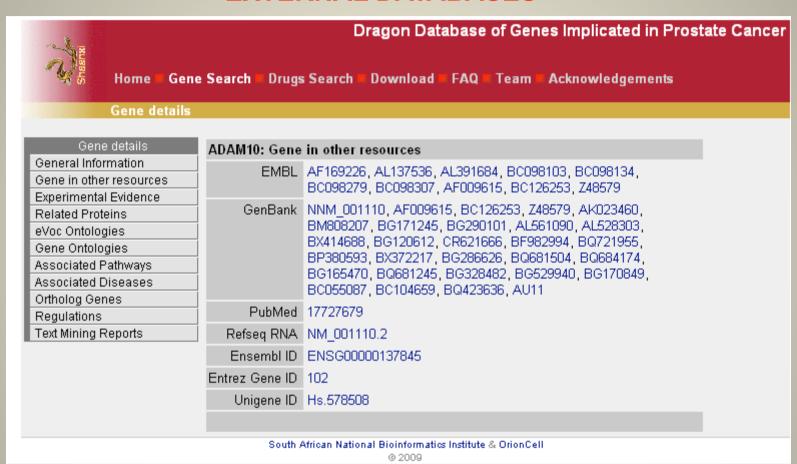
#### **LIST OF GENES**



# **GENE DETAILS**



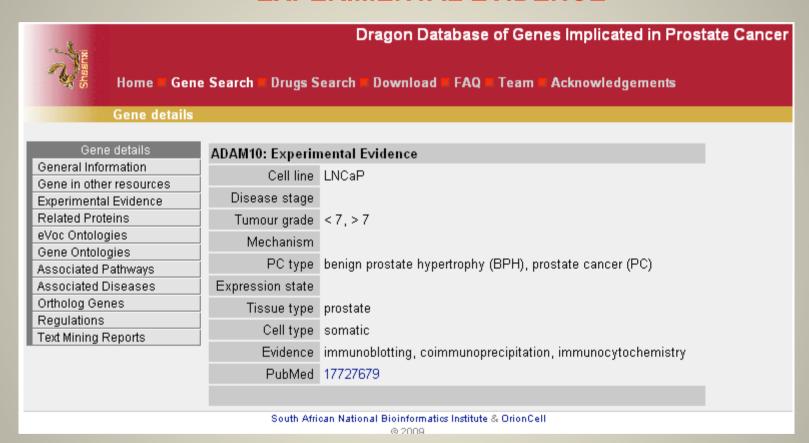
#### **EXTERNAL DATABASES**



# **EXTERNAL DATABASES**



# **EXPERIMENTAL EVIDENCE**



#### **EXTERNAL DATABASES**



# TRANSCRIPTION REGULATION

Dragon Database of Genes Implicated in Prostate Cancer

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Gene details

Gene details
General Information
Gene in other resources
Experimental Evidence
Related Proteins
eVoc Ontologies
Gene Ontologies
Associated Pathways
Associated Diseases
Ortholog Genes
Regulations
Text Mining Reports

ADAM10: Transcription Regulation						
TF ID 🔻	TF Symbol	EntrezID	UniprotID			
T00017	C/EBPbeta(p35)	12608	P28033			
T00018	AhR	11622	P30561			
T00019	AhR	25690	P41738			
T00033	AP-2alpha	21418	P34056			
T00035	AP-2alphaA	7020	P05549			
T00036	AP-4	7023	Q01664			
T00045	COUP-TF2	7026	P24468			
T00052	ATF-a	11016	P17544			
T00053	ATFa-isoform1	11016	P17544			
T00070	Pax-5	5079	Q02548			
T00100	CDP	1523	P39880-1			
T00104	C/EBPalpha	12606	P53566			
T00105	C/EBPalpha	1050	P49715			
T00107	C/EBPalpha	427549				
T00108	C/EBPalpha	24252	P05554			
T00109	C/EBPdelta	25695	Q03484			
T00111	c-Ets-1	23871	P27577			
T00112	c-Ets-1	2113	P14921			
T00113	c-Ets-2	2114	P15036			
T00114	c-Ets-1 54		P13474			
T00115	c-Ets-1 68	396235	P15062			
T00116	c-Ets-2 58-64		P10157			
T00122	c-Fos	14281	P01101			
T00123	c-Fos	2353	P01100			
T00124	c-Fos	314322	P12841			
T00125	c-Fos		P11939			
T00128	HOXA4		P17277			

#### **TEXT MINING REPORTS**

Human Genes+Proteins Metabolites+Enzymes Toxins Chemicals with pharmacological effects

Searching for: ABC2 ATP-BINDING CASSETTE PROTEIN

Abstracts found: 1

Page: 1

1) 11804192

The role of half-transporters in multidrug resistance.

