

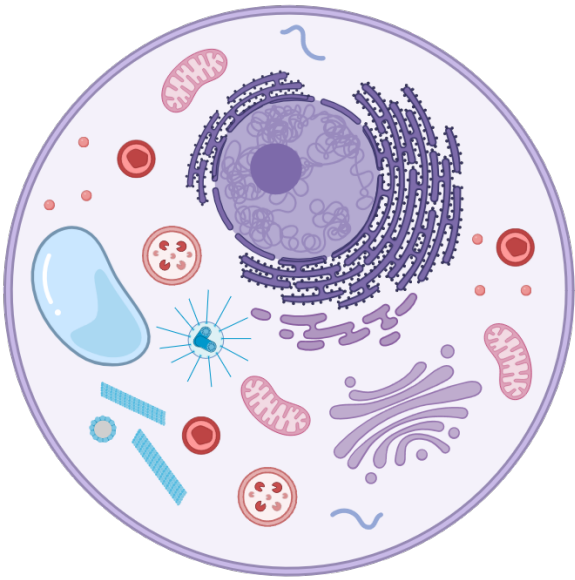
EURO^{4SEE}

Generating Mutant Protein Structures Using Advanced Techniques

Tandac Furkan Guclu

Sabancı University

Proteins?



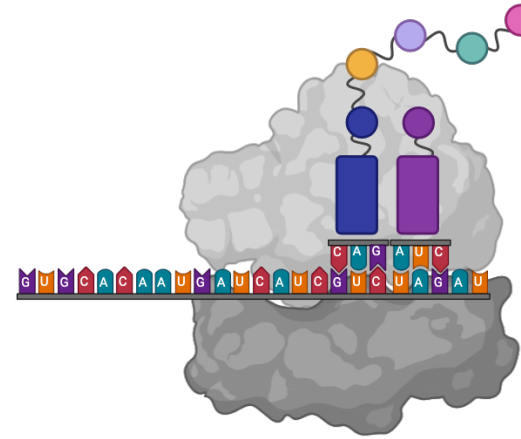
Cell



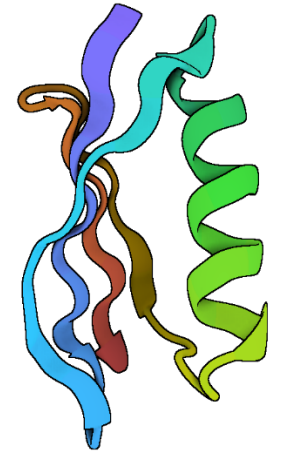
DNA



RNA



Protein
(Translation)

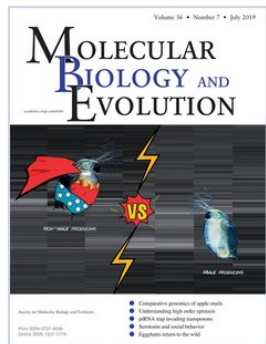


Protein
(Structure)



Antibiotic Resistance

MOLECULAR BIOLOGY AND EVOLUTION

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Volume 36, Issue 7
July 2019

