Team finds fungus-fighting compound

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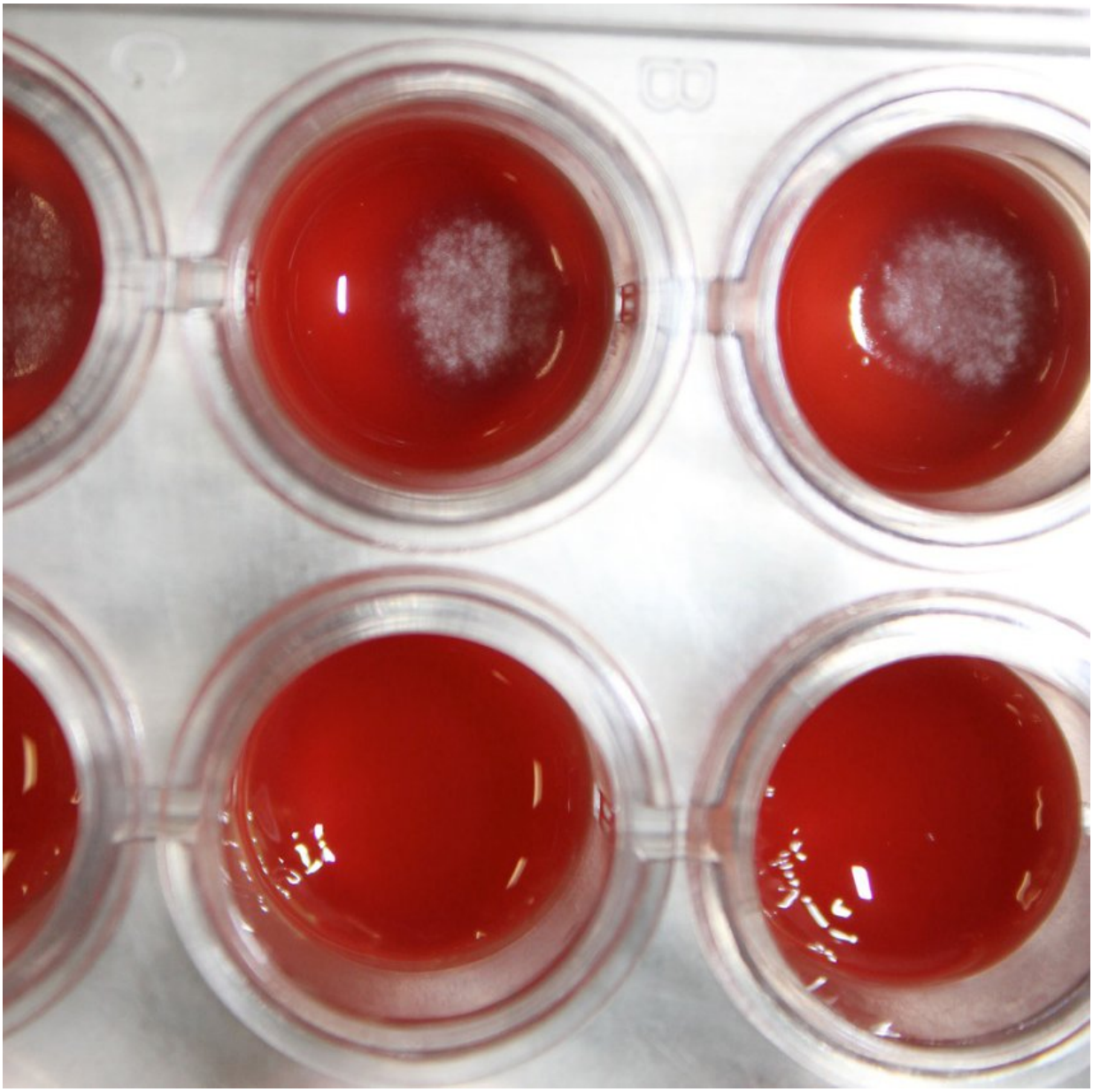

A. fumigatus growth in solid blood media. White spots in wells show fungal

growth while clear wells shows no growth because of SidA inhibition. Credit: Julia S. Martin del Campo

Researchers with the Virginia Tech Center for Drug Discovery have identified a compound that blocks the growth of a fungus that causes deadly lung infections and allergic reactions in people with compromised immune systems.

The research team targeted the switch that allows the fungus *Aspergillus fumigatus* to survive in iron-deficient conditions like the human body. Specifically, they targeted an enzyme known as SidA, which is essential for the synthesis of molecules called siderophores that are made during infection to steal iron from human proteins.

Furthermore, by performing high-throughput screening in the center's Drug Discovery Screening Laboratory, they found a compound called Celastrol that blocks the growth of iron-producing organelles in the fungus.

The results were published in the journal *ACS Chemical Biology*.

"This project shows what an asset the screening lab is to the community," said Pablo Sobrado, a professor of biochemistry in the College of Agriculture and Life Sciences and director of the screening laboratory. "Without the robots and chemical libraries available at the screening lab, this work would not have been possible. We are very fortunate at Virginia Tech to have this facility."

Aspergillus fumigatus is common and is typically found in soil and decaying organic matter. Most people are exposed to it daily with little consequence, but it can cause lung damage in people with compromised

immune systems, such as organ transplant recipients and people with AIDS or leukemia. The mortality rate of this population, when exposed to the fungus, is more than 50 percent, according to the authors.

"Growing antibiotic resistance is demanding the development of target-directed therapies," said Julia S. Martin del Campo, a postdoctoral research scientist in Sobrado's lab. "This approach requires the discovery of enzyme inhibitors that block essential pathogen pathways. The discovery of Celastrol as a SidA inhibitor represents the first building block in the development of drugs against A. fumigatus and related pathogens."

The Virginia Tech Center for Drug Discovery was established in 2012 and is an interdisciplinary group committed to continuing the growth and advancing the stature of the existing drug discovery and development programs at Virginia Tech. The center is housed in the College of Science, with support from the College of Science, the Fralin Life Science Institute, the Institute for Critical Technology and Applied Science, and the College of Agriculture and Life Sciences.

More information: Julia S. Martín del Campo et al. Inhibition of the Flavin-Dependent Monooxygenase Siderophore A (SidA) Blocks Siderophore Biosynthesis andGrowth, *ACS Chemical Biology* (2016). DOI: 10.1021/acschembio.6b00666

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