

The BacMet database as a tool for biocide resistance risk assessment

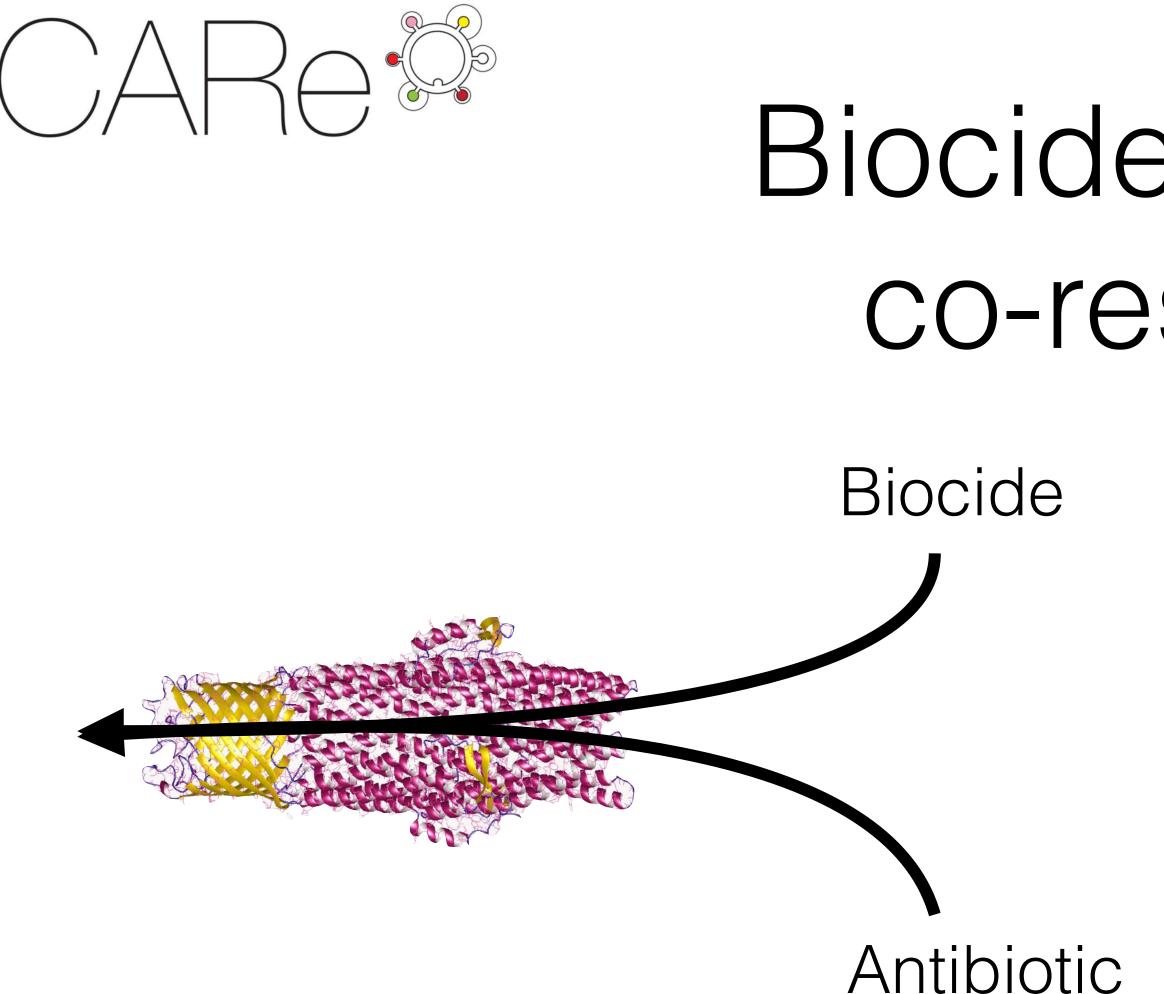
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