NUI GALWAY

Graded CodY Activity Prioritizes Metabolism and Virulence Gene Expression in *Staphylococcus aureus*

Nick Waters

December 4, 2015

Brinsmade Lab, Biology Department, Georgetown University

BACKGROUND

CODY

- Conserved among Firmicutes

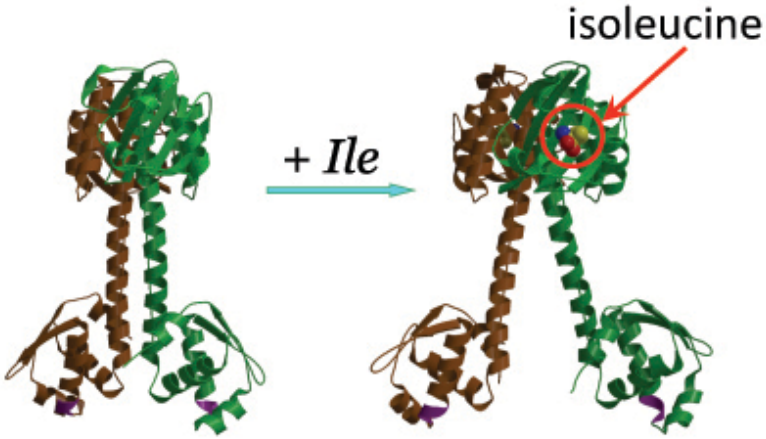

Figure 1. Crystal structure of unliganded CodY (largely inactive) and in the presence of the activator isoleucine. How GTP binds remains an open question. Credit: V. Levdikov and A.J. Wilkinson

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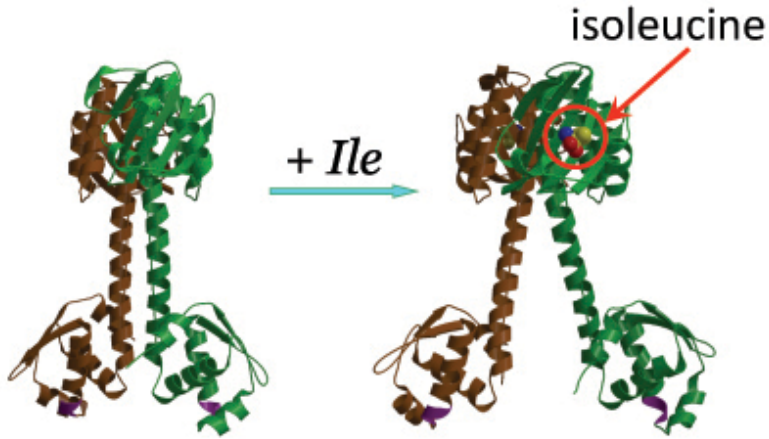

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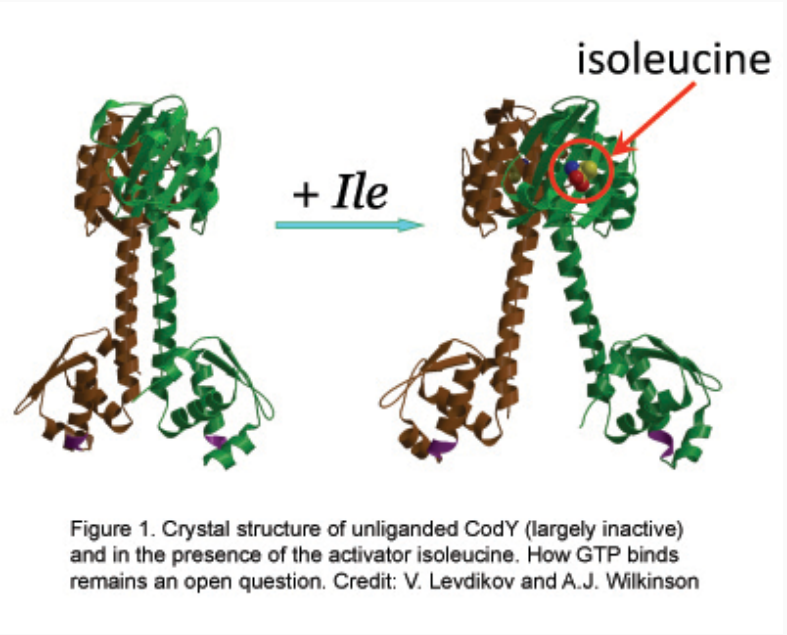

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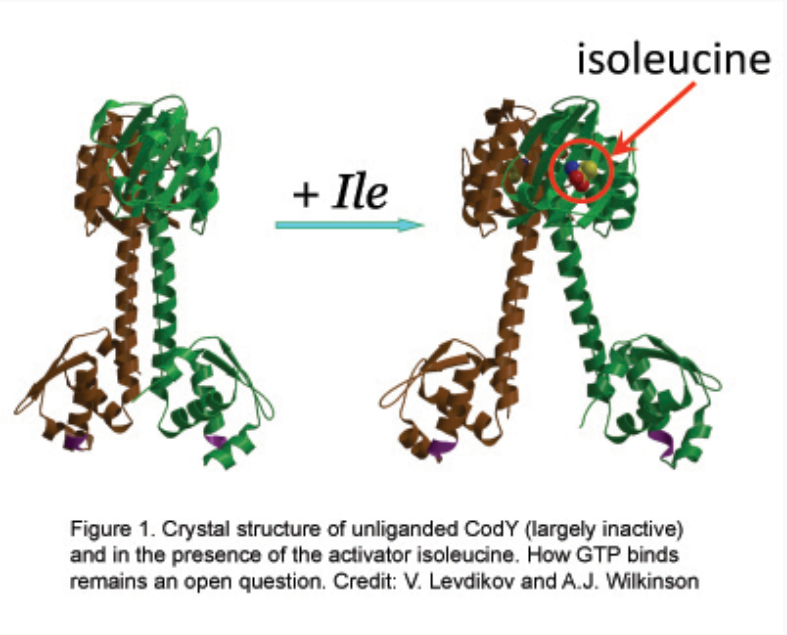