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JOURNAL ARTICLE

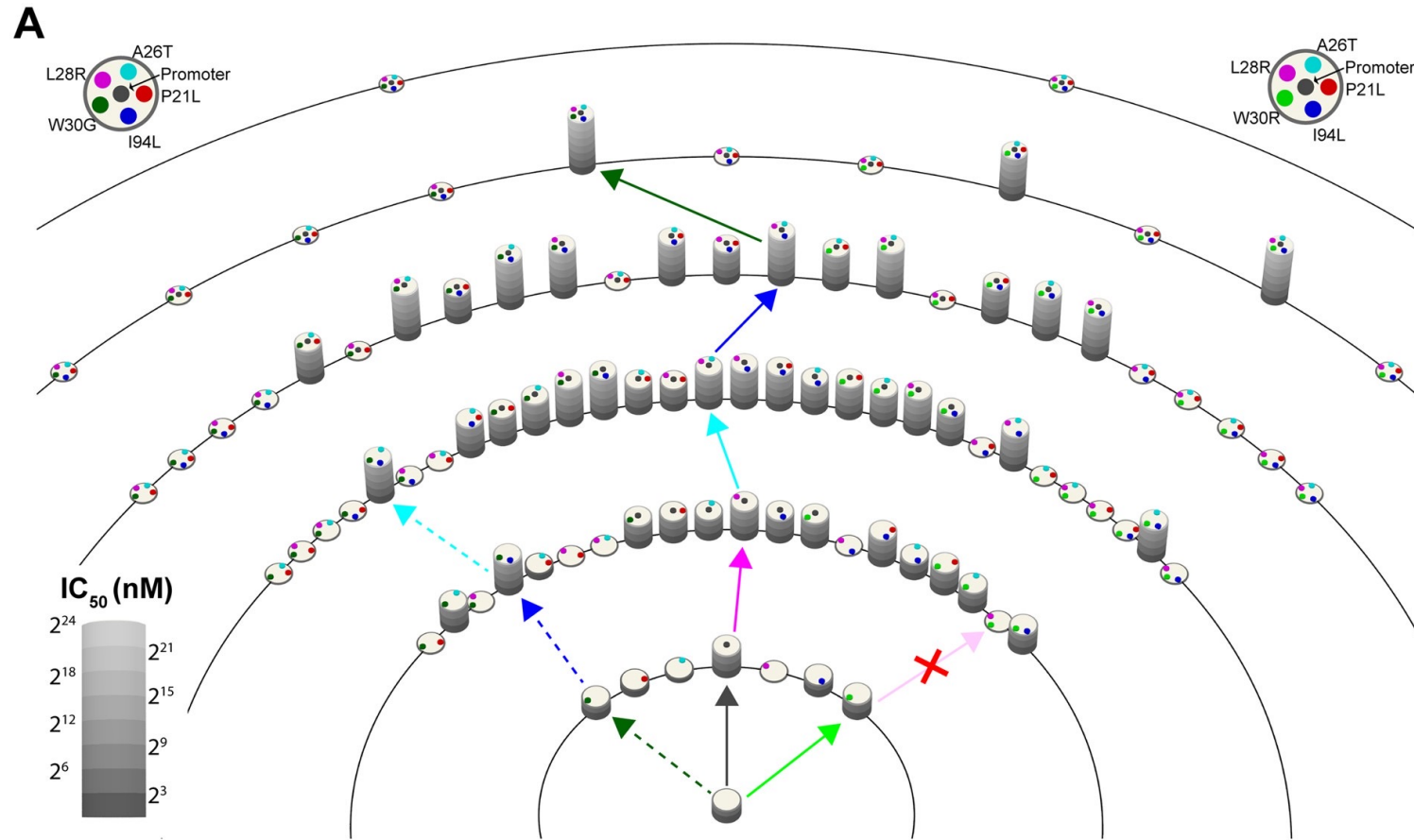
High-Order Epistasis in Catalytic Power of Dihydrofolate Reductase Gives Rise to a Rugged Fitness Landscape in the Presence of Trimethoprim Selection

Yusuf Talha Tamer, Ilona K Gaszek, Haleh Abdizadeh, Tugce Altinusak Batur, Kimberly A Reynolds, Ali Rana Atilgan, Canan Atilgan, Erdal Toprak 

Molecular Biology and Evolution, Volume 36, Issue 7, July 2019, Pages 1533–1550, <https://doi.org/10.1093/molbev/msz086>

