An Introduction to CARD & Biocuration

Brian Alcock

May 26, 2022

A Bit About Me...

- Born and raised in Newfoundland
- McMaster M.Sc. (Biology) - 2013-2015
- McArthur Lab - December 2015

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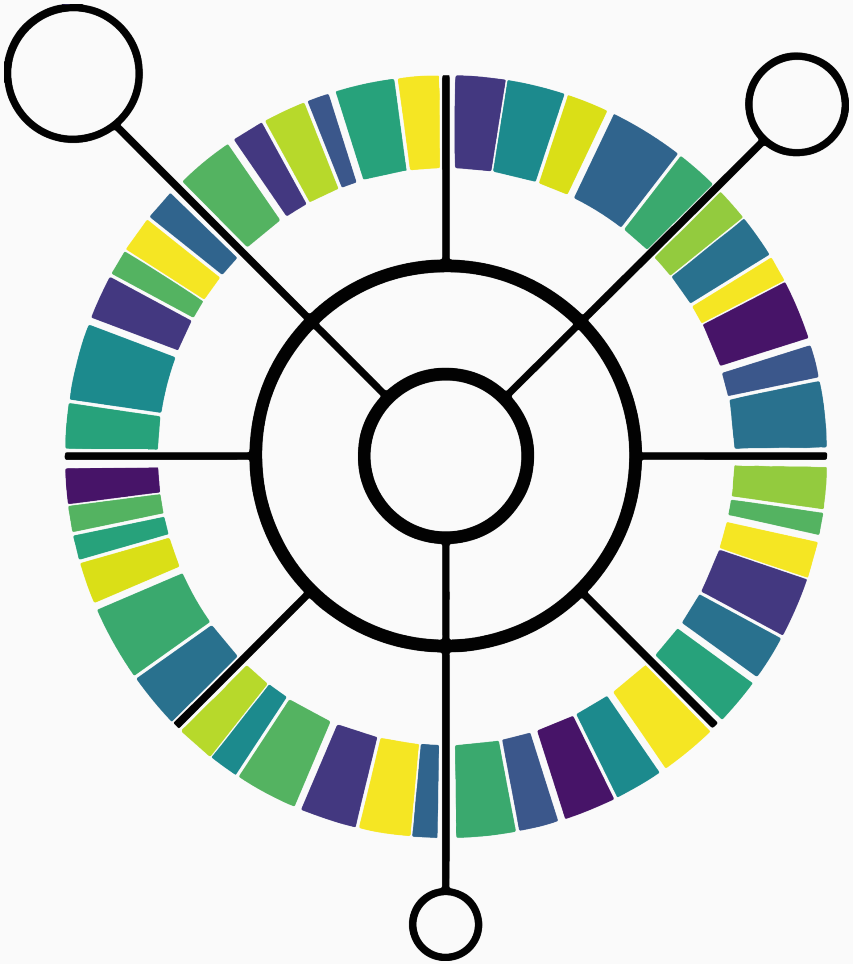
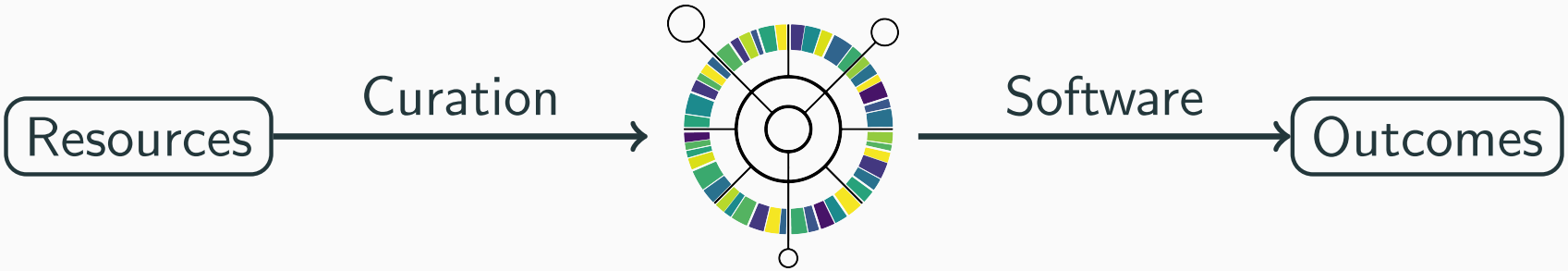
- *No background in CompSci prior to my MSc!*

What We Do



- **The Comprehensive Antibiotic Resistance Database**
- Antimicrobial surveillance and stewardship
- Biocuration and software development
- Data standardization and harmonization

