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EDITORIAL

# British Journal of Biomedical Science in 2020. What have we learned?

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**ABSTRACT**

Each year the British Journal of Biomedical Science publishes a 'What have we learned' editorial designed to introduce readers within the major disciplines of laboratory medicine to developments outside their immediate area. In addition it is designed to inform a wider readership of the advances in the diagnosis and treatment of disease. To this end, in 2020 the journal published 39 articles covering the disciplines within Biomedical Science in the 4 issues comprising volume 77. These included a review of COVID-19 in this issue, 27 original articles, 6 Biomedical Science 'In Brief' and 4 case histories. 27 of the articles involved molecular techniques, with one of these comparing results with a mass spectrometry based method. The preponderance of molecular genetic studies gives us a good idea of the likely future direction of the disciplines

**KEYWORDS**

Biomedical Science; Cellular Pathology; Clinical Chemistry; Cytopathology; Heamatology; Immunology; Microbiology; Transfusion Science; Virology

## Introduction

The *British Journal of Biomedical Science* is the leading international journal focussing on practice, research and education in all aspects of biomedical science as it applies to the diagnosis and treatment of human disease. The growing importance of the journal is highlighted by its recent increase in impact factor (to 2.712) and by its broad range of papers covering all the pathology disciplines, which is of increasing importance as the traditional boundaries become blurred with multidisciplinary working and cross-disciplinary techniques, particularly in molecular genetics. As will be apparent from the tables of contents of the journal in the last few years, molecular methods are becoming increasingly important in all the disciplines and perhaps point towards a future where a single laboratory uses these methods for analyses crossing all the traditional laboratory streams.

## Molecular genetic studies

Starting with molecular genetic studies therefore, issue 1 opened with an investigation of single nucleotide polymorphisms (SNPs) in the DNA repair gene also termed X-ray Cross Complementary gene-4 (*XRCC4*) which is located on chromosome 5, specifically at 5q14.2 and forms part of the non-homologous end joining (NHEJ) system [1]. This system has the function of repairing breaks in double-stranded DNA, and therefore defects in this system may have a critical role in cancer initiation and progression. Gupta and colleagues [2] showed a clear link between several of the genotypes and the development of cervical cancer, adding this to an association between SNPs in this gene and the development of cancers in a number of tissues including the bladder, breast, prostate, liver and GI tract, thyroid, lung, leukaemia and multiple myeloma (see [2] for references).

Another area investigated was a disorder of the cornea, keratoconus [3], which like the other conditions investigated in this year's volume of the journal involve a number of potential genes. The matrix metalloproteinases (MMPs) are a group of extracellular endopeptidases with a key role in extracellular matrix remodelling by degrading various types of collagen [4]. The study [5] examined the effect of SNPs in the genes for collagen type 4 (*COL4A3), TIMP-1* (a gene for one of the tissue inhibitors of MMPs) and *MMP-9*. As the TIMP-1 gene is on the X chromosome, male and female subjects were investigated separately. The authors also measured tear levels of TIMP1 and MMP-9, with the former showing decreased and the latter increased levels compared with controls. A SNP in each gene was associated with the presence of keratoconus.

A further area investigated in issue 1 was pregnancy loss, which showed a relationship between SNPs in two of the Toll-like receptors (TLRs) expressed in humans [6]. TLRs have an important role in the immune system, assisting in the recognition of antigens from invading microorganisms and the activation of the innate and adaptive immune systems. The developing foetus is a challenge for the immune system in the mother as clearly any immune response is likely to have a serious unwanted outcome [7]. The study investigated SNPs in TLR4 and TLR2 and showed a link between a SNP in TLR2 and recurrent pregnancy loss [6].

