كلية الطب

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Role of Long non-coding RNA NEAT-1 and Interleukin-6 in Pathogenesis of Vitiligo in Egyptian patients

Thesis

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summary

Vitiligo is a common multifactorial skin disorder with very complex pathogenesis. The cause and pathogenesis of vitiligo remain unclear. Uncovering the biological mediators and the molecular mechanisms that lead to metabolic defects therefore, melanocyte degeneration and autoimmunity is important to identify new therapeutic targets and drugs that could prevent, stop disease progression or even cure vitiligo. systemic biological therapies that target cytokines, might be successfully used in vitiligo.

Long noncoding RNAs (LncRNA) are essential to carry out key functions in regulating gene expression.LncRNA is a new transcript class that plays important roles in immune system disorders. An increasing number of studies suggest that lncRNAs have important biological roles ranging from regulation of development and differentiation to regulation of epigenetic processes by guiding chromatin-modifying enzymes to their sites of action playing a role in RNA modification, evolution and inheritance. Recent studies have implicated noncoding RNAs in epidermal development and keratinocyte differentiation, but the complexity of multilevel regulation of transcriptional programs involved in these processes remains ill-defined.

Interleukin-6 (IL-6) is involved in the pathogenesis of several autoimmune disorders, including vitiligo. LncRNAs, as important transcriptional regulators affecting gene expression and cell homeostasis, have demonstrated vital participation in the expression and signalling regulation of IL-6.

Our current study aimed to investigate the possible role of long noncoding NEAT-1and Interleukin-6 in the pathogenesis of vitiligo.

This case-control study was performed in the Medical Biochemistry and Molecular Biology Department, Faculty of Medicine, Fayoum University. After the approval of the Faculty of Medicine, Fayoum University's local ethical

committee of Human Rights in Research before the beginning of the study, **60** subjects were recruited from the Dermatology outpatient clinic, Faculty of Medicine, Fayoum University Hospital for the study and divided into 2 groups; **40** vitiligo patients and **20** normal healthy volunteers 10 males and 10 females aged from 30 to 50 years old as a control group. Informed consent was obtained from all the subjects enrolled in this study.

All patients were subjected to history taking and clinical evaluation to assess the extent of the disease (Body Surface Area) and its severity (VASI score). Serum samples were obtained from all subjects. The expression of LncRNA NEATT-1 was assessed using Quantitative RT-PCR in addition to ELISA for Interleukin-6 assay and biochemical blood investigations for measurements of CBC, ALT, AST, creatinine, urea, cholesterol, triglycerides, and HDL.

The results revealed a statistically significant increase in lncRNA NEAT-1 fold change expression in vitiligo patients compared to control (p value<0.001) and no significant difference in NEAT-1 level between male and female vitiligo patients (p-value =0.9).

Serum level of IL-6 was significantly higher in patients than controls (p-value < 0.001) and showed no significant difference in IL-6 level between male and female vitiligo patients (p-value =0.6).

The results show a significant increase in serum ALT and creatinine in vitiligo patients compared to controls (p-value =0.03, 0.045), respectively, otherwise no significant difference between the two groups regarding AST, urea, TG, cholesterol and HDL (p-value>0.05). No significant difference between vitiligo patients and control regarding Hb , platelets and WBCs count (p-value >0.05).

There were statistically significant **positive** correlations with p-value <0.05 between NEAT-1 and IL-6 (r= 0.276, p-value =0.033) and between age and onset (r=0.791, p-value <0.001), duration and onset (r= - 0.556, p-value <0.001) and also **positive** correlations between duration and VASI (r=0.321, p-value =0.044).

The correlation between NEAT-1 and VASI is significantly inverse (r= - 0.358, p-value =0.023).

The results show that NEAT-1 is significant and could be a diagnostic marker for vitiligo (p value<0.001, AUC=0.9) at a cut-off value of 1.15, a sensitivity of 90%, specificity of 99% and accuracy of 94.5%.

In conclusion, our findings indicate that NEAT-1 and IL-6 are important factors in the pathogenesis of vitiligo; it is not clear if the rise in the level of NEAT-1 and IL-6 reflects the consequence of the disease or the cause of the disease. Considering the mechanisms of epigenetics, it is essential to study the effect of environmental variables on the expression of the studied over-expressed LncRNA in the context of vitiligo. This LncRNA should be considered a potential target in future research dealing with new therapeutic options for vitiligo.