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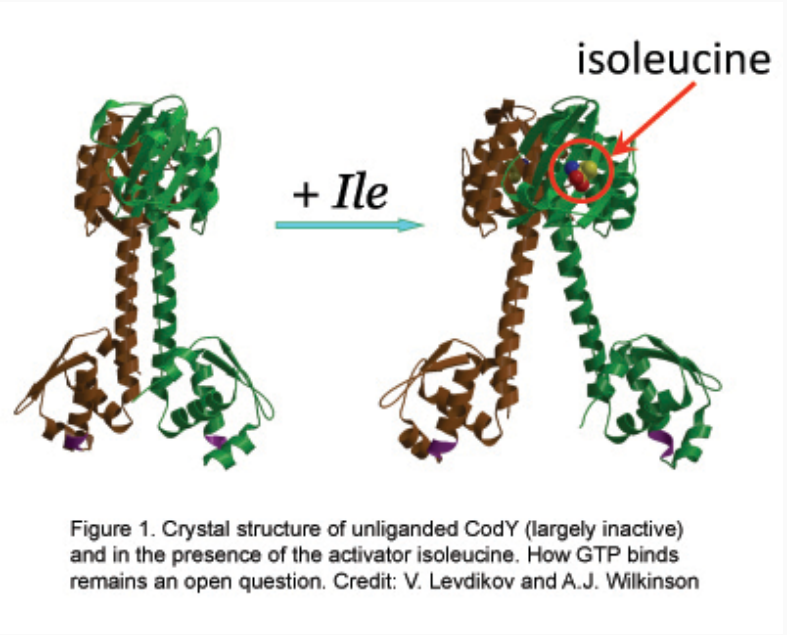

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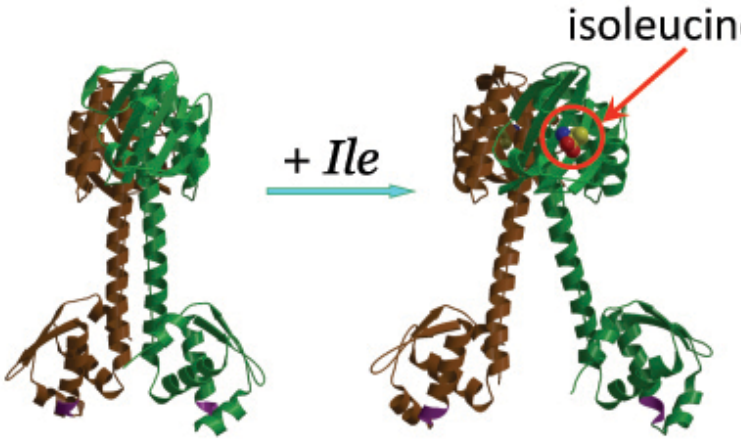

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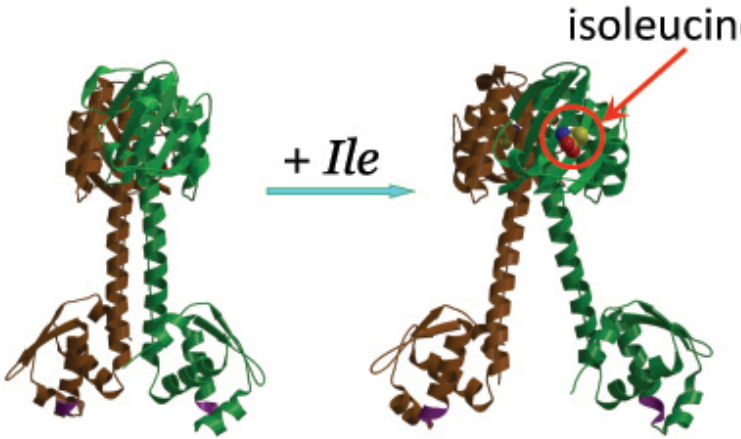
- Two Known Effectors: ILV and GTP
- Consensus Sequence: AATTTTCWGAAAATT



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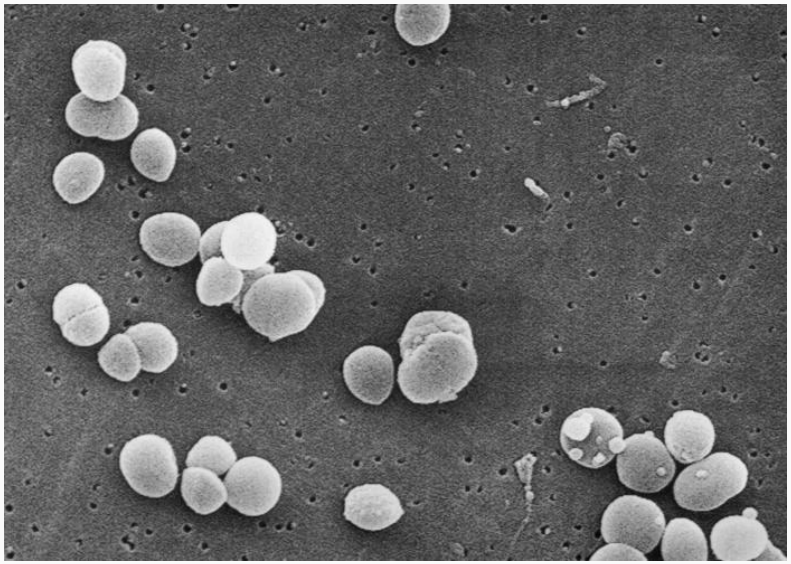
S. AUREUS

- Nosocomial



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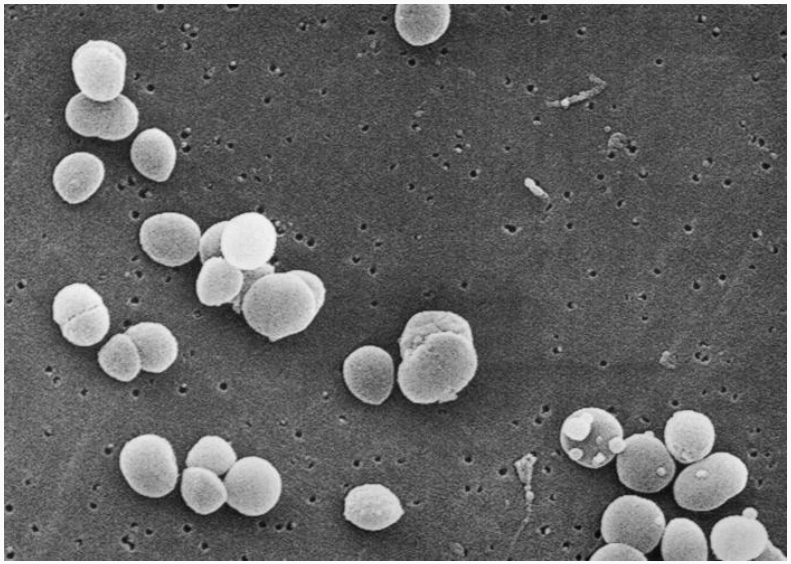
- Gram Positive