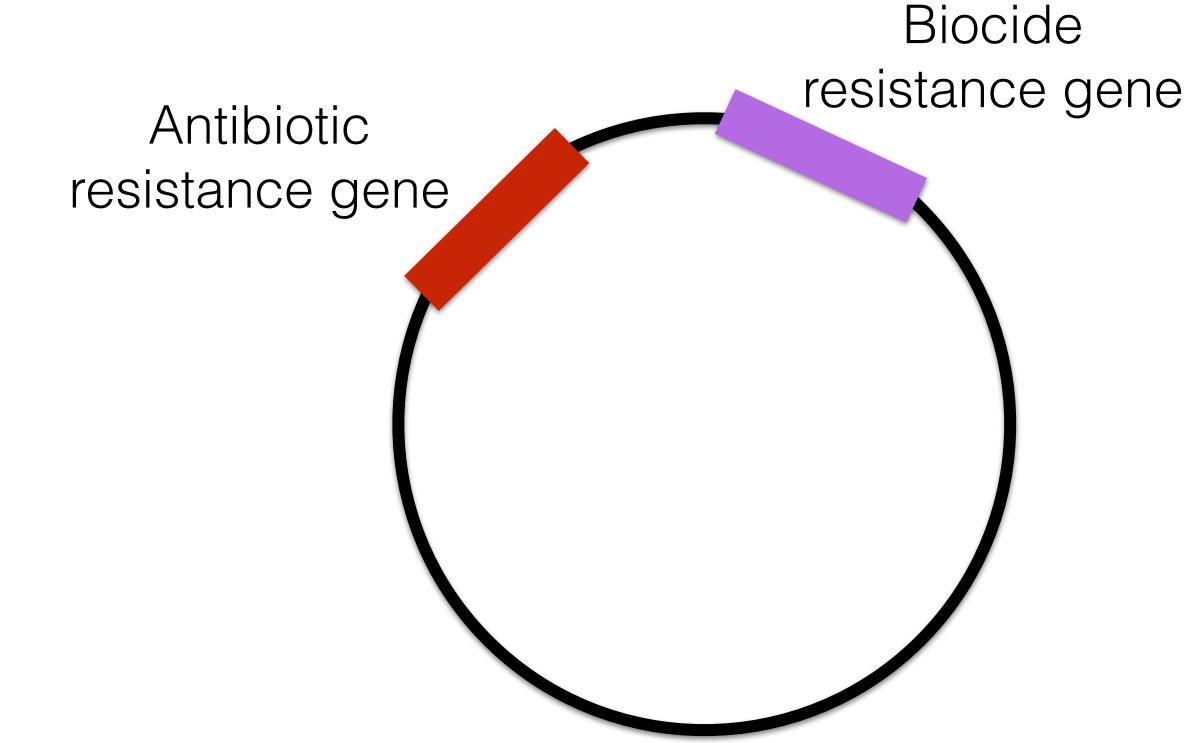
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Biocide-antibiotic co-resistance