What We Do



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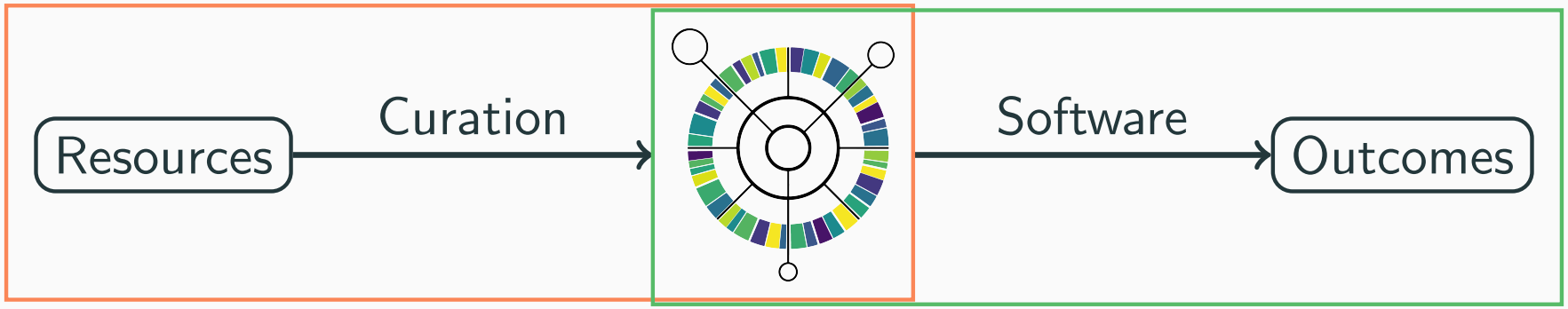

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What is (Bio-)curation?

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What Gets Included?

CARD's Golden Rule: to be included in CARD an AMR determinant must be described in a peer-reviewed scientific publication, with its DNA sequence available in GenBank, including clear experimental evidence of elevated minimum inhibitory concentration (MIC) over controls. (CARD 2020)

(Over time we've added some exceptions but let's not worry about those right now. . .)

How CARD is Structured

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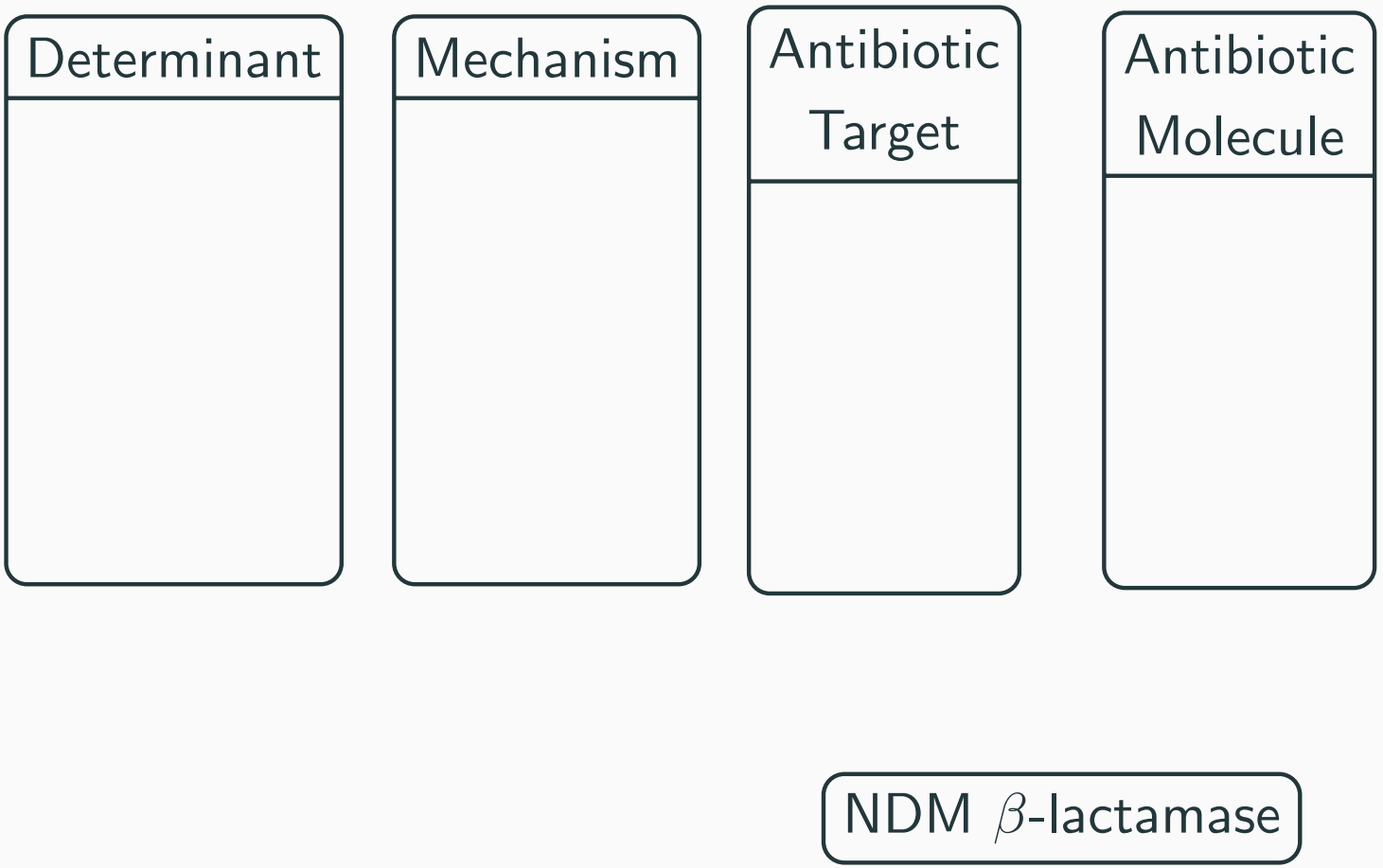