ATP-binding cassette proteins comprise a superfamily of transporter proteins, a subset of which have been implicated in multidrug resistance. Although P-glycoprotein was described over 15 years ago, the recent expansion in the number of transporters identified has prompted renewed interest in the role of drug transporters in clinical drug resistance. These newly identified transporters include additional members of the MRP family, ABC2, and a new half-transporter, MXR/BCRP/ABCP1. This half-transporter confers high levels of resistance to mitoxantrone, anthracyclines, and the camptothecins SN-38 and topotecan. At 72 kDa, MXR localizes to the plasma membrane in cells which highly overexpress the protein either through gene amplification or though gene rearrangement. Future studies will be aimed at identifying an inhibitor, and attempting to translate recognition of this new transporter into a target for anticancer treatment.

Page: 1

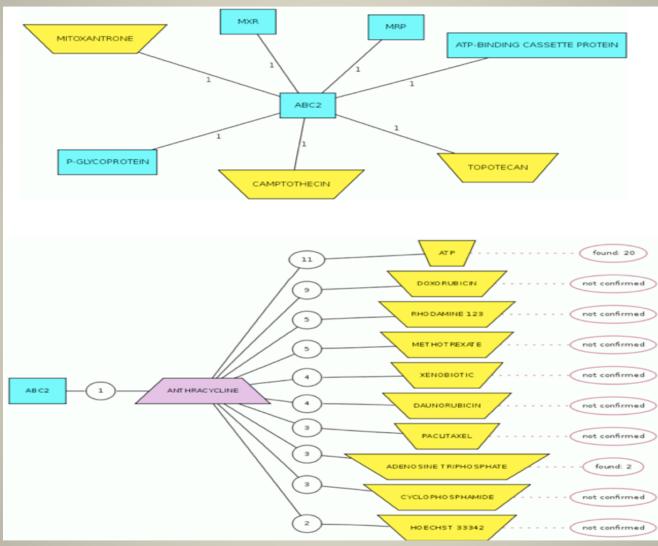
South African National Bioinformatics Institute & OrionCell

⊚ 2009

#### **SUMMARY OF RESULTS**

```
Change dictionary: Metabolites+Enzymes Toxins Chemicals with pharmacological effects
Human Genes+Proteins:
(0123456789ABCDEFGHIJKLMNOPQRSTUVWXYZ
Page: 1234
[ab] [ac] [ad] [ae] [af] [ah] [ak] [al] [am] [an] [ap] [aq] [ar] [at]
Α
ABC2 ->
 ATP-BINDING CASSETTE PROTEIN [1] MRP [1] MXR [1] P-GLYCOPROTEIN [1] CAMPTOTHECIN [1] MITOXANTRONE [1] TOPOTECAN [1]
 ANTHRACYCLINE [1]
 draw network | show hypotheses
ABCA1 ->
 ABCA12 [1] ABCA3 [1] ABCB1 [1] ABCB3 [1] ABCB5 [1] ABCC1 [1] ABCC11 [1] ABCC13 [1] ABCC5 [1] ABC
 [1] ABCF2 [1] ABCG2 [1] BCRP [1] BREAST CANCER RESISTANCE PROTEIN [1] CFTR [1] CYSTIC FIBROSIS
 TRANSMEMBRANE CONDUCTANCE REGULATOR [1] MAL [1] MRP1 [1] MULTIDRUG RESISTANCE-ASSOCIATED
 PROTEIN 1 [1] P-GLYCOPROTEIN [1] P-GP [1] ABC TRANSPORTER [2]
 5-FLUOROURACIL [1] CYCLOPHOSPHAMIDE [1] EPIRUBICIN [1] OLIGONUCLEOTIDE [1] PACLITAXEL [1] ATP [2]
 AIR POLLUTANTS [1] ABC [2]
 draw network | show hypotheses
ABCA12 ->
 ABC TRANSPORTER [1] ABCA1 [1] ABCB1 [1] ABCB3 [1] ABCB6 [1] ABCC1 [1] ABCC11 [1] ABCC13 [1]
 ABCC5 [1] ABCC7 [1] ABCF2 [1] ABCG2 [1]
 5-FLUOROURACIL [1] ATP [1] CYCLOPHOSPHAMIDE [1] EPIRUBICIN [1] OLIGONUCLEOTIDE [1] PACLITAXEL [1
 ABC [1]
 draw network | show hypotheses
```

# **DRAW NETWORK**



# **DRUG SEARCH**



Home



#### DDPC

Expert reviewed information summary about the genes implicated in prostate cancer, including comprehensive information about every specific gene.