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BacMet: antibacterial biocide and metal resistance genes database

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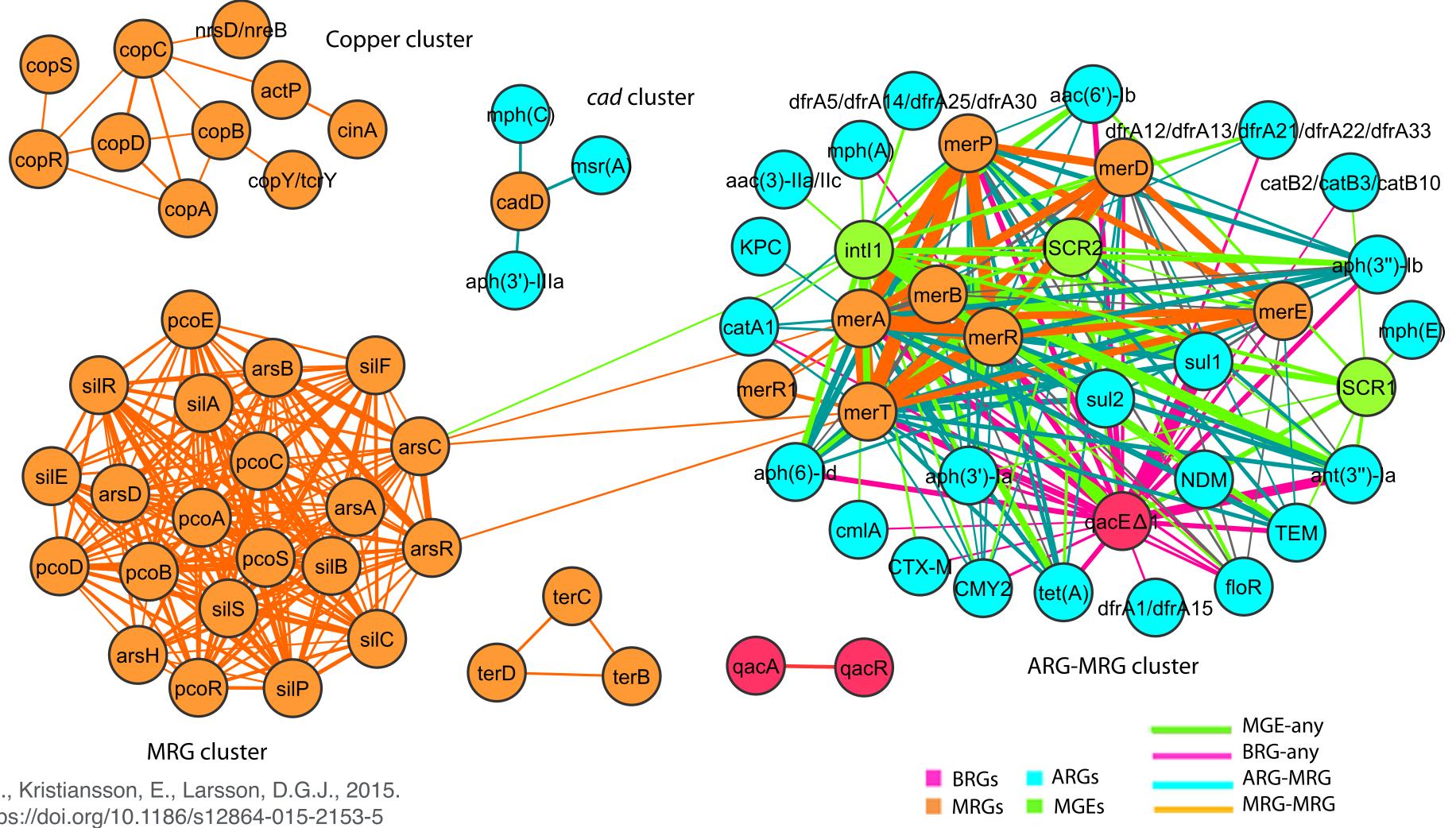








Gene co-occurences



Pal, C., Bengtsson-Palme, J., Kristiansson, E., Larsson, D.G.J., 2015. BMC Genomics 16, 964. https://doi.org/10.1186/s12864-015-2153-5

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BacMet Demo

http://bacmet.biomedicine.gu.se/

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BacMet is an easy-to-use bioinformatics resource of antibacterial biocide- and metal-resistance genes. BacMet consists of two databases:

- A manually curated database of genes with experimentally confirmed resistance function

Database Statistics	(version 2.0)
Last updated: 11 Ma	arch 2018

Predicted Resistance Genes: 155,512

Exp. Confirmed Resistance Genes: 753 Chromosomal-borne: 550 Plasmid/transposon-borne: 203

> Biocide resistance genes: 268 Metal resistance genes: 420 Genes with both biocide- and metalresistance potential: 65

Total Compounds: 111

Chemical classes: 43 Antibacterial biocides: 58 Metals: 23 'Other compounds' : 30

BacMet provides a high quality, manually curated database of bacterial genes that are experimentally confirmed to confer resistance to metals and/or antibacterial biocides, fully referenced to the scientific literature. BacMet also includes a database of predicted resistance genes, as the resistance genes may differ between species and/or occur in different forms that are not (yet) experimentally investigated. The database of predicted genes is generated by sequence similarity searches in public databases, using an uniform cut-off for genes found on plasmids, and individually set cut-offs for chromosomal genes.