Published: 15 April 2019

Antibiotic Resistance



Fitness Landscape

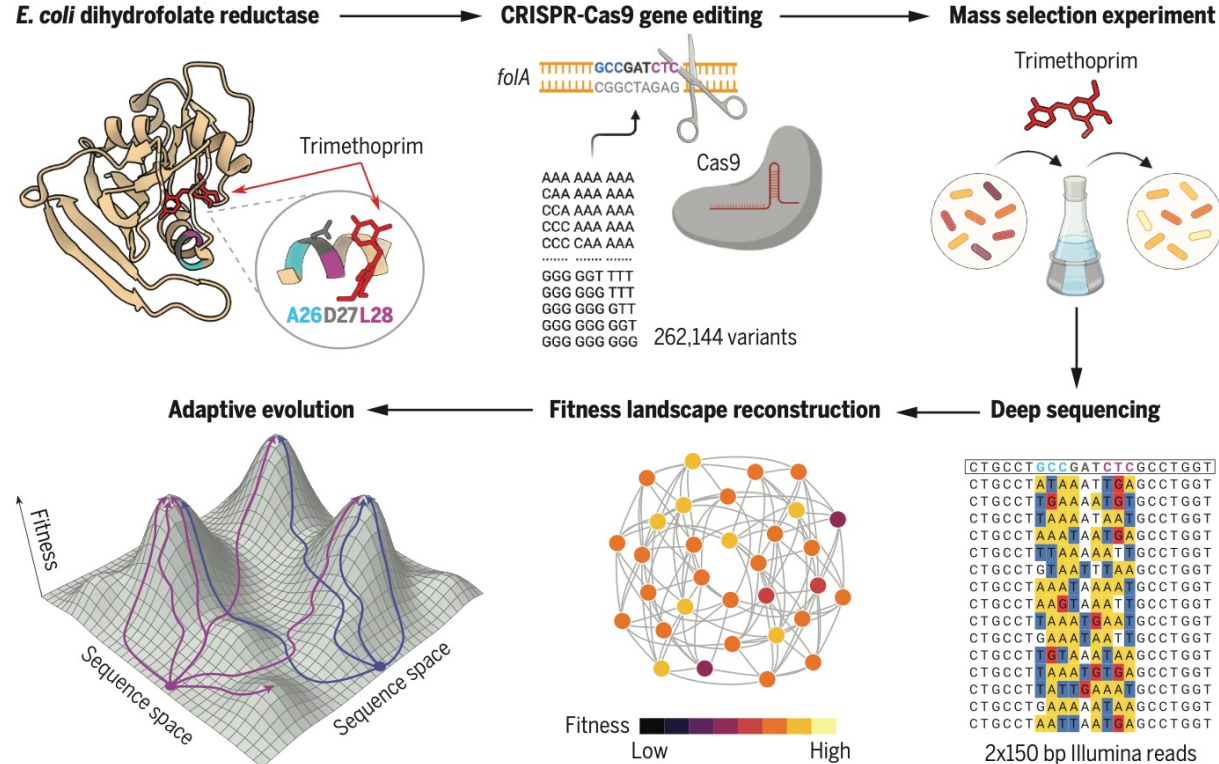
EVOLUTIONARY BIOLOGY

A rugged yet easily navigable fitness landscape

Andrei Papkou, Lucia Garcia-Pastor, José Antonio Escudero, Andreas Wagner*

Empirical fitness landscape of dihydrofolate reductase.

We edited the *E. coli* genome to create a fitness landscape of all 64³ codons encoding three consecutive amino acids (A, Ala; D, Asp; L, Leu) of the protein dihydrofolate reductase. We measured the fitness of each genotype in this landscape in the presence of the antibiotic trimethoprim using a mass selection experiment and deep sequencing. Even though the landscape is highly rugged, adaptive evolution can find the highest peaks from most starting locations via short and abundant fitness-increasing paths. [Created with BioRender.com]



Deep Mutational Scanning

nature

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Article | Published: 06 April 2022

