Anthrax bacterium's deadly secrets probed

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New insights into why the bug that causes anthrax behaves in the unusual way that it does have come to light thanks to a development under the UK e-Science Programme. Researchers at the North East Regional e-Science Centre have found that the proteins the anthrax bacterium secretes equip it to grow only in an animal host and not in the soil.

This finding sheds light on why Bacillus anthracis does not grow in soil, even though in many ways it resembles a soil-growing bacterium. It has the ability to lie dormant in soil for, in some cases, hundreds of years and then to cause a rapid, often fatal, illness when ingested by a suitable animal host. Bioterrorists have exploited this ability to deadly effect.

Dr. Anil Wipat, Professor Colin Harwood, Tracy Craddock and colleagues at the North East Regional e-Science Centre in Newcastle revealed the new insights after developing a method for deducing and characterising the proteins a bacterium secretes simply from a knowledge of its genome sequence.

Secreted proteins equip a bacterium to survive in its environment and so reveal much about its lifestyle. A soil-living bacterium, for example, secretes proteins that enable it to take up nutrients from the soil. A disease-causing bacterium may secrete proteins that subvert the host's immune system, enabling the bacterium to infect cells or survive in the bloodstream. Knowledge of a pathogenic bacterium's secreted proteins and how they function can therefore help with the search for treatments.

As genes carry the code for proteins, researchers are able to use knowledge of a bacterium's genes to deduce all the proteins it produces. Difficulty arises when trying to pick out only the proteins that are secreted. Methods exist to do this, but are very time-consuming, given that many bacteria secrete 4000 or more proteins. Now, however, the Newcastle researchers have developed an automatic method which makes the identification, analysis and comparison of bacterial secreted proteins from many organisms a realistic proposition.

Based on Taverna workflow technology, which was developed under myGrid, an e-Science project funded by the Engineering and Physical Sciences Research Council (EPSRC), it performs a series of analyses on all the proteins produced by a bacterium to create, by a process of selection and elimination, a list of secreted proteins and their properties. The results are stored in a database. Before this new method, researchers would have had to perform these operations manually, often retrieving algorithms for performing the analyses from separate, distributed computers.

The team decided to test their method on 12 members of the Bacillus family. Family members exhibit a variety of behaviours ranging from the friendly Bacillus subtilis, which lives in the soil, promotes plant growth and is used to produce industrial enzymes and vitamins, to the deadly Bacillus anthracis, which causes anthrax. The full complement of proteins produced by the Bacillus family was fed into the workflow. The number of secreted proteins predicted for each member ranged between 350 and 500.

The secreted proteins were then put through a second workflow which placed them into groups of proteins with similar functions. Of particular interest were groups containing proteins secreted only by pathogenic members and only by non-pathogenic members. Secreted proteins unique to the non-pathogenic bacteria have functions that enable them to live in their habitats, whereas almost all of those unique to the pathogenic family members were of unknown function.

The predicted secreted proteins from Bacillus anthracis help to explain its inability to grow in soil. “When we looked at the secreted proteins, we found that they’re not adapted to utilise molecules in the soil,” says Professor Harwood. However, they do enable Bacillus anthracis to grow in an animal host. Some breakdown animal protein such as muscle fibres, others are the toxins which eventually kill the host, but others belong to the group of proteins of unknown function unique to pathogenic bacteria. “We don’t know what these latter proteins do but we think they help the organism to evade the immune response,” says Professor Harwood. “We’re beginning to understand why Bacillus anthracis behaves in the way that it does –and how it has adapted only to grow in the host and not in the soil,” he adds.

The team is setting up a website to guide users through the process for any bacterium whose genome is known. By identifying the secreted proteins it will be possible to determine some of the previously unsuspected properties of a bacterium, including whether it is likely to be pathogenic or not. The method is also showing promise of commercial application as many enzymes sold commercially, such as plant-derived enzymes used for biofuel production, are proteins harvested from bacteria which secrete them naturally.

Source: Research Councils UK