BacMet provides tools for identification of biocide and metal-resistance genes in proteins and DNA sequences including full genomes. The genes in the databases can be accessed either through the browsing option, where one can browse genes by the compounds they confer resistance to or by their name. Alternatively one may use the search function to search for any term in the database, including for example gene name, name of biocide or metal and chemical class. Using the advanced search option, one may search specifically for e.g. plasmidborne or chromosomal-borne genes. The entire database can also be downloaded for off-line analysis of larger datasets.

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• A database of predicted resistance genes based on sequence similarity to genes with experimentally confirmed function

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Browsing Experimetal Confirmed database by biocides

Biocide Name	Chemical Class	Resistance Gene(s)
2-nitroimidazole	Imidazole	Click here
Acriflavine	Acridine	Click here
Alexidine	Biguanides	Click here
Benzylkonium Chloride (BAC)	Quaternary Ammonium Compounds (QACs)	Click here
Cetrimide (CTM)	Quaternary Ammonium Compounds (QACs)	Click here
Cetylpyridinium Chloride (CPC)	Quaternary Ammonium Compounds (QACs)	Click here
Chlorhexidine	Biguanides	Click here
Clorine Dioxide (ClO2)	Halogens	Click here
Crystal Violet	Triarylmethane	Click here
Dequalinium chloride	Quaternary Ammonium Compounds (QACs)	Click here
Dibrompropamidine	Diamidine	Click here
Dodine	Acetate	Click here
Diphenyl Ether	<u>Phenyl</u>	Click here
Empigen	Amine betaine	Click here
Ethidium Bromide	Phenanthridine	Click here
Ethylbenzene	Aromatic hydrocarbons	Click here
Ethylmercury chloride	Organo-mercury	Click here
<u>Glycerol</u>	Alcohol	Click here
Hexamidine	Diamidine	Click here
Hydrochloric Acid (HCl)	Acid	Click here
Hydrogen Peroxide (H2O2)	Peroxides	Click here
Linoleic acid	Free Fatty Acids	Click here
<u>m-xylene</u>	Aromatic hydrocarbons	Click here
Methylene Blue	Thiazinium	Click here

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Browsing BacMet compounds

Information of 2-nitroimidazole from BacMet

- **Compound name:** 2-nitroimidazole
- Chemical Class: Imidazole

Description: It is an industrial biocide. It is only effective against anaerobic organisms and it is effective against sulfate-reducing bacteria (SRB) and compatible with other chemicals. Used to prepare nitroimidazole substituted boronic acids as precursors for imaging hypoxic tissue. Also used to prepare potential site-selective radiosensitizers for estrogen receptor-rich tumors.

Database Links: <u>CHEBI:67135</u>

BacMet database and website is designed and maintained by Chandan Pal

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Compound Information





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BacMet – Antibacterial Biocide

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Browsing Experimentally Confirmed database

Gene_name	Experimentally Verified Resistance Gene Information	Predicted Resistance Gene Information
ruvB	 BacMet ID: BAC0293 Code for: Enzyme Family: Malic enzymes family Sequence: FASTA Cross-database IDs: Link Organism: Pseudomonas corrugata 28 Location: Chromosome Compound: Chromium (Cr), Cetylpyridinium Chloride (CPC) [class: Quaternary Ammonium Compounds (QACs)], Dodine [class: Acetate], 2-nitroimidazole [class: imidazole] Description: It is a fragment of ruvB gene product. It is a oxidoreductase from malic enzyme family. Length (amino acid): 379 Reference: Decorosi et al. 2009; Pubmed- 19768364 	Similar resistance genes in BacMet Predicted database

BacMet database and website is designed and maintained by Chandan Pal

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e & Metal	Resistan	ce Gen	es Da	atabase
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Result: Your query found 1 resistance gene(s) from the BacMet Experimentally Confirmed database





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BacMet Predicted Database

Result: Your query found 495 resistance gene(s) from the BacMet Predicted database