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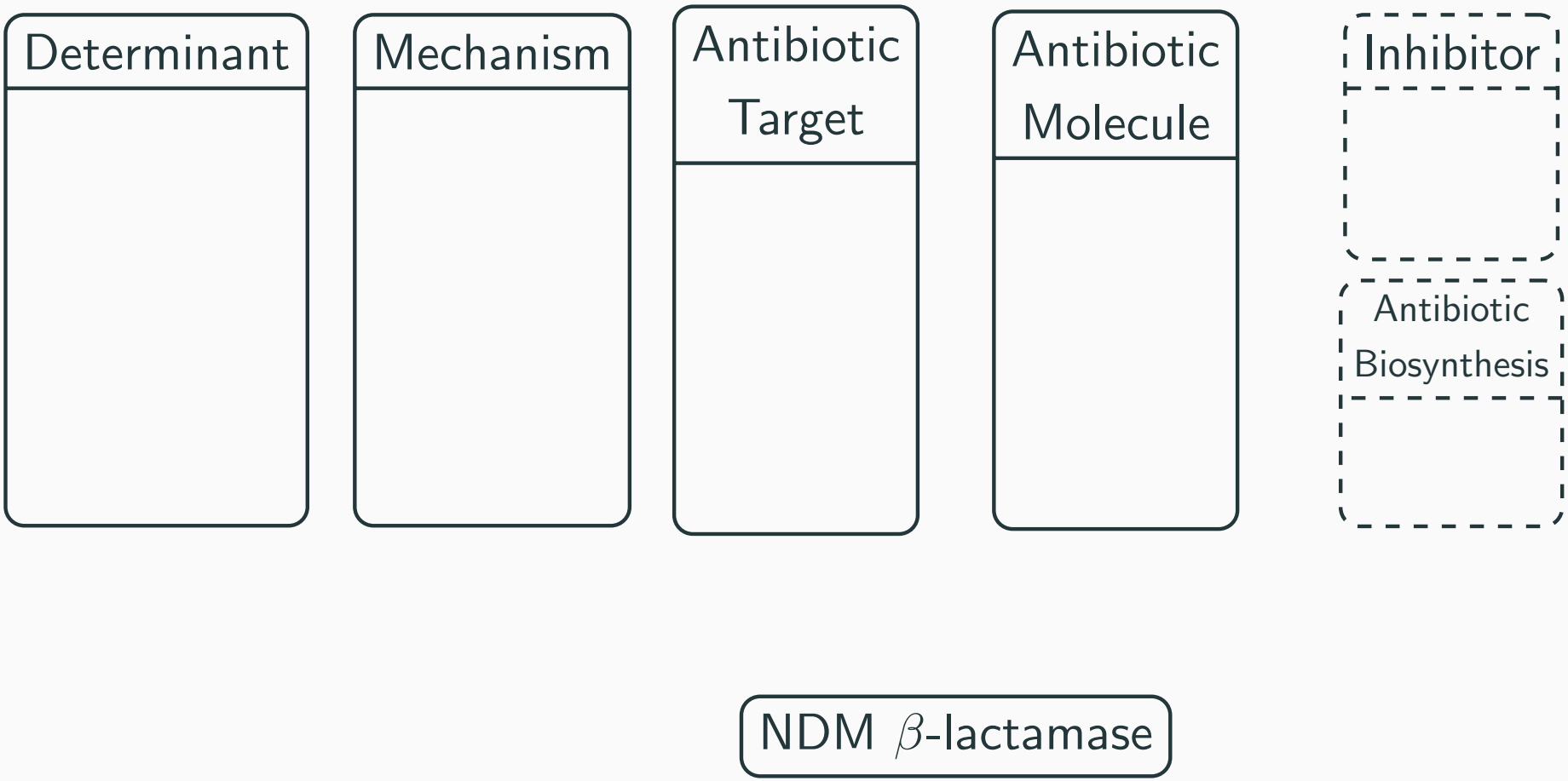