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Issue 4 continued this broad theme presenting three different studies investigating the role of SNP polymorphisms on issues pertaining to female infertility. The paper by Jodeiryzaer et al [8] tests the hypothesis that two oestrogen receptor alpha SNP's relate to female infertility. The biological functions of oestrogen are mainly mediated by binding to the oestrogen receptors (ERs), of which there are two isoforms, ERα and ERβ. ERα is encoded by the gene *ESR1* on chromosome 6q25.1 and is formed from 8 exons with more than 2200 SNPs [9,10]. Specific polymorphisms in *ESR1* may directly or indirectly lead to variations in its activity and have significant impacts on different diseases. Some have considered *ESR1* variants to be one of the important causative factors in female infertility [11]. One of the most studied SNPS on ESR1 is rs104893956 (Arg157Ter: C > T) found in exon 2 leading to a stop codon. A further SNP is rs121913044 (Val364Glu T > A) located at exon 4 which results in the substitution of Valine (Val) to Glutamic acid (Glu) at codon 364 [12] and which is located within the binding site of ERα protein. In the current study [8], found both SNPS to be associated with female infertility though the results for the rs104893956 variant to be the most convincing. In silico characterization of this SNP has previously suggested its role in disease by truncating or even inactivating ERα [12]. Jodeiryzaer and colleagues [8] provide translational evidence to support its potential role in female infertility.

The case-control study by Tajalli et al. [13] investigates the association of *hTERT* SNP (rs2736100) with implantation failure after *in vitro* fertilization and embryo transfer (IVF-ET). Human telomerase is a ribonucleoprotein complex composed of the telomerase reverse transcriptase (hTERT) and the telomerase RNA component (TERC) [14]. The authors find a significant association between this polymorphism and success of IVF-ET outcome, with the results suggesting that individuals with the CC genotype of the *hTERT* rs2736100 polymorphism may be at increased risk of implantation failure.

In the third paper in this issue related to infertility, Daghestani et al. [15] study the relevance of *KISS1* gene polymorphisms in susceptibility to polycystic ovary syndrome and associated endocrine and metabolic disturbances. Polycystic ovary syndrome (PCOS) is a gynaecological condition that occurs in 3–10% of women of childbearing age. It presents with menstrual irregularity, excessive hair growth, weight gain and infertility [16,17]. The *KISS1* gene contributes to regulation of the hypothalamic-pituitary-gonadal (HPG) axis. The authors hypothesise a link between *KISS1* SNPs in PCOS, and their effects on hormonal and metabolic parameters. The authors report a novel SNP rs1213704663 C/G identified in the 3′-untranslated region of the gene. Both the homozygous (GG) and heterozygous (CG) genotypes of rs1213704663 occurred at a significantly higher frequency in the PCOS group as compared to controls and points to a possible role of this polymorphism in PCOS associated luteinizing hormone and oestrogen hypersecretion.

The effect of SNPs in immune-system genes was also demonstrated in the association between the IL-28B genotype and the hepatitis C virus (HCV) [18], a field further complicated by the different genotypes of HCV itself. These SNPs were not only linked to the likelihood of spontaneous viral clearance, but other authors have shown links between SNPs in this gene to the development of fibrosis, cirrhosis and Hepatocellular carcinoma (HCC) and indeed response to antiviral therapy. Issue 3 included a report on the Fas cell surface death receptor (FAS) and its ligand (FASL) which play an important role in antiviral immunity [19]. Huang and colleagues [20] showed the polymorphism rs763110 in FASL to be linked to HCV infection. Computer modelling of the mRNA secondary structure suggested an effect on FASL mRNA translation which links with other studies showing altered binding of FASL to other transcription factors [21]. Taken together these data suggest decreased apoptosis (and therefore a greater risk of the infection taking hold) in persons with this particular polymorphism.

The links between SNPs and cancers continued in issue 2 with an association between a SNP in the vitamin D receptor gene and hepatocellular carcinoma (HCC) in patients with HCV cirrhosis [22]. The CC genotype for the SNP was a better marker for HCC than serum alphafeto protein (AFP), this finding adds to the involvement of SNPs in the vitamin D receptor in a number of other tumour types [23].

