On the trail of rogue genetically modified pathogens

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Bacteria can be used to engineer genetic modifications, thereby providing scientists with a tool to combat many challenges in areas from food production to drug discovery. However, this sophisticated technology can also be used maliciously, raising the threat of engineered pathogens. New research published in the online open access journal *Genome Biology* shows that computational tools could become a vital resource for detecting rogue genetically engineered bacteria in environmental samples.

Jonathan Allen, Shea Gardner and Tom Slezak of the Lawrence Livermore National Laboratory in California, US, designed new computational tools that identify a set of DNA markers that can distinguish between artificial vector sequences and natural DNA sequences. Natural plasmids and artificial vector sequences have much in common, but these new tools show the potential to achieve high sensitivity and specificity, even when detecting previously unsequenced vectors in microarray-based bioassays.

A new computational genomics tool was developed to compare all available sequenced artificial vectors with available natural sequences, including plasmids and chromosomes, from bacteria and viruses. The tool clusters the artificial vector sequences into different subgroups based on shared sequence; these shared sequences were then compared with the natural plasmid and chromosomal sequence information so as to find regions that are unique to the artificial vectors. Nearly all the artificial vector sequences had one or more unique regions. Short

stretches of these unique regions are termed 'candidate DNA signatures' and can be used as probes for detecting an artificial vector sequence in the presence of natural sequences using a microarray. Further tests showed that subgroups of candidate DNA signatures are far more likely to match unseen artificial than natural sequences.

The authors say that the next step is to see whether a bioassay design using DNA signatures on microarrays can spot genetically modified DNA in a sample containing a mixture of natural and modified bacteria. The scientific community will need to cooperate with computational experts to sequence and track available vector sequences if DNA signatures are to be used successfully to support detection and deterrence against malicious genetic engineering applications. Scientists would be able to maintain an expanding database of DNA signatures to track all sequenced vectors.

"As with any attempt to counter malicious use of technology, detecting genetic engineering in microbes will be an immense challenge that requires many different tools and continual effort," says Allen.

Source: BioMed Central