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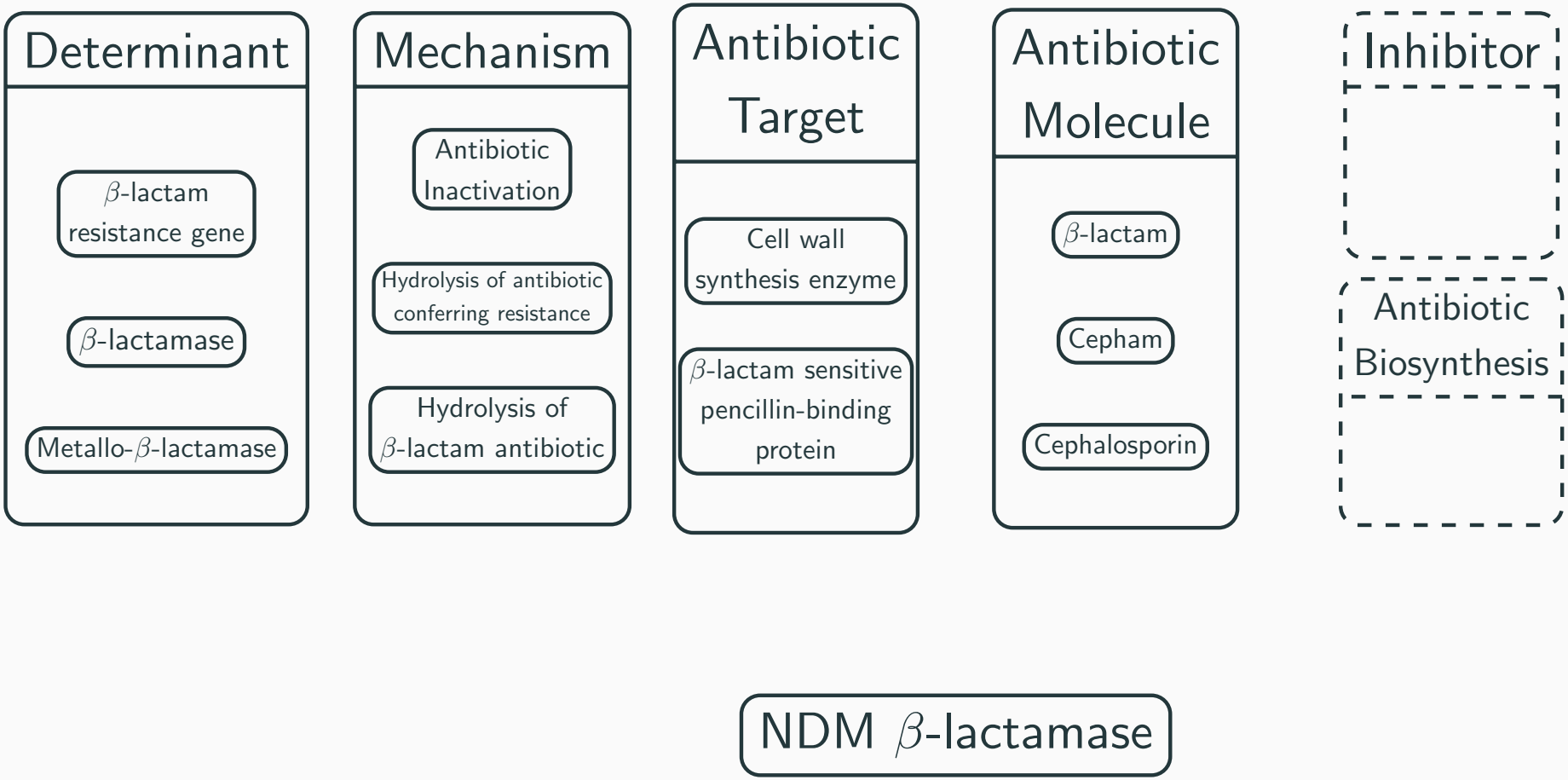