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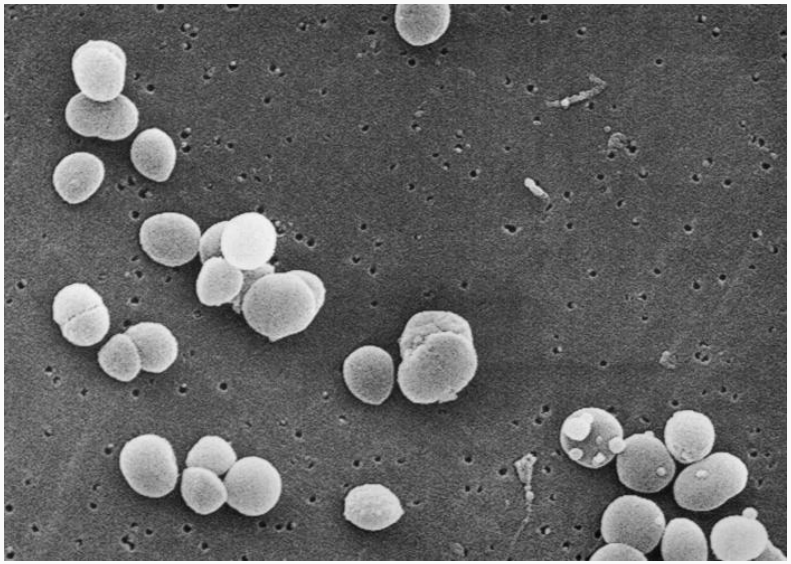
- Colonizes skin and nares asymptomatically



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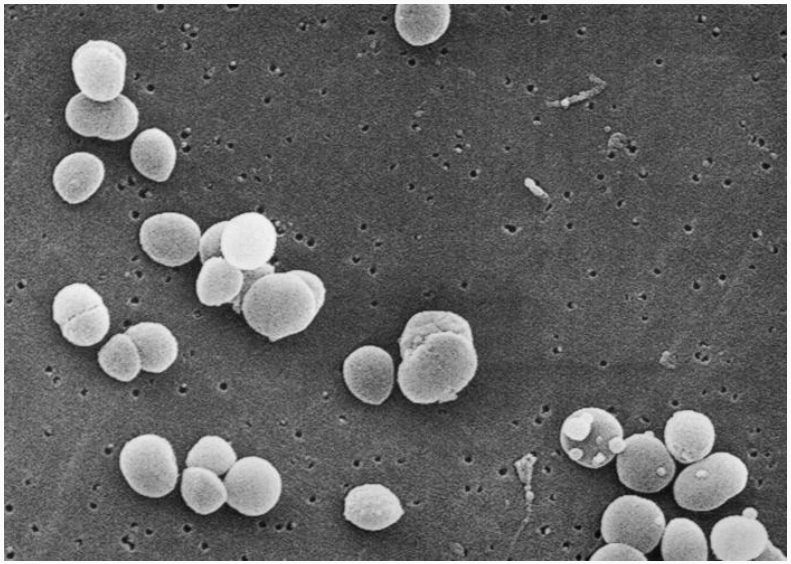
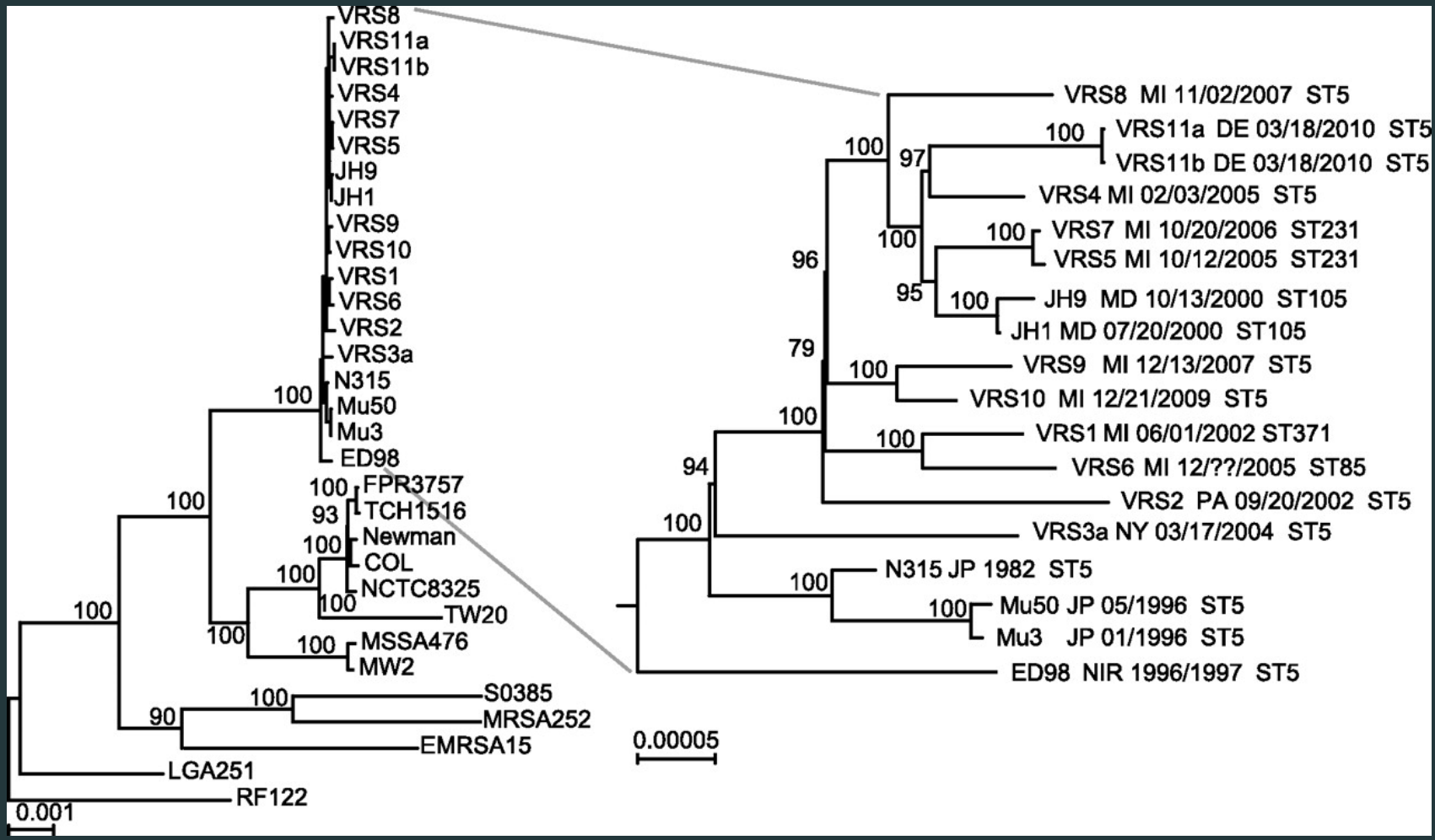
- Nosocomial until ~1990
- Gram Positive
- Colonizes skin and nares asymptomatically



LINEAGE


VRS8
VRS11a
VRS11b
VRS4
VRS7
VRS5
JH9
JH1
VRS9
VRS10
VRS1
VRS6
VRS2
VRS3a
N315
Mu50
Mu3
ED98
FPR3757
TCH1516
Newman
COL
NCTC8325
TW20
MSSA476
MW2
S0385
MRSA252
EMRSA15
LGA251
RF122
0.001
VRS8 MI 11/02/2007 ST5
VRS11a DE 03/18/2010 ST5
VRS11b DE 03/18/2010 ST5
VRS4 MI 02/03/2005 ST5
VRS7 MI 10/20/2006 ST231
VRS5 MI 10/12/2005 ST231
JH9 MD 10/13/2000 ST105
JH1 MD 07/20/2000 ST105
VRS9 MI 12/13/2007 ST5
VRS10 MI 12/21/2009 ST5
VRS1 MI 06/01/2002 ST371
VRS6 MI 12/??/2005 ST85
VRS2 PA 09/20/2002 ST5
VRS3a NY 03/17/2004 ST5
N315 JP 1982 ST5
Mu50 JP 05/1996 ST5
Mu3 JP 01/1996 ST5
ED98 NIR 1996/1997 ST5
0.00005

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- Does CodY modulate virulence?
- If so, what can we infer about CodY and pathogen strategy?