A link between polymorphisms in a number of cytokine genes (IL-1RN, IL-1β, IL-6 and TNFα) to cervical cancer [24]. They examined a group of patients with stages 11B to 111B of cervical carcinoma and a group of matched controls. They noted agreement with a study of gastric cancer in an Italian population [25] and cervical cancer [26]. The authors noted a link between these polymorphisms and survival though this was not significant suggesting other factors are involved in the development and prognosis of this disease.

Thyroid cancer has an increasing global incidence, with papillary thyroid carcinoma (PTC) accounting for 80–85% of cases [27]. Heidari and co-workers [28] hypothesised that known polymorphisms in the gene for caspase-3 (*CASP3*) which has a key role in apoptosis, would be associated with the development of this carcinoma. They noted no association between the polymorphisms studied and PTC, however the rs4647610 polymorphism was associated with a larger tumour size, and the rs4647602 was associated with lower tumour stage and thus might be protective.

Juvenile idiopathic arthritis (JIA) is the most common cause of chronic arthritis in children and is

thought to have a genetic element [29]. Ali and colleagues [30] investigated the link between JIA and one polymorphism each in *PAD14* (the gene for type IV peptidylarginine deaminanase, PADI), *PDCD1* (the gene for programmed cell death molecule, PD-1) and *CTLA4* (the gene for cytotoxic T-Lymphocyte antigen 4). A complex association of polymorphisms in the above genes was noted with an association between *PAD14* and *PDCD1* linked to the disease, but not its activity, *CTLA4* weakly linked to disease activity, *PAD14* linked to the childhood health assessment questionnaire (CHAQ) score, and *PDCD1* linked to anti-CCP antibodies, RF and the CHAQ score.

Smoking kills more than 5 million people every year worldwide, with more than 70% of deaths caused by lung cancer and chronic obstructive pulmonary disease COPD [31].The integrity of the alveolar surface in the lungs during the ventilation cycle is maintained by secreted products that include surfactant proteins (SPs): SP-A, SP-B, SP-C and SP-D [32]. El Gayed et al [33], in the current issue of the journal, suggest that a genetic factor renders some smokers more susceptible to developing COPD than others. Nicotine functions via neuronal and peripheral nicotinic acetylcholine receptors (nAChRs). The authors hypothesized a link between serum SP-D and the nicotinic acetylcholine receptors (nAChRs) (rs1051730) (G/A) gene polymorphism. The results showed this nicotinic acetylcholine receptor polymorphism, and specifically the AA genotype and A allele, to be significantly increased in smokers with COPD.

Finally in issue 3 an investigation into Behçet's disease which, although relatively rare, is a chronic multisystemic disorder with considerable morbidity and disability [34]. A polymorphism in the tumour necrosis factor superfamily member 15 gene (TNFSF15) was shown to be associated with the development of ocular lesions in this disorder [35]. The authors acknowledge the need for larger multi-centre studies to confirm the finding and to elucidate the mechanism behind the association of the gene with the disorder.

A further area for development in molecular techniques involves micro RNA (miRNA). These small single-stranded RNA molecules are becoming increasingly recognised as having a key role in the development of many types of cancer [36]. Issue 1 included 2 studies in this area: Firstly, Barhreini and colleagues [37] examined a polymorphism in mi-559 (rs58450758) and demonstrated using computer modelling techniques a predicted change in the secondary structure of the miRNA which would shorten its life-span, thus decreasing its inhibitory effect. Patients in this study with breast cancer had a significantly higher frequency of the TT genotype, and it can be hypothesised that the decreased inhibitory effect predisposes to this malignancy.

miR-125 has been widely conserved in evolution, with three members present in humans with changes in circulating level of each implicated in resistance to chemotherapy [38]. In a study examining miR-125a-3p and miR-125b expression in leukocytes it was noted that levels of the former significantly decreased and the latter significantly increased in subjects with breast cancer compared to controls [39].