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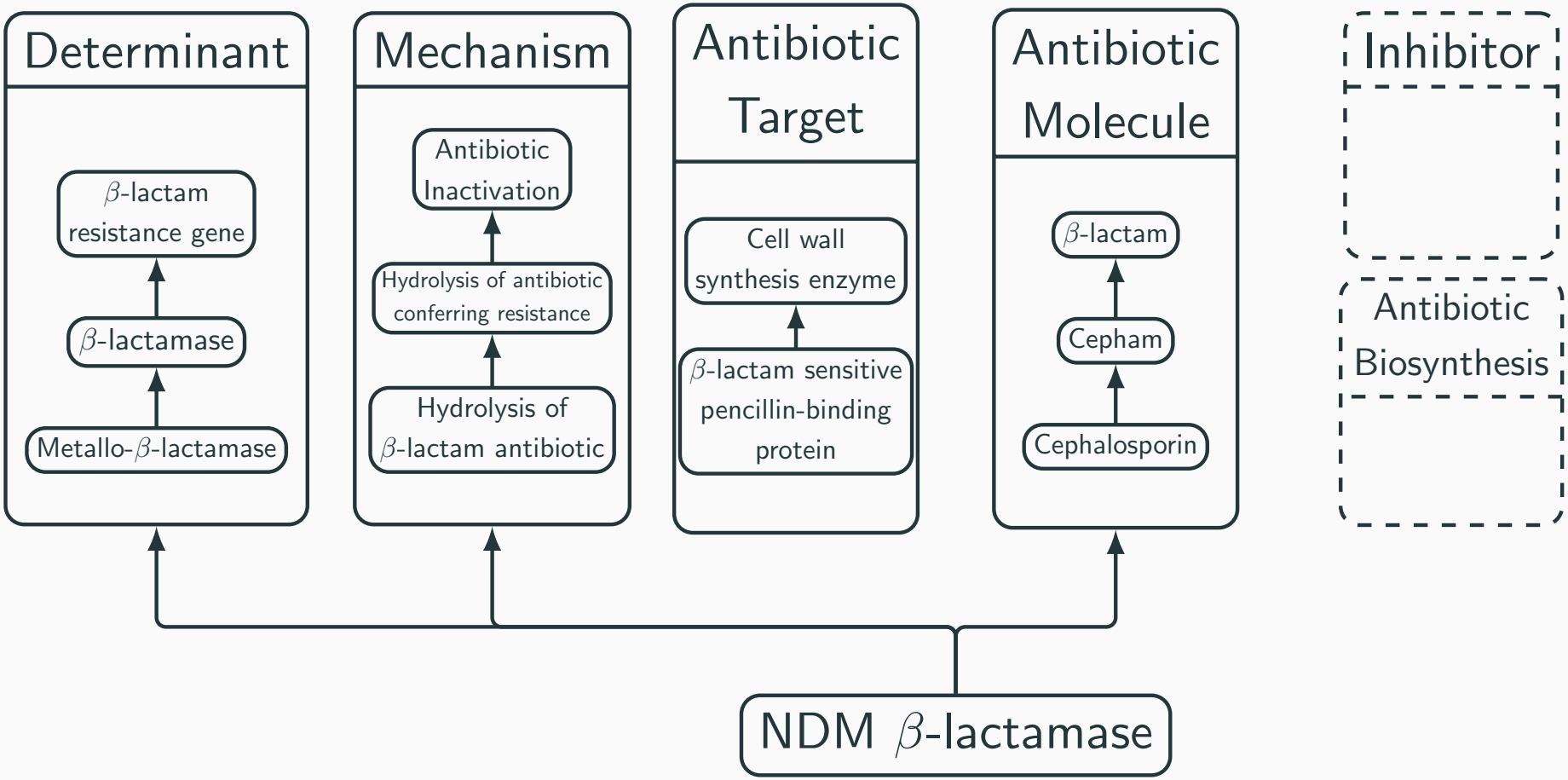