RESEARCH DESIGN

PREVIOUS WORK

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Re-annotation of UAMS-1 genome

GENOME KEGGER

Problem: Previous annotation used a automated process that referenced another poorly curated genome

Solution:

- Kyoto Encyclopedia of Genes and Genomes (KEGG) downloader script

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DIFFERENTIAL EXPRESSION ANALYSIS

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- Group Expression Profiles by k-means clustering

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Results of differential expression:

- 29 genes activated by CodY

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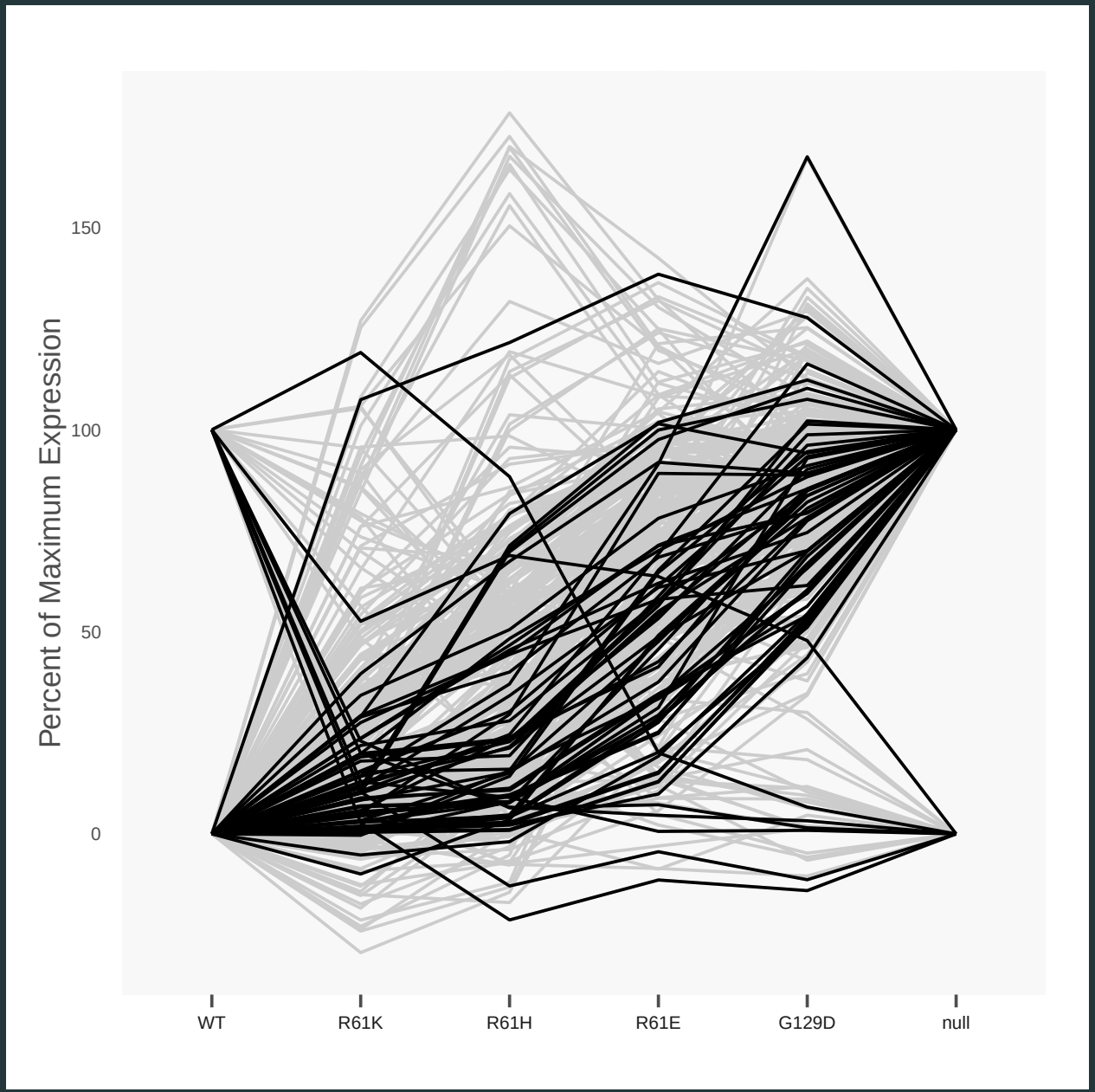
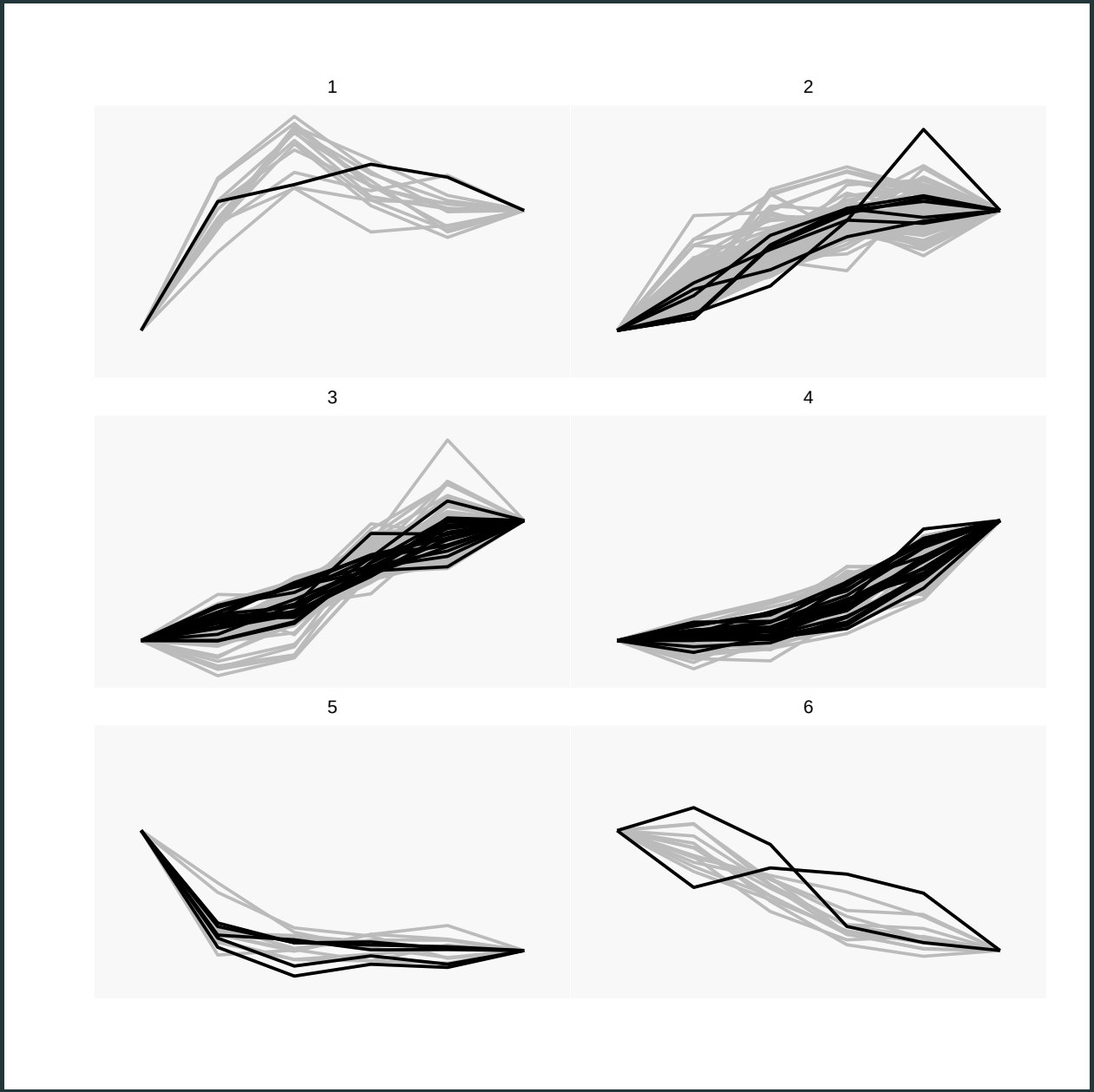
- around 83 virulence genes regulated by CodY/ / /

