Finding new ways to tackle environmental diseases

December 23 2010

Researchers at the University of Exeter have developed a new approach to studying potentially deadly disease-causing bacteria which could help speed up the process of finding vaccines.

Dr Andrea Dowling, from the Centre for Ecology and Conservation at the university's Cornwall Campus, has pioneered a simple screen which can help isolate the virulent parts of the gene structures of pathogenic* bacteria.

The screen allows researchers to simultaneously run thousands of tests where genes from the pathogen are pitted against the human blood cells that normally attack them.

"By looking at the results from these tests it is possible to determine which parts of a pathogen's genetic code allow it to override immune systems," said Dr Dowling.

"From there we can focus in on those key areas to find out how the pathogen works and how we can develop vaccines. The screen allows us to study and tackle the causes of disease and infection much quicker than other methods."

The screen has been used by Dr Dowling and other researchers at Exeter to look at genes in the important pathogen, *Burkholderia pseudomallei***, which causes the potentially deadly human disease, melioidosis. The research is published in the journal, PLoS ONE.

Burkholderia appears to be able to infect man directly from the environment via cuts and grazes. Normally any invading bacteria would be consumed by the body's immune system, but *Burkholderia* bacteria seem to resist being eaten and can spread to other parts of the body in a very nasty infection.

Using the screen, the researchers were able to isolate the unique parts of *Burkholderia*'s genetic code which could be responsible for its resistance to the human immune system.

Dr Dowling explained: "We used library-clones which each contain a genetic region of *Burkholderia*, and then studied each one's ability to kill immune cells to find what are known as virulence factors – basically the parts which allow it to override the immune system. Using the screen, we established the potential locations of that virulence factor much quicker than using normal methods.

"We can then study the mechanism for these factors using microbiological, cellular and biochemical techniques to see whether disrupting the virulence factor reduces the abilities of this bacteria to overcome the immune system."

Professor Richard Ffrench-Constant, a co-author of the research, said: "Knowledge gained from this research provides essential insights into how this poorly understood, but extremely serious human pathogen works to cause disease, and, crucially, it helps us identify candidates for the development of much needed vaccines."

The techniques used for this research are not only important in looking at *Burkholderia*, but can also be used on many other pathogens.

More information: Read the open-access, full-text article here: dx.plos.org/10.1371/journal.pone.0015693

Notes:

*Almost half of all human diseases are caused by pathogenic bacteria. Pathogens produce symptoms of disease by disrupting the normal cellular processes of their host by producing agents known as 'virulence factors'. Virulence factors can allow the bacteria to adhere, invade, replicate within and/or kill their host cells and tissues, allowing the pathogen to establish infection. Understanding how these virulence factors work enhances ability to combat disease.

**Burkholderia pseudomallei is a serious human pathogen which causes a disease known as melioidosis. Infection is usually caused by exposure of cuts on the skin to contaminated soil or water, or via inhalation. B. pseudomallei is widespread in South East Asia and Northern Australia where lethal infection can result in a mortality rate of up to 50%. This pathogen is highly resistant to antibiotics and is listed as a Category B bio-warfare threat making it an extremely high priority for research as no vaccine currently exists. B. pseudomallei have a complex intra-cellular lifestyle. The pathogen uses its virulence factors to attach, invade, replicate within and kill host cells thus establishing infection. These mechanisms of pathogenicity are not well understood and research into them will be critical in identifying the key novel virulence factors behind them, how they interact with the host cell, and how they may be used for vaccine development.

Provided by University of Exeter