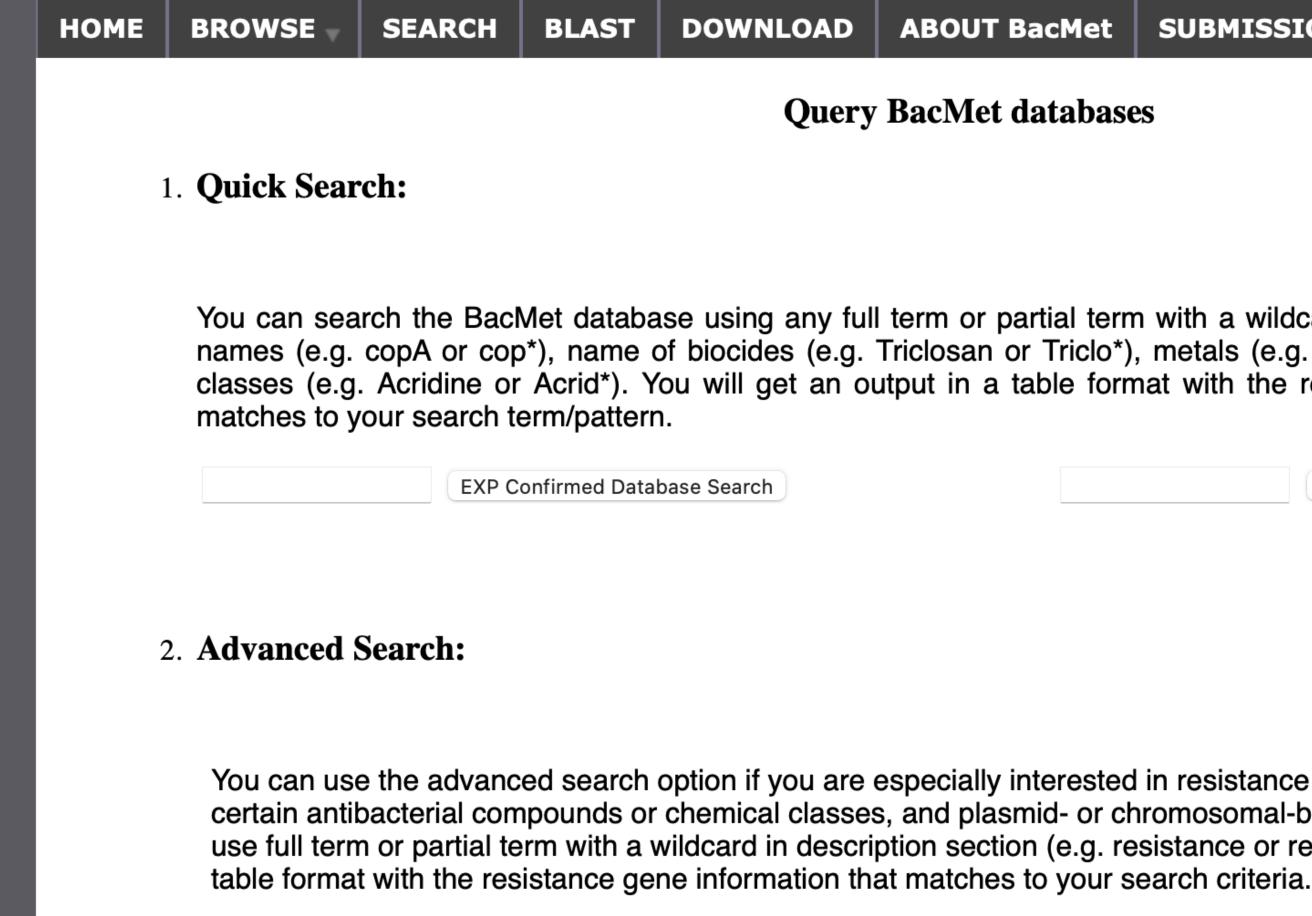
Gene name	GI number	GenBank ID	Sequence	e	Compound	NCBI annotation
ruvB	<u>15596164</u>	NP_249658.1	FASTA	Pseudomonas aeruginosa PAO1	Chromium (Cr), Tellurium (Te), Selenium (Se)	ruvB gene product
ruvB	<u>7443650</u>	PIR: JC5477	FASTA	aeruginosa	(Te), Selenium (Se)	DNA-binding protein ruvB - Pseudomonas aeruginosa
ruvB	<u>1183842</u>	BAA11819.1	FASTA	0	1	Holliday junction specific DNA helicase
ruvB	<u>152988470</u>	YP_001349890.1	FASTA	Pseudomonas aeruginosa PA7	Chromium (Cr), Tellurium (Te), Selenium (Se)	Holliday junction DNA helicase RuvB
ruvB	<u>289674672</u>	ZP_06495562.1	FASTA	Pseudomonas syringae pv. syringae FF5	Chromium (Cr), Tellurium (Te), Selenium (Se)	Holliday junction DNA helicase RuvB
ruvB	<u>28871122</u>	NP_793741.1	FASTA	Pseudomonas syringae pv. tomato str. DC3000	Chromium (Cr), Tellurium (Te), Selenium (Se)	Holliday junction DNA helicase RuvB
ruvB	<u>289626497</u>	ZP_06459451.1	<u>FASTA</u>	Pseudomonas syringae pv. aesculi str. NCPPB 3681	Chromium (Cr), Tellurium (Te), Selenium (Se)	Holliday junction DNA helicase RuvB
ruvB	<u>237800219</u>	ZP_04588680.1		Pseudomonas syringae pv. oryzae str. 1_6	Chromium (Cr), Tellurium (Te), Selenium (Se)	Holliday junction DNA helicase RuvB
ruvB	<u>71736556</u>	YP_275912.1		Pseudomonas syringae pv. phaseolicola 1448A	Chromium (Cr), Tellurium (Te), Selenium (Se)	Holliday junction DNA helicase RuvB
				Pseudomonas	Chromium (Cr) Tellurium	