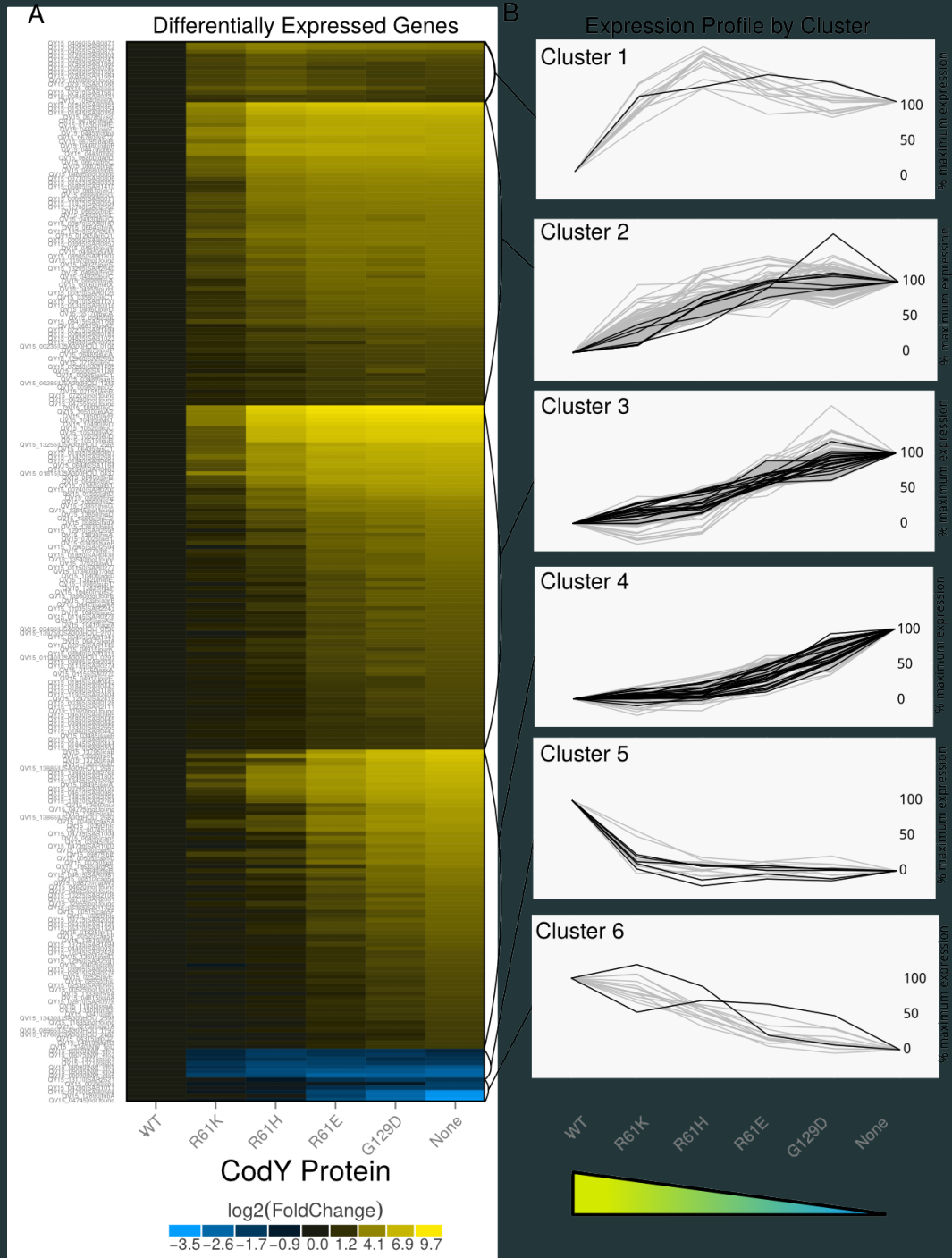
GRADED CODY REPONSE



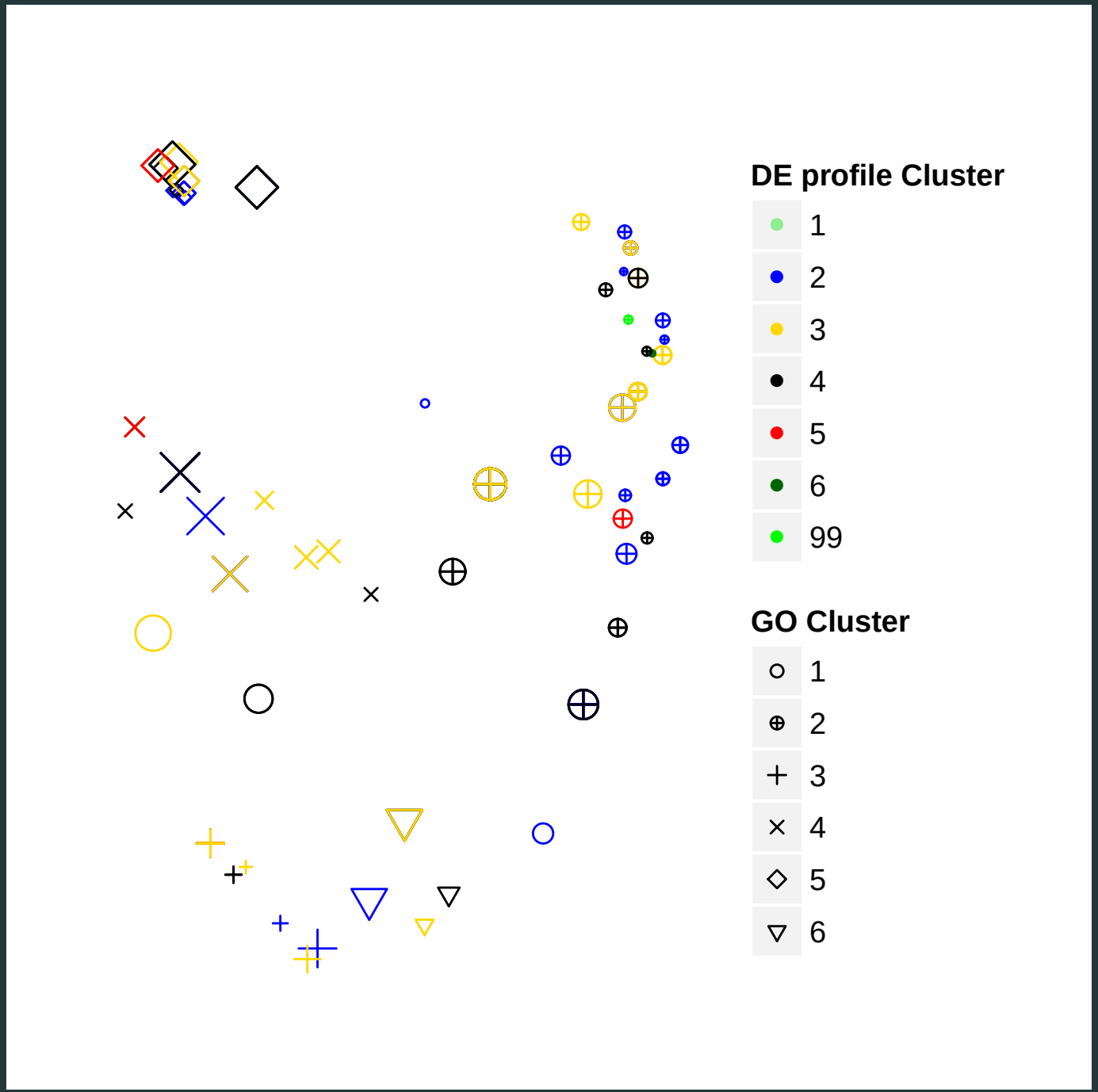
GRADED CODY REPONSE: CLUSTERED



GRADED CODY REPONSE: HEATMAP



