

EMMA™ TECHNOLOGY

METHOD

Improving sensitivity of electrophoretic heteroduplex analysis using nucleotides as additives: Application to the breast cancer predisposition gene *BRCA2*

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Abstract A new method for the detection of unknown mutations, enhanced mismatch mutation analysis (EMMA), is proposed. It is based on electrophoretic heteroduplex analysis (HDA). The resolution is considerably improved, thanks to the combination of high-resolution block-copolymer sieving matrix, and nucleosides as additives in the electrophoretic medium. The EMMA method is compared to denaturing HPLC (DHPLC) in a large-scale study of mutations in the breast cancer-associated gene *BRCA2*, involving 4655 DNA amplicons from 94 patients. The rate of false positives was 0.09%. The raw success rate, without optimization of the amplicons tiling, was 94%, a value much higher than that achieved earlier with HDA, and comparable with that obtained with DHPLC. An analysis of the missed mutations suggest that the success rate could be improved up to about 97%, simply by redesigning the amplicons, while retaining the speed, cost effectiveness, and simplicity of the method.