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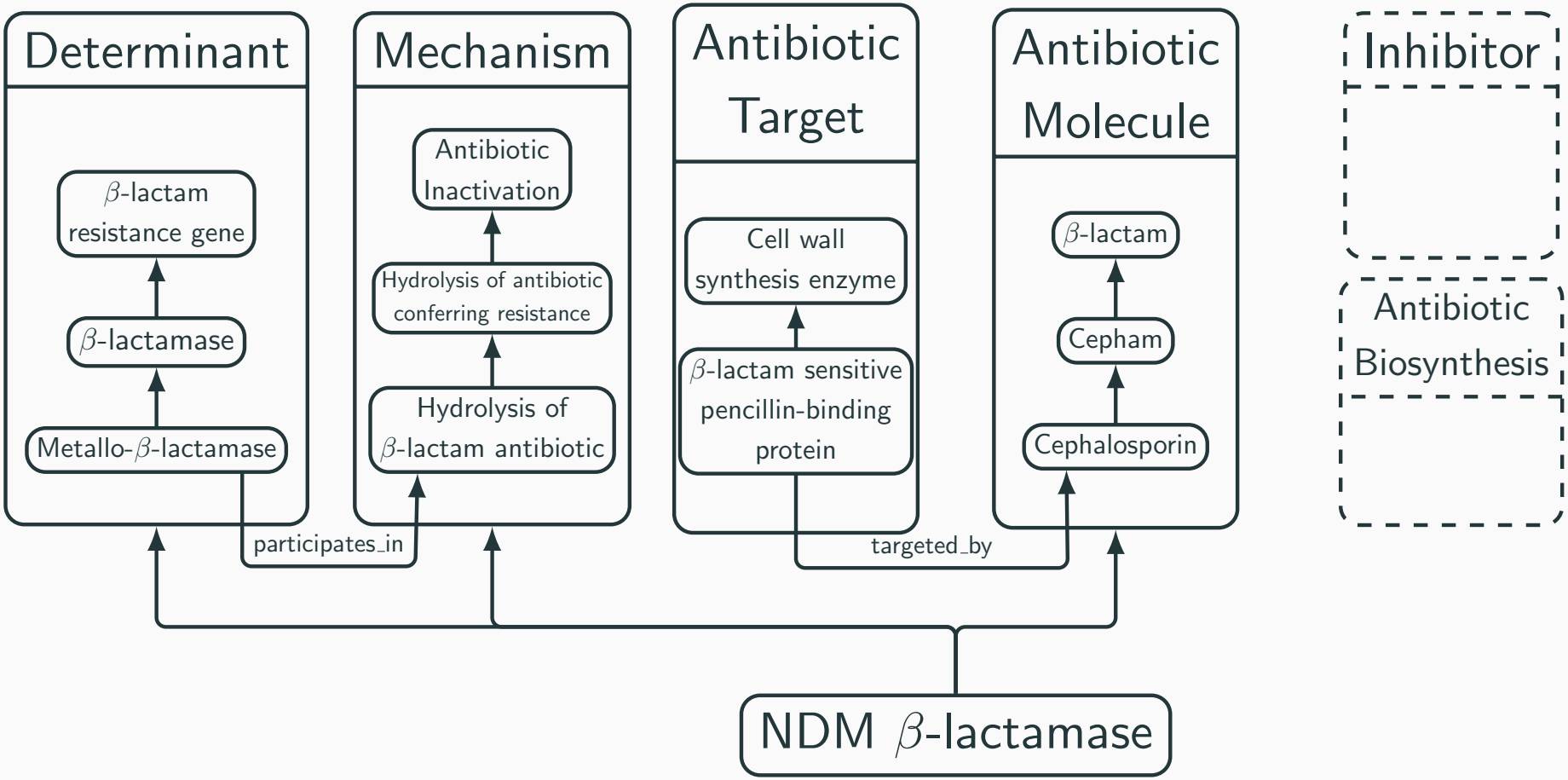

NDM on CARD

NDM beta-lactamase [AMR Gene Family]

Download Sequences

Accession	ARO:3000057
Definition	NDM beta-lactamases or New Delhi metallo-beta-lactamases are class B beta-lactamases that confer resistance to a broad range of antibiotics including carbapenems, cephalosporins and penicillins.
Drug Class	carbapenem, cephalosporin, cephamycin, penam
Resistance Mechanism	antibiotic inactivation
Classification	**13 ontology terms** | Hide + process or component of antibiotic biology or chemistry + antibiotic molecule + mechanism of antibiotic resistance + antibiotic inactivation [Resistance Mechanism] + beta-lactam antibiotic + determinant of antibiotic resistance + determinant of beta-lactam resistance + hydrolysis of antibiotic conferring resistance + antibiotic inactivation enzyme + hydrolysis of beta-lactam antibiotic by metallo-beta-lactamase + beta-lactamase + cephem + class B (metallo-) beta-lactamase
Parent Term(s)	**5 ontology terms** | Hide + *confers_resistance_to* carbapenem [Drug Class] + *confers_resistance_to* cephalosporin [Drug Class] + *confers_resistance_to* cephamycin [Drug Class] + *confers_resistance_to* penam [Drug Class] + subclass B1 (metallo-) beta-lactamase
Sub-Term(s)	**17 ontology terms** | Hide + NDM-1 + NDM-2

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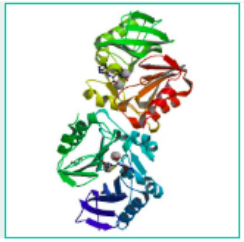
Adding a New Resistance Gene

One incredibly useful aspect of ontologies is we do not need to record redundant information for new genes:

NDM-1

Download Sequences



Accession	ARO:3000589
Definition	NDM-1 is a metallo-beta-lactamase isolated from Klebsiella pneumoniae with nearly complete resistance to all beta-lactam antibiotics.
AMR Gene Family	NDM beta-lactamase
Drug Class	penam, carbapenem, cephamycin, cephalosporin
Resistance Mechanism	antibiotic inactivation
Resistomes	*Acinetobacter baumannii*[g+wgs], *Acinetobacter nosocomialis*[wgs], *Citrobacter freundii*[p+wgs], *Enterobacter asburiae*[wgs], *Enterobacter cloacae*[p+wgs], *Enterobacter hormaechei*[p+wgs], *Enterobacter kobei*[wgs], *Escherichia coli*[p+wgs], *Klebsiella oxytoca*[wgs], *Morganella morganii*[g+wgs], *Proteus mirabilis*[p+wgs], *Providencia rettgeri*[g+p+wgs], *Providencia stuartii*[p+wgs], *Serratia marcescens*[p+wgs], *Shigella sonnei*[wgs], *Vibrio cholerae*[wgs], *Vibrio parahaemolyticus*[wgs]
Classification	**23 ontology terms** | Show
Parent Term(s)	**5 ontology terms** | Hide + *confers_resistance_to_drug* ertapenem [Antibiotic] + *confers_resistance_to_drug* meropenem [Antibiotic] + NDM beta-lactamase [AMR Gene Family] + *confers_resistance_to_drug* imipenem [Antibiotic] + *confers_resistance_to_drug* amoxicillin-clavulanic acid
Publications	Zhang H and Hao Q. 2011. FASEB J 25(8): 2574-2582. Crystal structure of NDM-1 reveals a common {beta}-lactam hydrolysis mechanism. (PMID 21507902) King D and Strynadka N. 2011. Protein Sci 20(9): 1484-1491. Crystal structure of New Delhi metallo-beta-lactamase reveals molecular basis for antibiotic resistance. (PMID 21774017)