GRADED CODY REPONSE: ALTERNATICE DUAL CLUSTERING



VALIDATION

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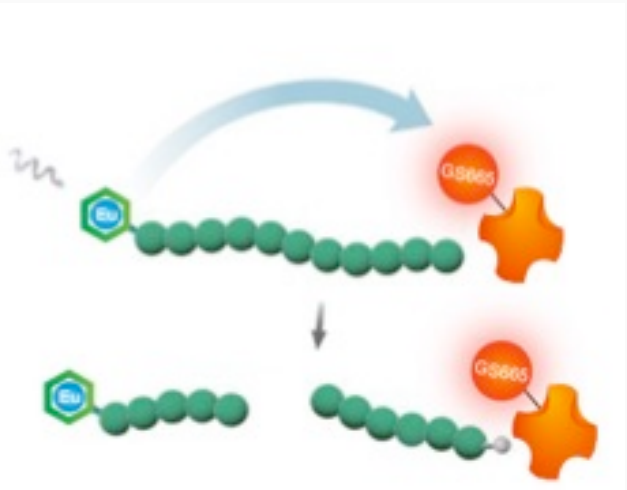
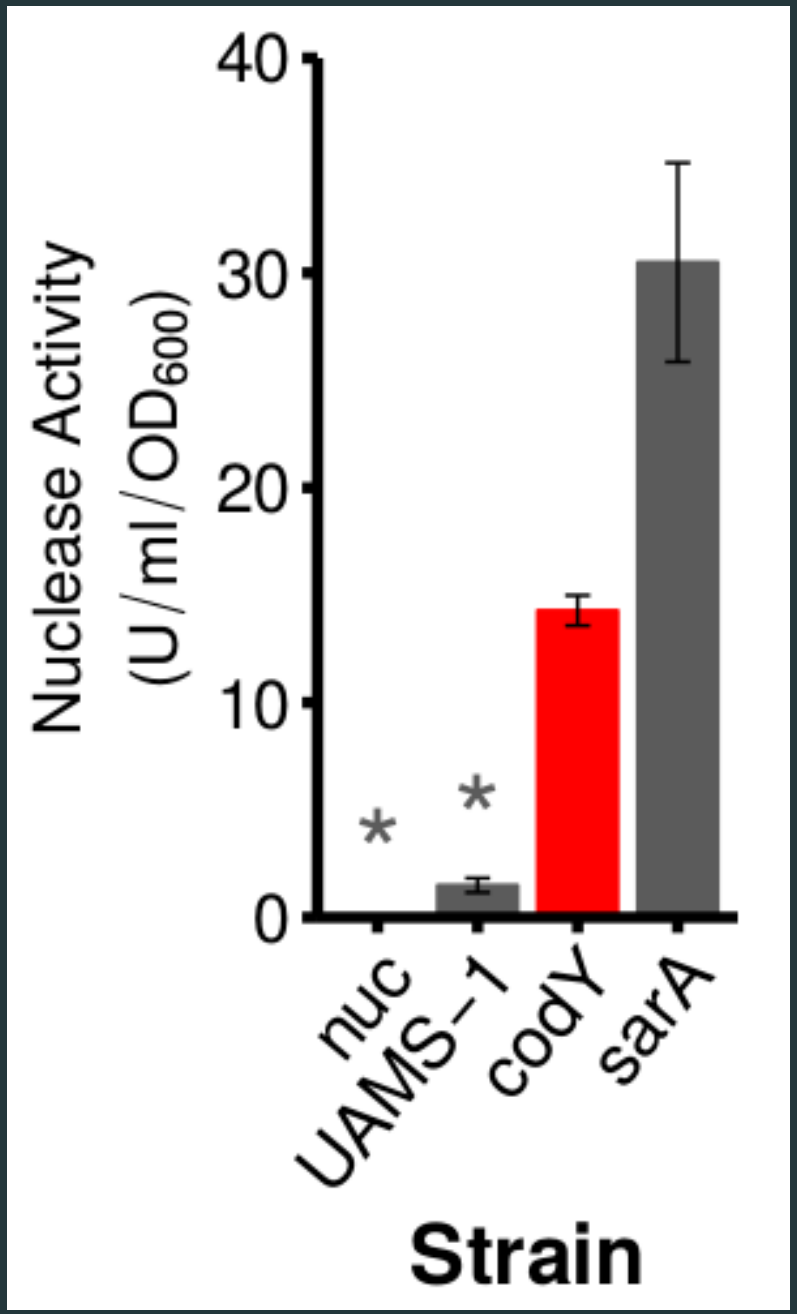