Turning again to micro MRAs in issue 2, a polymorphism in miR-627 (rs2620381) in patients with gastric cancer showed a significantly higher frequency of the C SNP compared to controls [40]. In silico analysis of the secondary structure of miR-267 showed an extra area without a paired base. The authors speculate that this difference in structure is implicated in the development of gastric cancer, but acknowledge that a prospective study is required to determine its use as a possible biomarker.

Colorectal cancer is the most common form of cancer worldwide [41] and miR-410 is implicated in the development of various cancers either as a suppressor or as an inducer [42]. This miRNA was shown to be expressed at higher levels in tumour tissue in patients suffering from colorectal cancer compared to adjacent non-cancerous tissues. Furthermore, patients expressing higher levels of this miRNA had a significantly poorer prognosis and this was independent of other risk factors [43].

Abdeltawab et al. [44] in this issue of the journal look at the association of micro RNA-223 and angiopoietin-like protein 8 as potential biomarkers of gestational diabetes mellitus. Gestational diabetes mellitus (GDM) affects approximately 7% of all pregnant women [45]. It leads to higher risks during pregnancy and the severity of the complications are proportional to the severity of the hyperglycaemia. The condition is defined as glucose intolerance diagnosed during the second or the third trimester of gestation with no previous history of diabetes outside pregnancy [46]. The pathophysiology of this condition is attributed to the insufficient adaptation of β-cells to peripheral insulin resistance [47]. Different miRNAs participate in the pathogenesis of diabetes [48] and angiopoietin-like protein 8 (ANGPTL8) is known also to play a role in the regulation of glucose homoeostasis. The authors found a significant increase in mean miRNA-223 and ANGPTL8 levels in women with GDM women compared to pregnant women without the condition.

A fourth paper in issue 4 concerned with gynaecological disturbances is the study by Asadi-Tarani et al [49] investigating the relationship between maternal and placental polymorphisms of the microRNA (miR)-196a2 and miRNA-499, with preeclampsia. Preeclampsia is a disorder of gestation that affects a small proportion of all pregnancies and is an important cause of maternal and perinatal morbidity and mortality [50]. Although several pathophysiologic mechanisms are involved in preeclampsia, the precise underlying reason for its onset are unclear but may

include abnormal spiral artery remodelling, endothelial cell dysfunction, oxidative stress, immune-system alterations, and systemic inflammation [51]. The authors hypothesise that altered miRNA levels may result in dysregulated expression of their target genes, abnormal function of the placenta and subsequent complications such as preeclampsia [52]. They focus on the links between maternal and placental rs11614913 and rs3746444 polymorphisms in miR-196a2 and miR-499 with preeclampsia and found that the maternal/placental rs3746444 CC genotype is associated with higher preeclampsia risk.

Another area of molecular techniques is epigenetics where modifications to gene activity can be passed from generation to generation or can lead to alterations in gene activity in life. Issue 1 included an examination of DNA methylation in HCC. Methylation of DNA has long been understood as a means whereby gene expression can be regulated by hypo or hypermethylation at gene promoter sites. This has been shown to occur in the development of HCC, chronic hepatitis and hepatic cirrhosis [53] and this may be additionally affected by HCV viral proteins [54]. The methylation of three tumour suppressor genes (*RUNX3, RASSF1A* and *E-Cadherin*) in a control population were compared with subjects with HCV-related cirrhosis and a further group with HCC. There was significant hypermethylation in patients with HCC, and regression analysis showed the *RASSF1A* and *E-Cadherin* hypermethylation predicted HCC within cirrhosis, but only *E-Cadherin* predicted HCC in patients with a low AFP, thus suggesting a diagnostic role of the hypermethylation of this gene in the early detection of HCC [55].

