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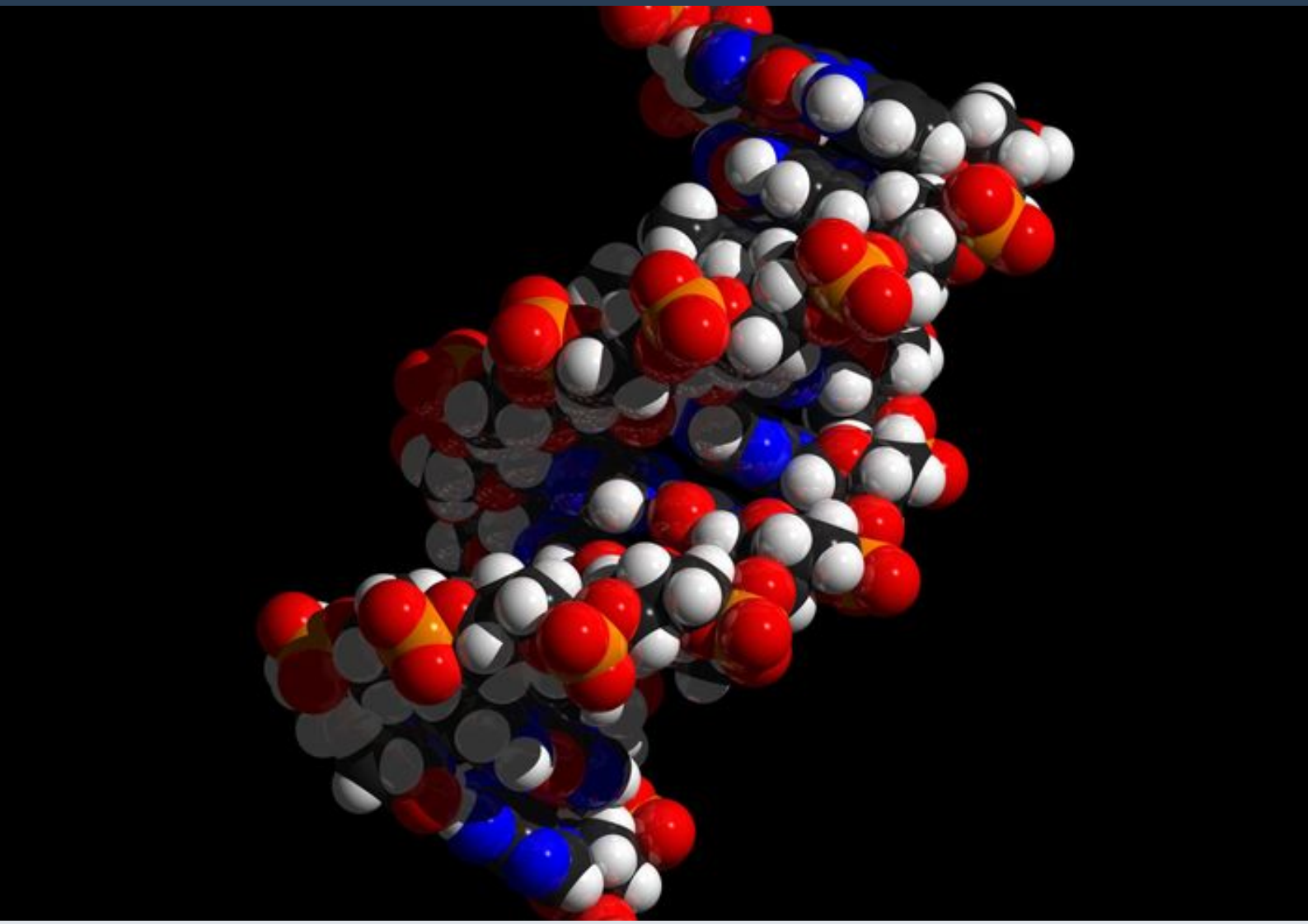
A Novel Method of Testing for Lynch Syndrome

A PCR based genetic testing method that does not require capillary electrophoresis equipment to complete



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About **University of Nottingham**

The University of Nottingham produces world-changing research by focussing on the problems and challenges that affect societies and people on a wide scale. More than 80% of Nottingham research is ranked in the highest categories ‘world-leading’ or ‘internationally excellent’.

Background

Lynch Syndrome is a form of hereditary cancer affecting approximately 2-5% of the population. The cancers arising in Lynch Syndrome are mainly colorectal cancers and these are characterised by (i) a feature known as microsatellite instability (MSI) and (ii) by an absence of mutations of the BRAF gene. Currently only at risk people are tested for the presence of Lynch Syndrome but NICE guidance is imminent which will recommend that ALL patients with colorectal cancer undergo testing for Lynch Syndrome. The guidance (currently out for consultation) will recommend a strategy whereby tumours are tested for both MSI and BRAF mutation.

Currently the testing for MSI and BRAF mutations involves multiple steps and specialist instrumentation.

MSI testing: this involves testing tumour DNA using 5 different PCR reactions. The products of these reactions are then analysed on a Capillary Electrophoresis (CE) machine.

BRAF mutation testing: this involves testing tumour DNA using 1 PCR reaction. The products of this reaction then undergo Sanger sequencing.

Tech Overview

This improved technology represents a simplified work stream as detailed below:

- MSI testing - this involves testing tumour DNA using 5 different PCR reactions with HRM performed as part of this reaction.
- BRAF mutation testing - this involves testing tumour DNA using 1 PCR reaction with HRM performed as part of this reaction.

The primers used for both MSI and BRAF testing have been designed in-house by the researchers and are not published.

Thus, both current practice and this test involve PCR. However, the current technology does not require the second step of CE or Sanger sequencing as the HRM is done as part of the PCR. This significantly cuts down the amount of work necessary to achieve the same result. Implementation of this test in Molecular Diagnostics Labs will therefore save money both in terms of manpower and consumables compared to current practice. Given the imminent NICE guidance will result in an increase in workload for testing for Lynch Syndrome, the savings may be significant.

This test requires real-time PCR machines with HRM capability. These are common and would be present in most Molecular Diagnostic labs. In contrast, the capillary electrophoresis machines and sequencing machines are not required.

Stage of Development

The current practice for MSI testing with this test on a retrospective series of 60 colorectal cancers has been compared. The results were nearly identical and therefore the researchers are happy that their test is sufficiently robust for clinical practice. The researchers are in the process of comparative testing of some cases prospectively for further evaluation of the test.

Benefits

- Negates the requirement for expensive specialist instrumentation
- Reduced steps in the workflow compared to current practice
- As robust as the current practice

Applications

The test is designed for the specific application of screening for Lynch Syndrome in clinical molecular diagnostics laboratories.