

In This Issue**Editor's Summaries of the Articles Published in This Issue of Molecular Medicine Communications****Editorial Staff**

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In this issue Yusuf and colleagues investigated the association of association of fat, mass and obesity (FTO) gene polymorphism with diabetes and prediabetes in Pakistani population, Mannan and colleagues did a variant analysis of FOXE1 gene in non-syndromic cleft lip and palate in Peshawar, Pakistan, Zaib et al determined the frequency of p53 mutations and Epstein-Barr virus in Pakistani gastric cancer patients and investigated their association with the tumor grade, Rehman and her colleagues made an analysis of comparative effectiveness & renoprotective effects of hypoglycemic drugs for type 2 diabetes mellitus, and Ain et al reviewed the sources and mechanisms of chemoresistance in hepatocellular carcinoma.

Association of Fat, Mass and Obesity (FTO) Gene Polymorphism with Diabetes and Prediabetes in Pakistani Population

Obesity and Type 2 Diabetes Mellitus (T2DM) have become the most prevalent public health issue around the world. A study by Yusuf and colleagues, comprising 300 participants grouped into normal, pre-diabetics and diabetics, showed that there was statistically significant difference among the three groups in terms of their lipid profile parameters. Frequency of *FTO*-rs9939609 genotype distribution, however, was not significantly different in the three groups but patients with AA genotypes are 1.34 and 1.59 times more likely to develop prediabetes and diabetes as compared to patients with TT genotypes. Lack of statistical association with *FTO*-rs9939609 SNP notwithstanding, their data reinforced the link between dyslipidemia, obesity and glycemic index.

Variant Analysis of FOXE1 Gene in Non-Syndromic Cleft Lip and Palate Patients of Peshawar, Pakistan

One of the most common structural birth defects is the cleft lip and palate, having an incidence rate of 1:700 live births worldwide. The gene Fork-head Box protein E1 (*FOXE1*) has been documented to be involved with cleft lip and palate. A study by Mannan and her colleagues comprising 100 participants show that a point mutation (c.274C>T, rs3021526) in *FOXE1* gene was detected in 15 samples. Based on phenotype, males and isolated cleft palate type was commonly involved with bilateral occurrence, and moderate cases were frequently seen among the enrolled patients. In this study, a missense substitution was observed in gene *FOXE1*. This study provides a foundation for genetic counseling for families at risk and offer valuable insights for prevention and management plans.

Frequency of p53 Mutations and Epstein-Barr Virus in Pakistani Gastric Cancer Patients and Their Association with the Tumor Grade

Gastric carcinoma (GC) is the fourth most common cause of cancer-associated death worldwide. Zaib and her colleagues investigated the prevalence of *TP53* mutations and Epstein-Barr virus (EBV) infection in GC and to find any association with the tumor grade. A total of 108 formalin-fixed-paraffin-embedded tissue blocks (98 gastric adenocarcinomas and ten controls) were collected, and DNA was extracted from them. Histopathology revealed that of the 98 adenocarcinoma samples, 63.3% (n=62) were

poorly differentiated, whereas 36.7% (n=36) were moderately differentiated. Signet rings were present in 30.6% (n=30), and EBV was detected in 18.4% (n=18). Mutation analyses indicated that 76% of the samples were mutated, of which 8% had single nucleotide variations (SNVs) in exon 5 (g.17371G>A and g.17521A>C). Moreover, 76% of the samples had the same SNV (g.18316T>C) in exon 7. We also discovered three novel SNVs; two in exon 5 (g.17371G>A and g.17521A>C) and one in exon 7 (g.18316T>C). No difference in the expression of caspase-3 was observed. The chi-squared test indicated no significant correlation between *TP53* mutations with EBV infection and tumor grade. In their cohort, young males had a higher prevalence of GC. The detection of EBV suggests it might be a risk factor for GC in their population.

A Comparative Effectiveness & Renoprotective Effects of Hypoglycemic Drugs for Type 2 Diabetes Mellitus

Type 2 Diabetes Mellitus (T2DM) is a huge burden on healthcare systems globally and it can lead to impaired kidney function, albuminuria, end-stage renal disease (ESRD). In a review article, Rehman and her colleagues highlight the need for selecting suitable drugs for a patient, as the optimal treatment significantly depends upon the patient-specific conditions. T2DM impact on the kidneys could result in diabetic nephropathy (DN) or diabetic kidney disease (DKD). The authors emphasize the need for new pharmacologic strategies for T2DM, that could prevent the development of DN and

safeguard the kidneys. They overview the recent clinical data pertaining to novel therapeutic approaches for the management of DN. Moreover, this review evaluates comparative effectiveness of hypoglycemic drugs like sodium-glucose cotransporter-2 inhibitors (SGLT2-i), glucagon-like peptide-1 receptor agonists (GLP1-RA), dipeptidyl peptidase-4 inhibitors (DPP4-i), and finerenone in treating T2DM and their renoprotective effects.

A Review On the Sources and Mechanisms of Chemoresistance in Hepatocellular Carcinoma

Degenerative Hepatocellular carcinoma (HCC) is one of the leading causes of cancer-related deaths worldwide, with surgical resection followed by chemotherapy being the primary treatment method. However, the complex nature and high metastatic potential of HCC often render treatment plans ineffective, and acquired drug resistance frequently results in disease relapse in patients. In this review, Ain and her colleagues performed an extensive literature search of different databases, including Medline, Scopus, and Cochrane, to identify studies that have addressed chemoresistance in HCC. They argue that novel therapies that counter these resistance mechanisms need to be developed to better manage and control the disease. This would increase the patient survival rate and help decrease the use of multiple chemotherapeutic agents that greatly increase the risk of toxicities encountered by patients.

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