The genome contains areas of DNA termed microsatellites which are sequences of repetitive DNA units, which can lead to errors in the DNA mismatch repair system. This leads to microsatellite instability (MSI) which can be detected in the DNA of peripheral cells. This screening is used in detecting Lynch syndrome, where there is a 50–70% lifetime risk of developing colorectal cancer, and a 40–60% risk of developing endometrial and other malignancies [56]. Issue 3 opened with a report from Sanchez and colleagues [57] examined a MSI in the Caspase 2 gene (*CAT25*), BAT 25 which occurs in the *c-kit* and BAT26 located in *hMSH2*. The authors showed CAT25 analysis to be fast as it can use high-resolution PCR rather than the usual capillary electrophoresis and has a 100% predictive value for a tumour having high MSI.

Issue 3 also included a study of a long intergenic non-protein coding RNA (LINC). These molecules are at least 200 nucleotides in length and have roles in the innate and adaptive immune systems [58,59]. Furthermore, they may be present in the circulation and have been shown to have roles in the development of cancers and disease pathogenesis. Wahba et al. [60] showed an association between LINC00305 which was significantly increased in the blood of rheumatoid arthritis (RA) patients, and CRP, ESR and the 28-joints disease activity score (DAS). Furthermore, a polymorphism in this LINC is associated with increased severity and activity of RA.

And finally in the area of molecular genetic studies, membranous nephropathy is the major cause of nephrotic syndrome in adults, and can be idiopathic (IMN) or secondary (SMN) to a number of causes including systemic lupus erythematosus (SLE), hepatitis B virus (HBV) and HCV [61]. IMN accounts for about 70% of MN cases and has a varied outcome from spontaneous resolution in a third of cases, with another third developing thrombotic or thromboembolic events, UTIs or cardiovascular disease. The remainder will suffer from a progressive decline in renal function with 35% of them developing end-stage renal disease within 10 years. IMN is characterised by antibodies to the M-type phospholipase A2 receptor (PLA2R) which are not detectable in patients with SMN or other autoimmune diseases, and SNPs in the gene for this receptor have been associated with IMN in European [62], Korean [63] and South Asian [64] populations. A further study in issue 1 examined two distinct populations in China [65] showed an association between SNPs in the gene and IMN, but with differences in the SNPs implicated in the Chinese as opposed to the studies in other nationalities. Furthermore, they found one SNP to be associated with SMN.

## Summary of the molecular genetic papers

A typical issue with studies of genetic markers is a restriction to a clearly defined population, with a clearly defined disease state. As our knowledge of the interactions between genes increases it will become increasingly important to broaden the populations included in the studies to begin to isolate other genes affecting the condition. Commendably authors pointed out that they had not examined all the known SNPs in these genes, or due to low sample numbers had not been able to perform subgroup analyses. As with a lot of studies of SNPs they tend to investigate a fairly narrow population or disease type; therefore, mass population screening using these findings will require much larger studies across the world. However, their importance in identifying at risk individuals within a particular population cannot be overestimated. Furthermore, the inter-relationship between genes needs to be determined – what is deleterious in one condition may be protective for another, or a SNP may only become important when acting in concert with a deleterious SNP in another gene.

## Biomarkers

More traditional biomarkers have also been investigated. In issue 1 the involvement of autoantibodies in RA. This is a chronic systemic autoimmune disease with a global prevalence of 0.51%. It is characterised by inflammatory lesions in synovial tissue which develop quickly (75% of cases within 2 years) leading to joint destruction and function with ensuing disability [66]. The pathogenesis of the disorder has yet to be defined; however various cytokines and inflammatory mediators have been implicated [67]. Early diagnosis of the disease is complicated by the diverse nature of the disorder and a lack of a good early serological marker, but is clearly important. Huang and colleagues [68] investigated a series of markers known to be raised in RA, namely high-mobility group box-1 (a DNA chaperone that acts as a proinflammatory cytokine), anticitrullinated peptide antibodies (anti-CCP) which are the most specific for RA and predict joint damage, rheumatoid factor (RF, widely used in clinical practice), anti-mutated citrullinated vimentin antibodies (anti-MCV) and a new marker serum 14-3-3η which is highly specific and related to the severity of the disease. Despite this battery of markers there has been little comparison of their diagnostic use. This study comparing patients with RA, those with other connective tissue disorders and controls showed 14-3-3η followed by RF, whereas the combination of anti-CCP and anti-MCV was the most specific and sensitive for diagnosis of RA.

