Newly discovered plague proteins could help fight bioterrorism and disease

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16-Mar-2007， The Black Death, the great pestilence, bubonic plagueamiliar names for a disease documented since antiquity that has at times caused epidemics throughout the world, most notably during the Middle Ages when it wiped out roughly one-third of Europe population.

Caused by the bacterium Yersinia pestis, which can infect humans through the bite of a rat flea carrier, plague did not disappear into the dusty pages of history but still exists today. In fact, the Centers for Disease Control and Prevention considers Y. pestis a high-priority organism for study because of its potential use for bioterrorism. The bacterium is a potent human health threat that has the power to overcome its host immune defenses. To improve detection and enable the design of new vaccines and treatment, the biological processes that determine the bacterium life cycle and ability to cause disease need to be identified. At Pacific Northwest National Laboratory, scientists recently discovered unique proteins in Y. pestis specifically related to their growing environment that are potential biomarkers for use in detecting the disease and intercepting its progress.

Biomarkers are indicators of change in a biological system that can yield information about the state of a disease, susceptibility and exposure. PNNL scientists Mary Lipton and Kim Hixson, along with colleagues at Lawrence Livermore National Laboratory, re-created the growing environment for Y. pestis in flea carriers and mammal hosts using unique proteomic equipment (a proteome is a survey of proteins in a cell) and cultured the bacteria to express virulence-related proteins. They compared abundance changes of 992 proteins under four different growth conditions at two different temperatures with and without calcium. An increase in temperature and decrease in calcium concentration are two known regulators that trigger the expression of proteins related to the organism ability to cause disease. Changes in these two conditions simulate changes the bacteria encounter as they are transmitted between flea and host. Identifying abundance changes of proteins under the environmental conditions that promote or inhibit the disease can provide insights into the bacterium life cycle.

Lipton and Hixson found 176 proteins and likely proteins in Y. pestis whose numbers rise and fall according to the disease virulence. Of these, 89 were found to have similar changes in abundance to 29 proteins known to be linked to virulence, indicating they are biomarkers related to virulence.

The scientists also uncovered another 87 ypothetical?proteins as unique biomarkers associated with disease condition. A hypothetical protein is defined by the Institute for Genomic Research as one identified by a genefinding algorithm whose sequence matches that of no other known protein and for which there is no other evidence showing it to be a gene product.

These unique biomarkers have promise for use as detection tools in public health, medical and defense applications. Drug and vaccine designers could potentially use these biomarkers to develop new agents to disrupt a biological pathway and intercept the bacteria ability to infect a host.

The approach used in this research is also being applied to search for biomarkers across a wide range of biological systems, from other infectious bacteria such as Salmonella to soil microbes of interest for cleaning up toxic waste. This research study was published in the November 2006 Journal of Proteome Research.

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