Classic Spotlight: Crowd Sourcing Provided *Penicillium* Strains for the War Effort

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The discovery of penicillin by Scottish-born microbiologist Alexander Fleming (1) and its development as a drug are one of the great stories of 20th-century medicine. Fleming's important discovery might have remained in the realm of microbiologists were it not for the subsequent pursuit of research essential to its practical application. In 1939, at the dawn of World War II, Howard Florey, Boris Chain, Norman Heatley, and colleagues at Oxford University reinitiated work on penicillin and demonstrated its therapeutic efficacy as an antibiotic. However, several obstacles stood in the way of large-scale production. Two major challenges were the small quantity of penicillin produced by *Penicillium* strains and the need to grow them on solid surfaces rather than in submerged cultures. With the war progressing in Britain, investigations on the industrialization of penicillin production shifted to the United States, coordinated by researchers in the Fermentation Division of the newly established U.S. Department of Agriculture's Northern Regional Research Laboratory (NRRL) in Peoria, IL.

A flurry of research on penicillin occurred in the 1940s, with 82 publications in the *Journal of Bacteriology* in the 5-year period from 1944 to 1948—some delayed by war-related strategy, as indicated in article footnotes (2). Among these publications was a classic article by Robert Coghill and colleagues Kenneth Raper and Dorothy Alexander (3). The team at NRRL, assisted by technician Mary Hunt and anonymous citizens, collected molds from natural sources and isolated 241 strains that they classified within the *Penicillium notatum-chrysogenum* group. They developed an assay for penicillin production, placing agar plugs from plates of *Penicillium* on lawns of *Staphylococcus* and scoring for zones of inhibition. The development of this novel assay, at the time considered high throughput, enabled identification of strains with high levels

of penicillin production on solid surfaces, which were then characterized more extensively using quantitative analyses for penicillin production in submerged cultures. The team documented great variation in penicillin production, concluding that “penicillin production is a strain, rather than a species, characteristic.” The investigations identified several strains superior in yield to the strain used previously for production of penicillin in submerged cultures. Most importantly, this research established a strategy and methodologies that facilitated identification of even higher-yield strains in subsequent years, enabling production of the “miracle drug” that is estimated to have saved more than 80 million lives.

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