Mapping the energetic and allosteric landscapes of protein binding domains

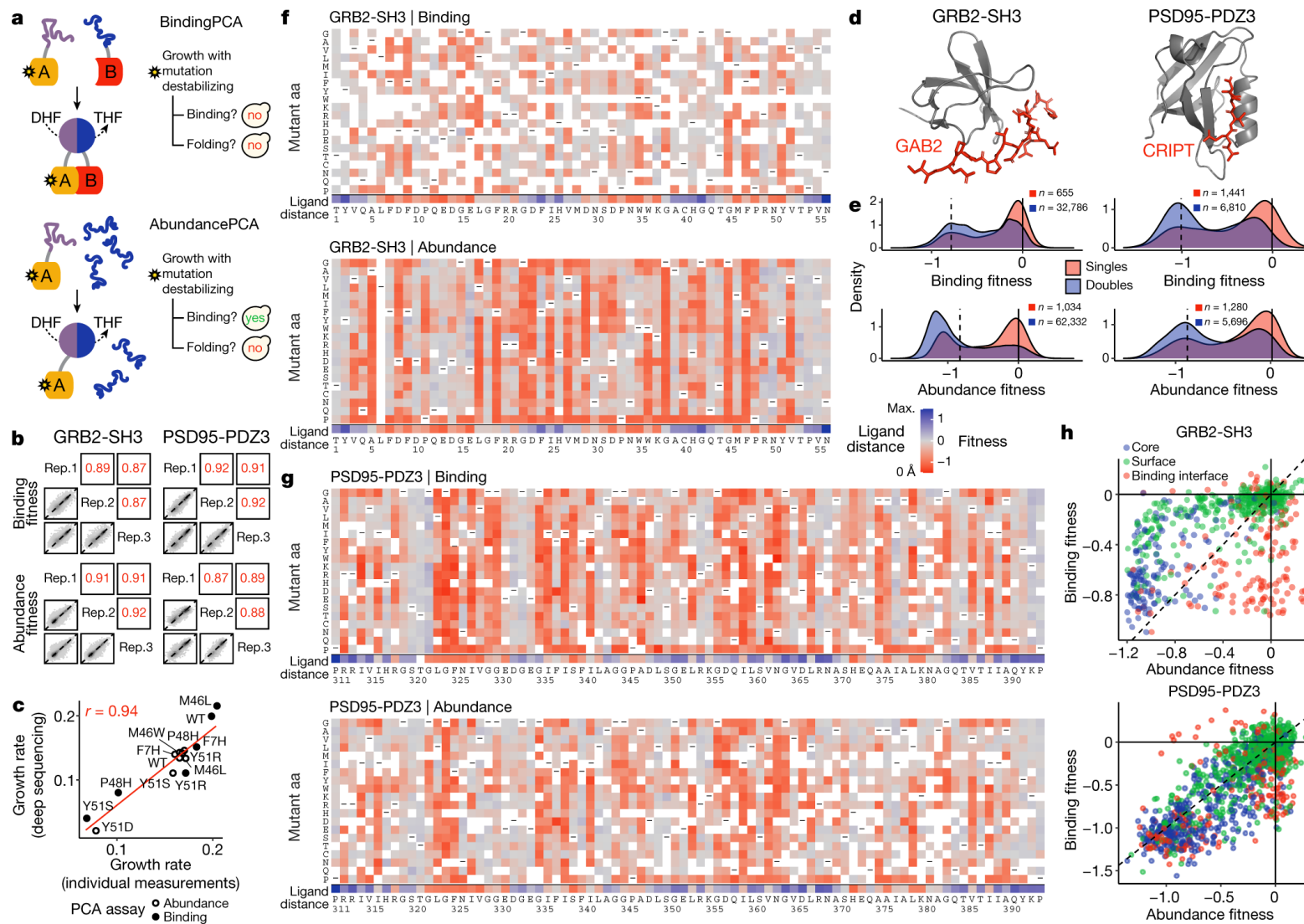
[Andre J. Faure](#), [Júlia Domingo](#), [Jörn M. Schmiedel](#), [Cristina Hidalgo-Carcedo](#), [Guillaume Diss](#) & [Ben Lehner](#) 

[Nature](#) **604**, 175–183 (2022) | [Cite this article](#)

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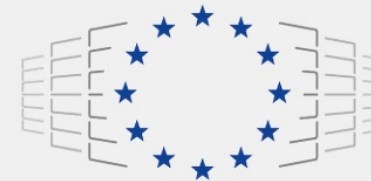
Deep Mutational Scanning



Thanks!



Co-funded by
the European Union



EuroHPC
Joint Undertaking

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