<u>Article 6</u>

<u>The emerging role of lncRNA MEG3 and MEG3 rs7158663 in hepatocellular</u> <u>carcinoma</u>

Abstract:

Introduction: Hepatocellular carcinoma (HCC) is the most common primary liver malignancy in Egypt. Genetic and environmental factors play a role in its development. This study explored the association between the long non coding RNA (lncRNA) MEG3 rs7158663 polymorphism, MEG3 expression, and the risk of HCC and other clinicopathologic characteristics in an Egyptian population.

Methods: This case–control study included 114 patients with HCC and 110 healthy controls. TaqMan real-time PCR was used to analyze lncRNA MEG3 rs7158663. Serum MEG3 expression levels were measured using RT-PCR.

Results: The AA, GA+AA, and A alleles were associated with increased risk for HCC (adjusted odds ratio (OR) 11.84%, 95% CI 4.07–34.45, p < 0.0001; adjusted OR 3.18, 95% CI 1.79–5.67, P < 0.0001; and adjusted OR 2.87, 95% CI 1.91–4.34, p < 0.0001, respectively). The mutant genotype and allele were linked to an increased risk in male patients and patients \geq 50 years old. MEG3 serum expression level was downregulated in HCC patients. The rs7158663 G > A polymorphism and downregulated MEG3 were significantly associated with larger tumor size and advanced disease stage.

Conclusions: MEG3 rs7158663 Single nucleotide polymorphisms and downregulated lncRNA MEG3 were associated with HCC risk and may represent diagnostic and bad prognostic factors for HCC patients.

Key Words: Hepatocellular carcinoma, LncRNA MEG3, Maternally expressed gene 3 polymorphism, Rs715866