Supplementary Information

Experimental

DNA Extraction

A Qiagen™ QIAamp DNA Mini Kit was used to extract DNA from CSF and blood. Briefly this involved an initial Proteinase K liquefaction step followed by lysis with guanidine hydrochloride and DNA adsorption onto the QIAamp silica-gel membrane columns. Multiple wash steps were used to reduce inhibitors and DNA was eluted with buffer. This method produces high quality DNA suitable for PCR.

PCR

PCR was carried out using a Stratagene MX3005P fluorimeter and a commercially available Qiagen PCR kit which includes: PCR buffer, $MgCl_2$, dNTPs and Taq polymerase. Each reaction had a total volume of 25 µL; 2.5 µL of Qiagen reaction buffer (10x), 1 µL of $MgCl_2$ solution (25 mM), 0.4 µL of deoxynucleoside triphosphates (10 mM), 1 µL of forward primer (10 µM), 1 µL of reverse primer (10 µM), 0.5 µL of Taq Polymerase (5 U), 1 µL of pathogen DNA and made up to the total volume (25 µL) with DEPC treated water. PCR was then carried out using the following thermal profile: 10 min at 95 °C, followed by 45 cycles of 95 °C for 30 s, 58 °C for 1 min then 72 °C for 1 min and a final extension for 1 min at 72 °C.

SERS Assay

A biotinylated modified sequence and a 5' phosphate/fluorophore modified sequence underwent a sandwich hybridisation event with the amplified bacterial pathogen DNA from clinical samples using a Minicycler PTC-150 system. An aliquot of each DNA sequence (10 µL, 1 µM) was added to a PCR tube containing phosphate buffered solution (70 µL, 0.3 M). The temperature was held at 90 °C for 10 min, and then was lowered to 10 °C for 10 min. For the no target control (NTC), pathogen DNA was omitted from the PCR amplification and replaced with distilled water. Once the sequences were hybridised, 15 µL of Streptavidin coated magnetic beads were added to the PCR tubes and left at room temperature for 30 min. Three washing steps were carried out using phosphate buffered solution (70 µL, 0.3 M). The beads were then resuspended in exonuclease buffer (30 µL, 1x) and lambda exonuclease was added (2 µL, 1U) for digestion to occur for 90 min at 37 °C. SERS analysis was performed post-digestion.

SERS Analysis

SERS analysis was performed using an Avalon Plate Reader (Belfast, UK), with an excitation wavelength of 532 nm. A 96 well plate was placed onto a stage and the instrument's software was used to automatically move the stage so that spectra could be recorded from each well. The accumulation time was 1 s. A single well can hold 300 µL. Prior to SERS analysis, the supernatant was removed that contained the free fluorescent dye (30 µL) and was added to the well that contained citrate reduced silver nanoparticles (0.2 nM, 150 µL), spermine tetrahydrochloride (0.1 M, 20 µL) and distilled water (100 µL). Spectra were baseline corrected using a multipoint polynomial fit and level and zero mode using Grams software (AI 7.00).