Abelhardy et al. [69] in this issue of the journal consider the prognostic value of bone marrow MUC4 expression in acute myeloid leukaemia (AML), an aggressive haematological malignancy affecting adults and linked to a combination of environmental factors, chromosomal aberrations, and gene mutations. It is a cytogenetically, and molecularly heterogeneous disease characterized by over-proliferation and accumulation of myeloid blasts in the bone marrow and blood [70,71]. Although the survival rate in AML has improved, relapse remains an issue [72] and accurate prognosis of the disease is difficult. The *MUC4* gene is located at chromosome locus 3q29 and encodes the transmembrane protein mucin-4 (MUC4) [73]. With its epidermal growth factor (EGF)-like domains, MUC4 binds to human epidermal growth factor receptor (HER2), to facilitate signal transduction, cell proliferation, and cell survival [74,75]. Interestingly, the authors found bone marrow MUC4 expression to be significantly raised in AML patients. Low levels of MUC4 expression was associated with persistent remission, whilst high levels were associated with worse overall and disease-free survival, suggesting a useful prognostic role for MUC4 in the management of AML.

HCC is around the sixth most common cancer in the world [76]; however, the traditional serum marker, alpha-fetoprotein (AFP) is a poor marker being raised on only a small proportion of HCC cases and may also be raised in patients with chronic liver disease [77]. Use of collagen-III and matrix metalloproteinase-1 in combination with the standard 'liver function tests' has allowed the development of an HCC-ABC diagnostic test comprising alkaline phosphatase level x total bilirubin x (Collagen-III/MMP-1) x log AFP level giving an 81% sensitivity and 93% specificity in identifying the early stages of HCC [78].

A further study of HCC showed serum malondialdehyde (MDA, a product of lipid peroxidation) and CRP levels to increase as the Child-Pugh scores increased with higher MDA levels in larger tumours. The authors indicate the MDA is likely to come directly from the tumour as free radical production increases leading to lipid peroxidation with subsequent generation of MDA [79]. The increase in CRP is less well defined and may be linked to immune processes, or to cancer cells expressing CRP

Bladder cancer occurs in around 3% of the population and has a poor prognosis with a five-year survival rate of 50–80% [80]. Therefore, prognostic biomarkers are required to guide post-surgical treatment, two such putative markers CD44 and Nanog expression were investigated: Cluster of differentiation 44 (CD44) is expressed in the basal layer of the bladder and interacts with extra-cellular matrix protein and promotes stem-cell-like properties. It also interacts with Nanog, an embryonic stem-cell transcription factor, which inhibits MDR-1 and causes efflux of chemotherapy drugs in a number of tumour types. High CD44 and nannog expression were both associated with decreased survival [81] as independent prognostic factors along with lymph node status. The authors developed a combined CD44/Nanog score and suggest a use in risk stratification and for prognosis.

Issue 1 also included a new development on a long-established biomarker: Alkaline phosphatase levels are known to be increased in epilepsy, with received wisdom being this is a consequence of the medication, in addition patients with epilepsy are more prone to metabolic bone disease and fractures linked to increased serum ALP [82]. In a study comparing drug naïve and treated patients with epilepsy and normal controls ALP levels were highest in drug naïve patients with recent seizure activity. This suggests a link between epilepsy and bone turnover and that high ALP levels in patients should not be ascribed to an effect of the medication [83].