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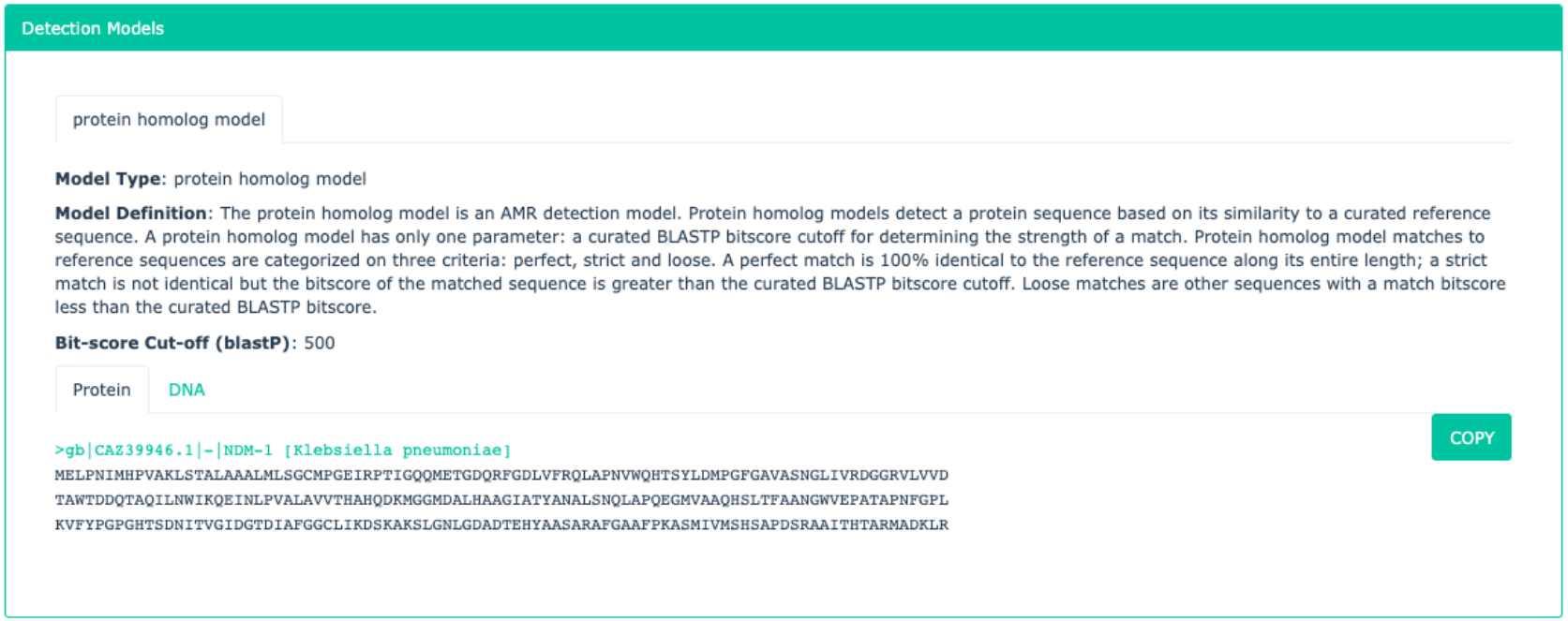
AMR Detection Models

We append "resistance genes" with genetic sequence, mutation and bit-score information to create an AMR Detection Model — a bioinformatic tool to detect resistance genes from genomes:



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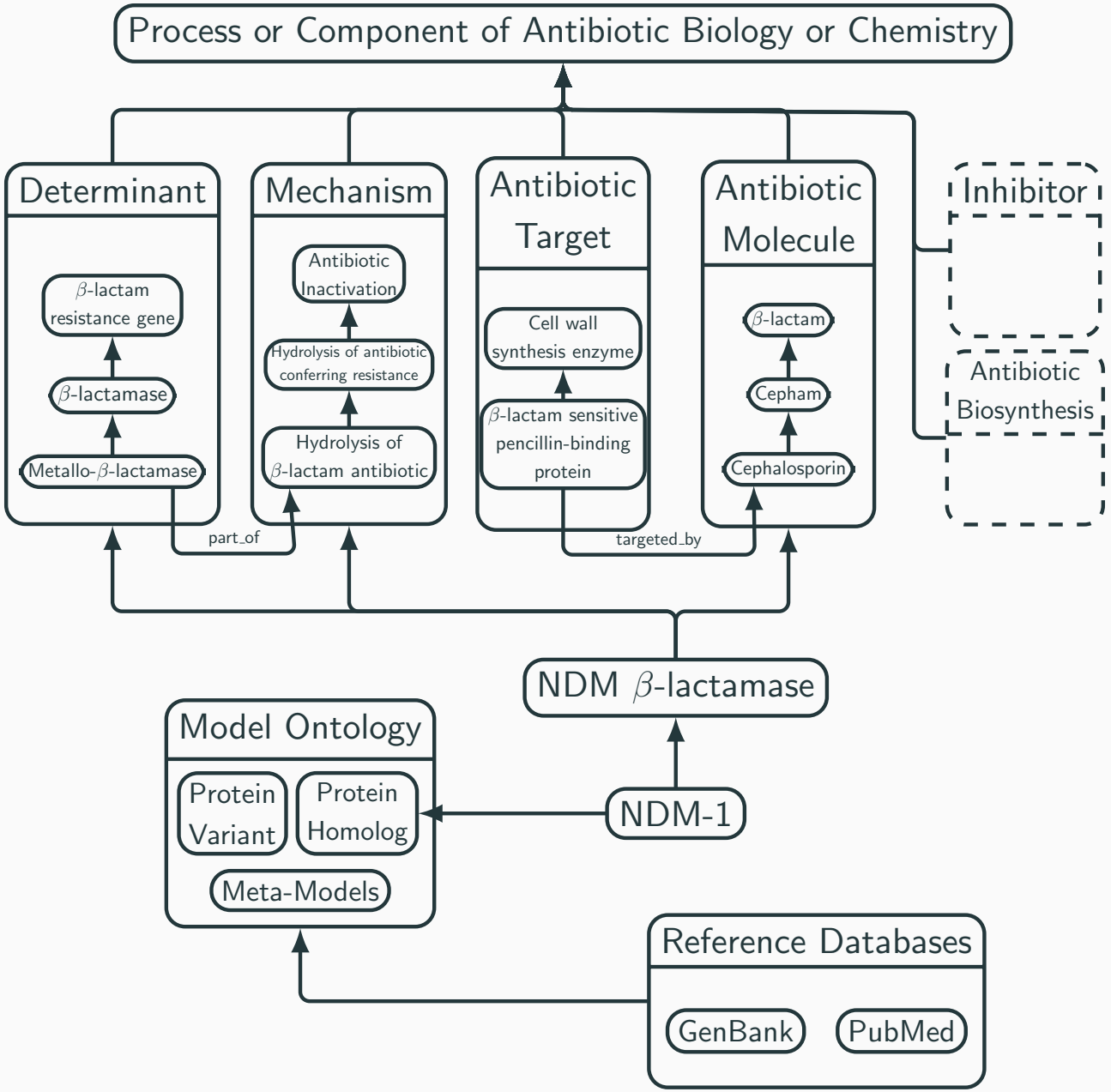
Putting it Together



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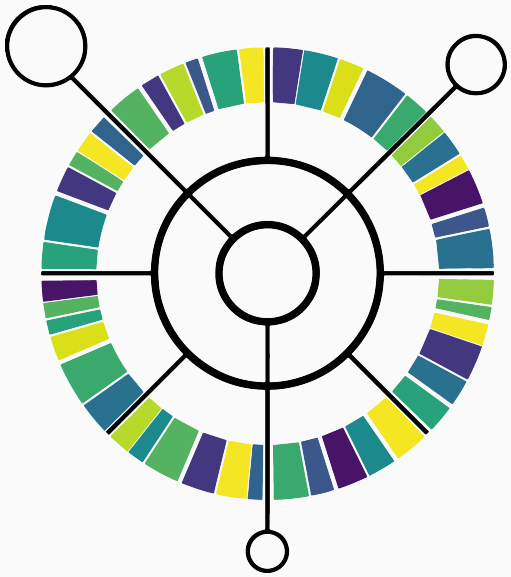
2. ARO is critical for providing a controlled vocabulary - universally understood AMR language
3. Biocuration is both the collection and presentation of these data for improved user experience
4. Our software uses these data structures and AMR detection models for computational AMR prediction

Thanks for listening!

(Questions are welcome!)



David Braley Centre
for Antibiotic Discovery

Michael G. DeGroote
INSTITUTE FOR INFECTIOUS DISEASE RESEARCH