

UNIVERSITY OF
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WHAT IS A METAEFFECTOR?

The diagram illustrates the interaction of *Legionella* with a host cell. A *Legionella* bacterium is shown entering the host cell. Inside, it can deliver effectors directly (labeled 'direct') or indirectly (labeled 'indirect'). Directly delivered effectors are shown as red diamonds, while indirectly delivered effectors are shown as blue triangles. These effectors can target host proteins (labeled 'Effectors target host proteins') or other bacterial effectors (labeled 'Metaeffectors directly target other effectors'). The indirect pathway involves a 'HOST TARGET' (red hexagon) that interacts with both the bacterial effectors and the host proteins. The overall interaction is labeled 'Yin-Yang effectors'.

Effectors are proteins delivered to host cells via dedicated bacterial translocation machineries. The intracellular bacterial pathogen, *Legionella pneumophila*, uses a Type IV translocation system to deliver over 300 effectors to the eukaryotic host cell (~10% of its proteome). The canonical role of effectors is to modify host targets. Metaeffectors (or effectors of effectors) directly modify other translocated bacterial proteins rather than the host. Yin-Yang effectors behave like canonical effectors, but indirectly interact through counteracting modulation of a shared host target.

The scatter plot shows the relationship between the percentage of confirmed and putative DITS (N = 392) and normalized yeast fitness (DITS/control). The x-axis ranges from 0 to 100, and the y-axis ranges from 0 to 1.6. A red horizontal line is drawn at y = 0.8, and a red vertical line is drawn at x = 37. The data points show a positive correlation, with a sharp increase in fitness as the percentage of DITS increases from 0 to 37, followed by a more gradual increase.

L. pneumophila infects a broad range of eukaryotic hosts (from protozoa to humans) and modulates conserved eukaryotic pathways. Because they target conserved pathways, 37% of *L. pneumophila* effectors cause a yeast growth defect of $\geq 20\%$ when heterologously expressed. Normalized spot sizes of effector-expressing yeast clones grown at 1,536 spot density.

USING YEAST TO FIND THEM.

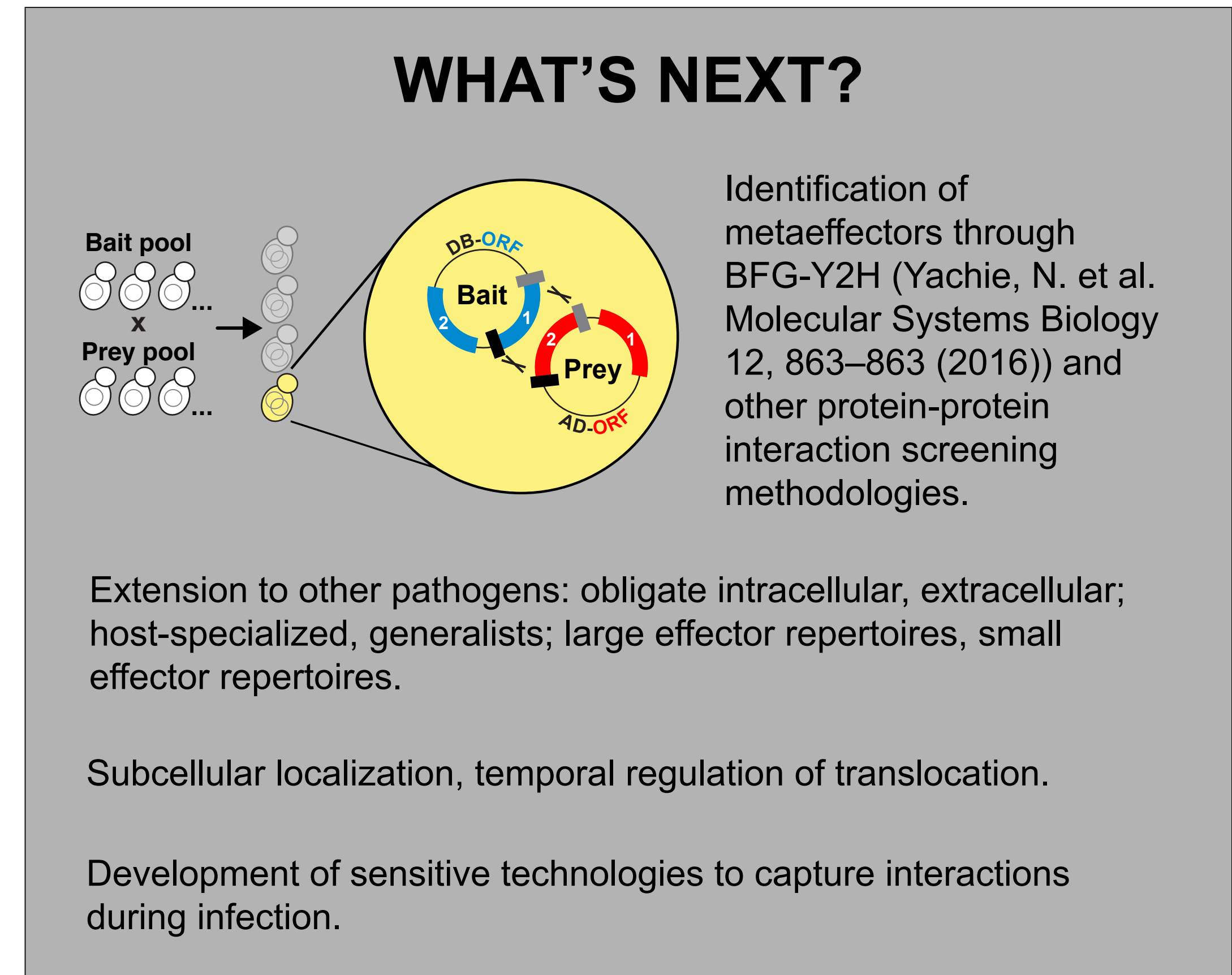
Induce expression. Image diploid spot size:

Query (MAT α , URA3) $\times$ Array (MAT α , HIS3) $\rightarrow$ Diploid (MAT α/α , HIS3, URA3)

sidD (lpg2465)

sidM/drrA (lpg2464) query screen

Results from a 330 x 330 *L. pneumophila* effector screen (>108,000 pairwise combinations). For more information, see: Urbanus, ML, Quail AT et al. Molecular Systems Biology (2016)12:893.



FOR MORE INFORMATION, SEE: <https://www.ensmingerlab.com/>