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Poster #107: An Lsr2-like Xenogeneic Silencer Confers Immunity Against AT-Rich Bacteriophage Infection

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In Actinomycetota, Lsr2-like xenogeneic silencer proteins are widespread nucleoid-associated proteins that preferentially bind AT-rich foreign sequences, oligomerize across promoters and intergenic regions, and hinder transcription. While they function as a global regulator for virulence genes or biofilm promoting genes has been described in the past, its role durin bacteriophage infection, one of the most direct encounters with foreign DNA, remain mainly unexplored. In Corynebacterium glutamicum, the Lsr2-like protein CgpS is encoded within CGP3, a 187 kb mobile genetic element rich in AT-sequences, and is known to silence transcription of foreign DNA within this region (1).
In a recent study, we demonstrate that the CGP3-encoded Lsr2-like silencer CgpS functions as an antiviral factor by restricting infection by the AT-rich bacteriophage JeanGrey (2). CgpS binds and oligomerizes on phage-derived AT-rich sequences, repressing early phage transcription and thereby preventing productive replication. The redistribution of CgpS delays the phage program development and enables a coordinated activation of host defense pathways, including the LexA-regulated SOS response and cell division regulators.
To place these observations in a broader evolutionary context, we extended our analysis by examining the distribution and genomic regions of Lsr2 homologues across actinobacterial lineages.
Our findings expand the known functional landscape of xenogeneic silencers and introduce chromatin-like silencing as a regulatory layer in bacterial antiviral defense, underscoring the remarkable functional diversity of this ancient protein family.

Reference #1

Pfeifer, E. et al (2016) doi: 10.1093/nar/gkw692

Reference #2

Badia Roigé, B. et al (2026) - in review. doi: 10.21203/rs.3.rs-9446490/v1

Reference #3

Author: BADIA ROIGÉ, Biel (IBG1)

Co-authors: Dr POZHYDAIEVA, Nadiia (Department of Bionanoscience, Delft University of Technology, The Netherlands); Prof. OMBELINE, Ombeline (Université Paris-Saclay, CEA, CNRS, Institute for Integrative Biology of the Cell (I2BC), 91198, Gif-sur-Yvette, France); Dr KALOGEROPOULOS, Konstantinos (Center for Translational Protein Design, Technical University of Denmark, Søltofts Plads, DK-2800, Kongens Lyngby, Denmark); Prof. MAXWELL, Karen L. (Department of Biochemistry, University of Toronto, Toronto, Ontario, Canada); Prof. BROUNS, Stan J. J. (Kavli Institute of Nanoscience, 2629 HZ Delft, The Netherlands); Prof. PFEIFER, Eugen (Université Paris-Saclay, INRAE, AgroParisTech, MICALIS, 78350 Jouy-en-Josas, France); Prof. FRUNZKE, Julia (HHU Düsseldorf, Faculty of Mathematics and Natural Sciences Institute of Microbial Interactions, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany)

Presenter: BADIA ROIGÉ, Biel (IBG1)

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