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Select 'chemical class'/'compound' (resi	istant to): class: Any
Select location: OAny OChromosome	e OPlasmid (for EXP confirmed database only)
Protein description contains text	(e.g. resistance)
Peptide sequence length greater than	50 (for EXP confirmed database only)
Peptide sequence length less than	2000 (for EXP confirmed database only)
Select database: BacMet Predicted of the second s	database <a>o BacMet Experimentally Confirmed database

Query BacMet databases

You can search the BacMet database using any full term or partial term with a wildcard, including for example gene names (e.g. copA or cop*), name of biocides (e.g. Triclosan or Triclo*), metals (e.g. Arsenic or Arsen*) or chemical classes (e.g. Acridine or Acrid*). You will get an output in a table format with the resistance gene information that

Predicted Database Search
Predicted Database Search

You can use the advanced search option if you are especially interested in resistance genes that confer resistance to certain antibacterial compounds or chemical classes, and plasmid- or chromosomal-borne resistance genes. You can use full term or partial term with a wildcard in description section (e.g. resistance or resis*). You will get an output in a



Moving towards a risk assessment tool

Incorporate data on selective concentrations and **co-selection opportunities**

and management

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Make BacMet useful for practical risk assessment







BacMet Update

- Current data will remain and be expanded upon
- **Substance-based** rather than gene-based focus commonly the starting point for risk assessment
- MICs and LOECs for different species, PNECs for resistance selection and HGT
- **New genes** will be added (from literature and this project)
- **Context information** (hosts, mobility potential, co-location with other resistance genes), based on available genome data
- Relative abundance in different environment types

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- Chandan Pal
- Joakim Larsson
- Erik Kristiansson
- Christopher Rensing
- Funding from FORMAS

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Discussion tasks

- Short introduction round (3-4 sentences per person) Who takes the minutes?
- authorization of biocides?
- Proposed structural changes?
- Proposed new categories?
- Proposed links with other relevant databases?

Who would like to present the results?

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http://bacmet.biomedicine.gu.se/

How can the BacMet database support biocide resistance risk assessment during approval/

What needs to be changed to be able to use the BacMet database for the regulatory process?

BacMet currently is a substance-based database. How to incorporate results for products?