NUCLEASE ACTIVITY



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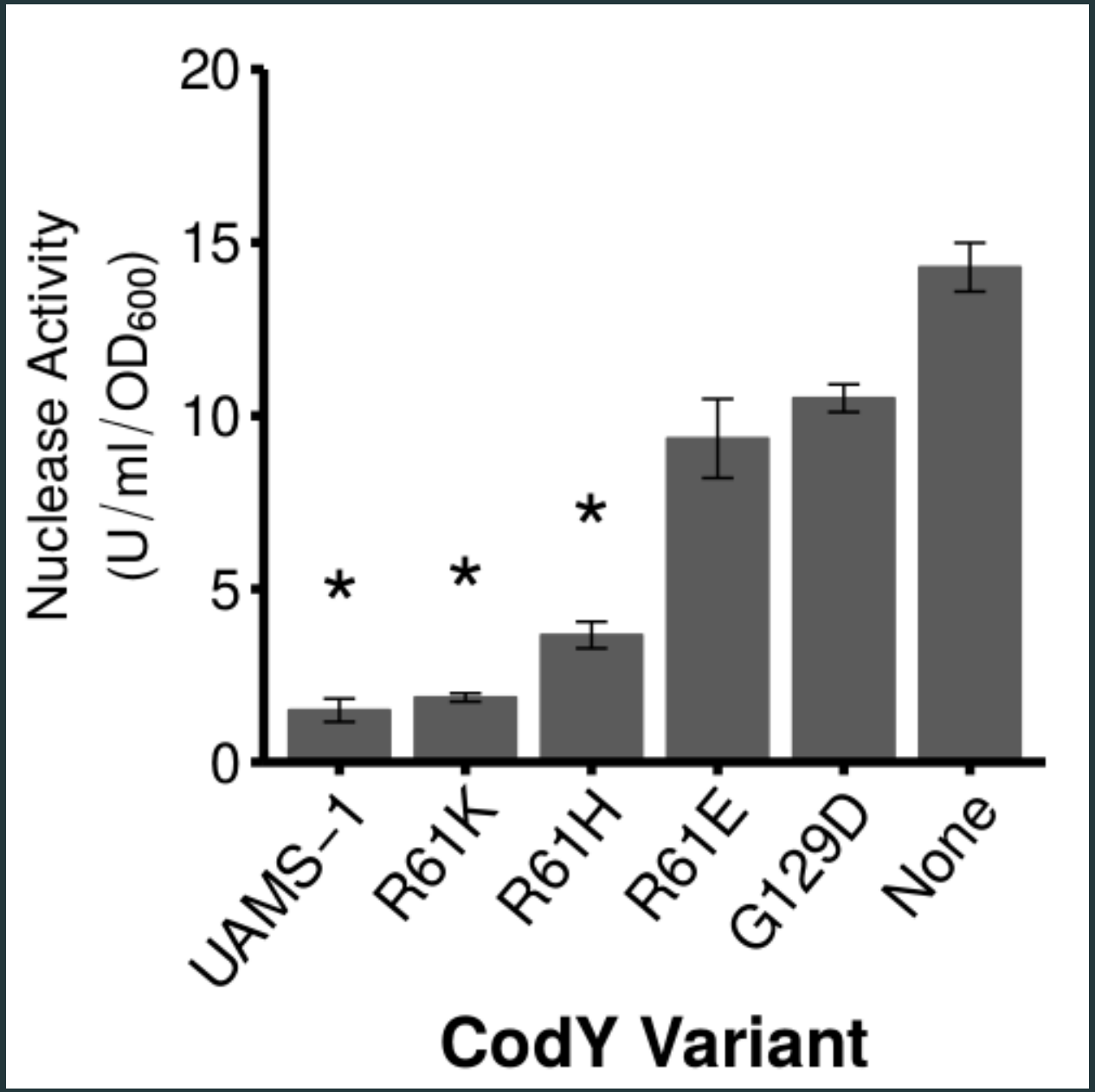