## Case histories

Case histories continue to provide interesting insights into pathology, and whist often examining very rare diseases, can alert laboratories to unusual presentations of typical markers, or can point towards areas for development in more common diseases. In issue 1

a case of type 1 Madelung disease was described. This rare disease is more common in the Mediterranean population, but was unknown in the population local to the authors. This rare disease should be considered where a diagnosis of Cushing's disease is a probable but does not fit the expected clinical picture [84]. Issue 2 included two interesting case reports: The first described a case of xanthogranulamatous pyelonephritis [85]. This rare chronic bacterial infection that was only diagnosed after excision of the mass, thought to be a cystic renal cell carcinoma. The patient was treated with appropriate antibiotics. The authors caution that radiographs are often ambiguous and suggest a pre-operative biopsy or an intra-operative frozen section may assist in decision-making and speed up appropriate antibiotic therapy. Also in this issue an association between bilateral renal artery dissection and antiphospholipid (aPL) antibodies suggests a mechanism for this very rare disorder. A pro-inflammatory environment was noted in the acute phase of the disorder, and treatment with standard anticoagulation was continued as aPL IgM antibodies remained [86], but given the rare nature of this disorder fresh cases to confirm this finding will take time.

Issue 3 included a case study involving a couple seeking infertility treatment showed a marked effect of infection on sperm concentration. The patient required treatment for post-operative infection after repair of a pectoral muscle tear, whilst sepsis was not diagnosed using current guidelines the patient was given iv antibiotics for 23 days. The authors [87] discuss the factors that can reduce the quality of semen and emphasise the need for retesting during the fertility management pathway should there be a significant impact on the health of the male partner.

## Methods

Last, but by no means least in importance are methodological papers. In issue 2 the detection of carbapenemase-producing enterobactererales (CPS) is highlighted as a diagnostic problem as not all resistant bacteria produce the carbapenemase and not all are universally resistant to carbapenens. Cafferkey and colleagues [88] discuss the improvements in their service over time offering a faster service combining molecular and inactivation assays.

In situ hybridisation (ISH) is a technique for localising genetic material to particular cells in heterogeneous tissue samples. This localisation has been recommended alongside total expression levels for miRNA [89]. Warford and colleagues [90] compared locked nucleic acid (LNA) probes with conventional oligonucleotide (COP) probes for the localisation of two miRNAs in formalin-fixed paraffin wax samples. Both methods gave equivalent results and whilst the use of COP was less expensive, the LNA methodology allowed for more rapid analysis.

MALDI-TOF mass spectrometry has enabled a marked improvement in the speed and accuracy of identification of bacterial species in clinical practice [91]. A comparison between molecular methods and MALDI-TOF for the identification of mycobacteria showed the former method to have a considerable number of advantages in the identification of mycobacteria. The authors [92] note the need for pure growth of mycobacterial species and that it cannot currently differentiate between members of the mycobacterium tuberculosis complex and high capital cost, however this is offset due to lower running costs, ease of use, smaller footprint, no requirement for batching, and a much larger library and the ability to add new species as these appear in the patient population.

## COVID-19 review

Lastly, in this issue of the journal, Salvamani and colleagues [93] provide a comprehensive review of the COVID-19 pandemic, starting with a short catalogue of the events leading to the global spread of the SARS-CoV-2 virus. They then explain the molecular structure of the virus, in comparison to other similar coronaviruses, namely those responsible for the previous Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS) outbreaks. They continue with a description of the pathophysiology of the disease and a review of the vaccines under development. Interestingly, they describe the results from a large Spanish epidemiological study showing only a low level of seroprevalence in the community with respect to antibodies to SARS-CoV-2, and insufficient to provide herd immunity [94]. However, they conclude the review on a note of optimism with a focus on fundamental research from the US investigating the dynamics of CD4 and CD8 responses to the virus. The results showing a degree of pre-existing immunity in 40–60% of individuals unexposed to SARS-CoV-2 in samples dating from 2015 to 2018 [95]. The authors of the review emphasise the importance of this type of fundamental biomedical research, in addition to large epidemiological studies in understanding the behaviour of the virus and immunity to it. The results of such research are likely to have a profound impact on how we control the pandemic, its effects and therefore the lives of everybody.

## Disclosure statement

No potential conflict of interest was reported by the authors.

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