Sociedad Argentina de Microbiología General

XIX CONGRESO DE LA SOCIEDAD ARGENTINA DE MICROBIOLOGÍA GENERAL

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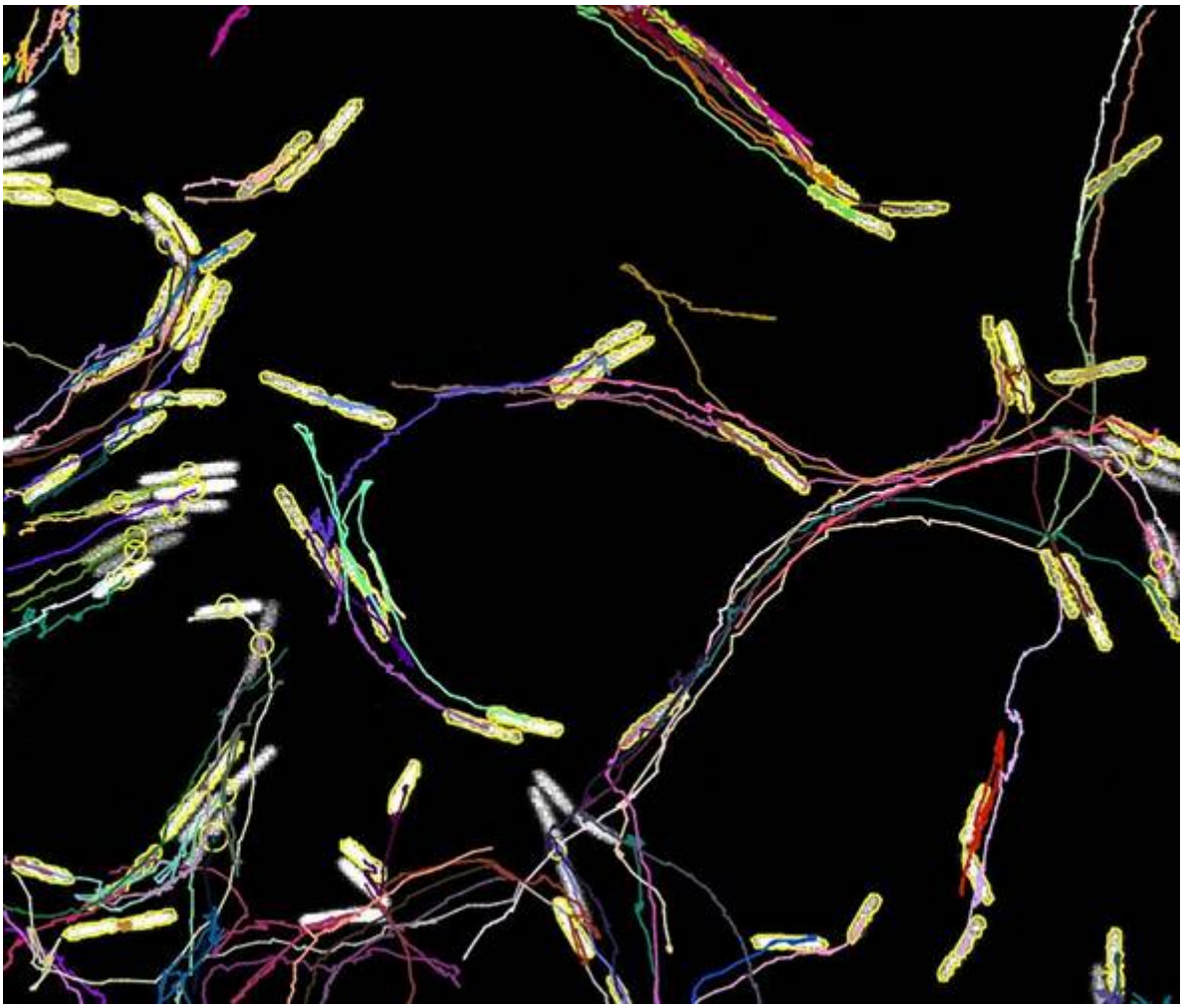

Foto: Se hace camino al andar. Celeste Dea. 1er puesto. Concurso fotográfico SAMIGE 20 años.

YGAV-MEDIATED REACTIVE SULFUR SPECIES HOMEOSTASIS IN *Escherichia coli*

Juncos, Maria Juliana[1] - Mastrogiovanni, Mauricio[2,3] - Fakhoury, Joseph[4] - Gonzalez-Gutierrez, Giovanni[5] - Radi, Rafael[2,3] - Durán, Rosario[6] - Giedroc, David[4,5] - Cuevasanta, Ernesto[2,7] - Capdevila, Daiana A.[1]

1) Fundación Instituto Leloir, Instituto de Investigaciones Bioquímicas de Buenos Aires (IIBBA-CONICET), Ciudad Autónoma de Buenos Aires, Argentina.
2) Centro de Investigaciones Biomédicas (CEINBIO), Universidad de la República, Montevideo, Uruguay.
3) Departamento de Bioquímica, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay.
4) Department of Chemistry, Indiana University, Bloomington, USA.
5) Department of Molecular and Cellular Biochemistry, Indiana University, Bloomington, USA.
6) Unidad de Bioquímica y Proteómica Analítica, Institut Pasteur de Montevideo, Montevideo, Uruguay.
7) Laboratorio de Enzimología, Instituto de Química Biológica, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay
Contacto: maria.juliana207@gmail.com

Hydrogen sulfide (H2S) is a gasotransmitter produced primarily by gut microbiota and has emerged as an important signaling molecule in gut bacteria, as beneficial levels can protect pathogenic bacteria from oxidative stress that arises from inflammatory responses or antibiotics, and microbiota-derived H2S can be toxic for invading bacterial pathogens in the gut. Protein and small molecule Reactive Sulfur Species (RSS) derived from H2S, such as persulfides (RSSH), mediate these beneficial and toxic effects by modifying reactive cysteines through a post-translational modification called persulfidation. Therefore, maintaining RSS homeostasis is essential to leverage their benefits while preventing toxicity. Bacteria achieve this homeostasis by expressing persulfide-sensing transcriptional regulators whose regulon encodes for sulfur detoxification genes. The transcriptional responses that allow this homeostasis in bacteria have been described for several human pathogens, however, little is known about the microbiome's response to rising H2S concentrations and how RSS affect most gut pathogens' metabolism and colonization. Here, we examine RSS homeostasis in non-pathogenic gut bacteria, using *Escherichia coli* as a model organism with the persulfide sensing transcriptional repressor, ArsR familiy member, EcYgaV. Our metabolic profiling and RT-qPCR experiments show that when low molecular weight persulfide increases intracellularly, YgaV upregulates YgaP, the only membrane-bound sulfurtransferase in *E. coli*. Due to the reaction with persulfide-containing mixtures, YgaV forms a pentasulfide bridge between its sensor cysteines, as evidenced by our intact protein mass spectrometry and crystallography results. Pentasulfide formation allosterically inhibits DNA binding

and allows the expression of YgaP, which contributes to clearing sulfide-induced stress. Our proteomics analysis identified a set of genes that respond to sulfide concentrations comparable to those found in the gut, reinforcing the critical role of YgaV in managing sulfide stress. This work highlights the broader impact of persulfidation on the adaptive mechanisms of gut bacteria in response to their chemical surroundings, providing new insights into the delicate balance of RSS homeostasis.

Palabras clave: HYDROGEN SULFIDE - REACTIVE SULFUR SPECIES - HOMEOSTASIS - TRANSCRIPTIONAL REGULATION - GUT MICROBIOTA