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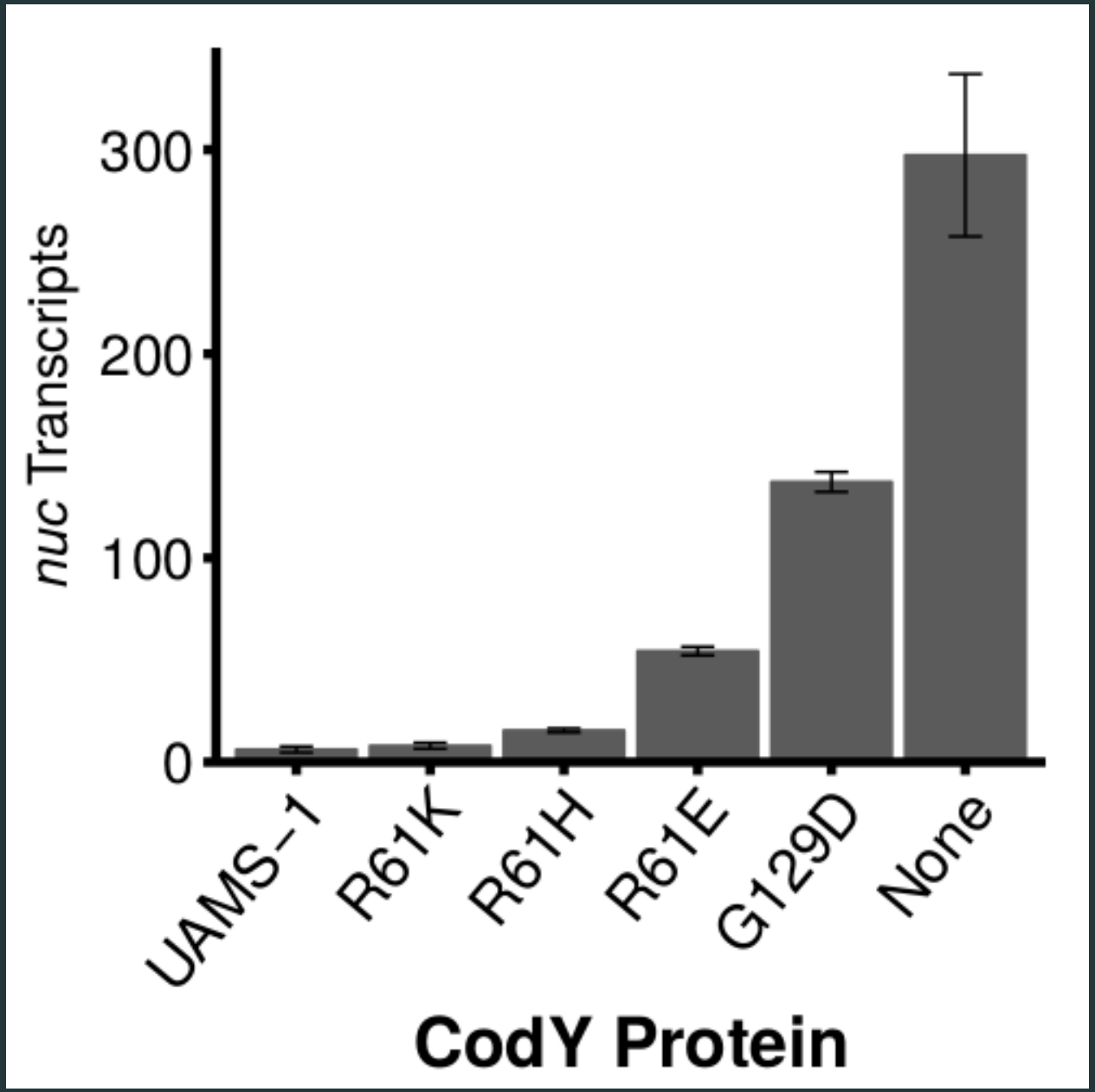

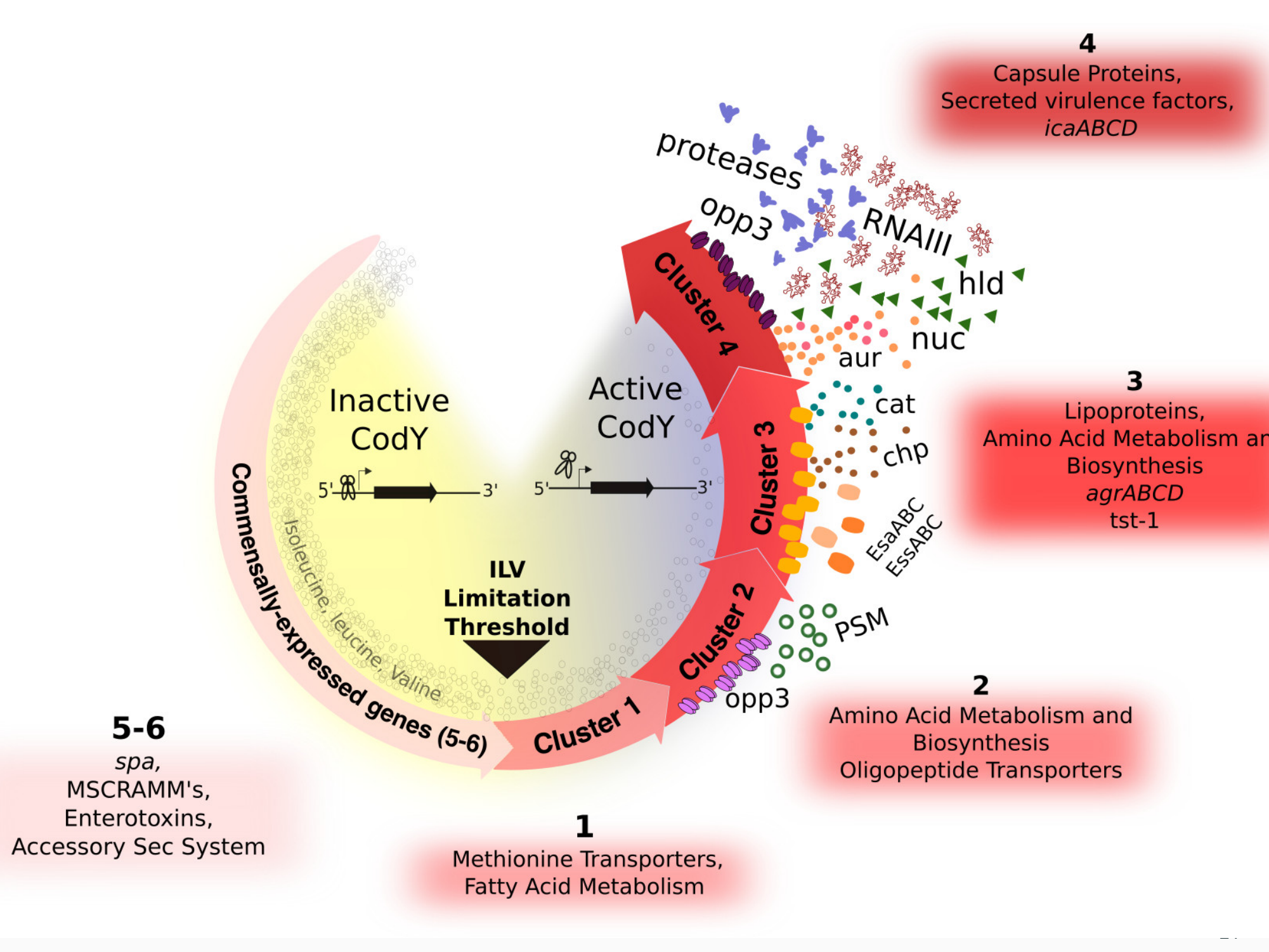
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Capsule Proteins,
Secreted virulence factors,
icaABCD
proteases
opp3
RNAIII
hld
nuc
aur
cat
chp
EsaABC
EssABC
PSM
opp3
Cluster 4
Cluster 3
Cluster 2
Cluster 1
Inactive
CodY
Active
CodY
5'
3'
5'
3'
ILV
Limitation
Threshold
Isoleucine, leucine, Valine
Commensally-expressed genes (5-6)
3
Lipoproteins,
Amino Acid Metabolism an
Biosynthesis
agrABCD
tst-1
2
Amino Acid Metabolism and
Biosynthesis
Oligopeptide Transporters
1
Methionine Transporters,
Fatty Acid Metabolism
5-6
spa,
MSCRAMM's,
Enterotoxins,
Accessory Sec System

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