A centralized resource for researchers to support functional characterization and analysis of molecular processes related to prostate cancer.

Start exploring...

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@ 2009

# **LIST OF DRUGS**

Home Home	Dragon Database of Genes Implicated in Prostate Cance  Gene Search Drugs Search Download FAQ Team Acknowledgements			
Drugs Search				
1. Abarelix	For palliative treatment of advanced prostate cancer.			
Alfuzosin     Aminoglutethimide	For the treatment of the signs and symptoms of benign prostatic hyperplasia.  For the suppression of adrenal function in selected patients with Cushing's syndrome, malignant neoplasm of the female breast, and carcinoma in situ of the breast.			
Bicalutamide     Capromab	For treatment (together with surgery or LHRH analogue) of advanced prostatic cancer.  For diagnosis of prostate cancer and detection of intra-pelvic metastases			
6. Cephalexin	For the treatment of respiratory tract infections caused by Streptococcus pneumoniae and Streptococcus pyogenes; otitis media due to Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Streptococcus pyogenes, and Moraxella catarrhalis; skin and skin structure infections caused by Staphylococcus aureus and/or Streptococcus pyogenes; bone infections caused by Staphylococcus aureus and/or Proteus mirabilis; genitourinary tract infections, including acute prostatitis, caused by Escherichia coli, Proteus mirabilis, and Klebsiella pneumoniae.			
7. Chlorotrianisene	Used to treat symptoms of menopause, deficiencies in ovary function (including underdevelopment of female sexual characteristics and some types of infertility), and in rare cases, prostate cancer. Chlorotrianisene may also be used to prevent breast engorgement following childbirth.			
8. Ciprofloxacin	For the treatment of the following infections caused by susceptible organisms: urinary tract infections, acute uncomplicated cystitis, chronic bacterial prostatitis, lower respiratory tract infections, acute sinusitis, skin and skin structure infections, bone and joint infections, complicated intra-abdominal infections (used in combination with metronidazole), infectious diarrhea, typhoid fever (enteric fever), uncomplicated cervical and urethral gonorrhea, and inhalational anthrax (post-exposure).			
9. Conjugated Estroger	For the treatment of moderate to severe vasomotor symptoms associated with the menopause, atrophic vaginitis, osteoporosis, hypoestrogenism due to hypogonadism, castration, primary ovarian failure, breast cancer (for palliation only), and Advanced androge dependent carcinoma of the prostate (for palliation only)			

# **DRUG INFORMATION**

	Dragon Database of Genes Implicated in Prostate Cancer		
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	Ноте		
Drug name	Alfuzosin		
Description	Alfuzosin (INN, provided as the hydrochloride salt) is an alpha-adrenergic blocker used to treat benign prostatic hyperplasia (BPH). It works by relaxing the muscles in the prostate and bladder neck, making it easier to urinate. [Wikipedia]		
DrugBank	Primary Accession Number: DB00346		
DIN	02245565		
Туре	Approved, Investigational, Small Molecule		
Indication	For the treatment of the signs and symptoms of benign prostatic hyperplasia.		
Mechanism of Action	Alfuzosin acts by inhibiting the postsynaptic alpha(1)-adrenoceptors on vascular smooth muscle. This inhibits the vasoconstrictor effect of circulating and locally released catecholamines (epinephrine and norepinephrine), resulting in peripheral vasodilation.		
Absorption	Absorption is 50% lower under fasting conditions		
Toxicity	Side effects are dizziness (due to postural hypotension), upper respiratory tract infection, headache, and fatigue.		
Protein Binding	82%-90%		
Interactions	DrugBank: Interaction Insert Showing Interaction Insert for Alfuzosin		
	Drug-Drug Interactions: The pharmacokinetic and pharmacodynamic interactions between UROXATRAL and other alpha-blockers have not been determined. However, interactions may be expected, and UROXATRAL should NOT be used in combination with other alpha-blockers.		
RXList	http://www.rxlist.com/cgi/generic/uroxatral.htm		
KEGG	drug: D01692 / compound: Not Available		
PubChem	compound: 2092 / substance: 682525		
PharmGKB	PA164774795		

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