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Universal Microbial Diagnostics

The accurate, efficient, and rapid identification of bacteria and other microorganisms is of mounting importance in the fields of health care, disease management, and environmental monitoring (*1*–*3*). In the absence of a rapid identification method, patients are often treated with broad-spectrum antibiotics, which can produce significant, undesirable side-effects, and promote long-term antibiotic resistance. Treatment with such antibiotics is expensive and generates exorbitant expenditures for the both hospital and the patient. Currently, the predominant method for bacterial identification in the clinic relies on culturing (a process which can take anywhere from 24-72 hours), generally followed by gram-stain analysis and antibiotic susceptibility testing. While alternative methods of clinical bacterial identification have been developed (e.g., RT-PCR and DNA microarray based diagnostics), these methods are insufficient for the clinic. They either require *a priori* knowledge of the microbial agent (species-specific), have limited sensitivity, or need a long time to produce reliable results which often worsen patient prognosis during the detection/identification period. These limitations reveal a great need to develop a rapid and accurate clinical bacterial identification system.

Here we propose a new microbial diagnostic platform that satisfies the above desiderata. In common with microarrays and PCR-based techniques, our Universal Microbial Diagnostics (UMD) platform exposes a microbial sample (which may contain more than one genus/species) to a set of random, target-agnostic DNA probes. By measuring the degree to which the sample hybridizes with the collection of random probes, we set up a statistical inverse problem to detect the *presence* and *estimate the concentrations* of the various bacteria in the sample. Using signal recovery techniques from the recently developed theory of compressive sensing (*4*, *5*), we show below that it is possible to stably solve this inverse problem even when the number of probes is significantly smaller than the size of the library of possible bacteria of interest. The proposed UMD platform is not only *universal*, but also, inexpensive, rapid, and phylogenetically informative (as random probes bind to arbitrary spots on the genome). Moreover, due to the universal nature of its probe design, UMD can classify not only known organisms, but also novel mutants with their closest known relatives, such as clinical strains.

We believe the proposed diagnostic can significantly improve clinical treatment decisions for bacterial infections in in-patient settings, and promote more appropriate use of antibiotics for such cases. Our promising preliminary results have been recently published in *Science Advances* journal[1].