RETRACTED ARTICLE: The pivotal role and mechanism of long non-coding RNA B3GALT5-AS1 in the diagnosis of acute pancreatitis

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\textbf{ABSTRACT}

The present study planned to dig the potential impacts of long non-coding RNA B3GALT5-AS1 in acute pancreatitis (AP). A total of 66 patients who were diagnosed with AP using ultrasonic imaging were enrolled in the study. Expression levels of B3GALT5-AS1 in the serum of AP patients were determined. Afterwards, rat pancreatic AR42J acinar cells were disposed with caerulein to produce AP-like injury. The levels and molecular mechanisms of B3GALT5-AS1 in AP were explored through \textit{in vitro} cell experiments. The levels of IncRNA B3GALT5-AS1 were observed to be lessered in patients with AP relative to healthy controls. In addition, caerulein was observed to induce injuries in the AR42J cells (depressed cell viability, enhanced cell apoptosis, cytokines production, and levels of amylase). Overexpression of B3GALT5-AS1 alleviated the caerulein-produced injury in the AR42J cells. Moreover, it was determined that miR-203 showed a downside expression by B3GALT5-AS1 regulation, and the overexpression of B3GALT5-AS1 retrained caerulein-produced injury through the suppression of miR-203. In addition, it was observed that miR-203 lessened the level of nuclear factor interleukin-3 (NFIL3) and that NFIL3 was targeted by miR-203. Lastly, the impacts of B3GALT5-AS1 on caerulein-induced cell injury were manifested through the NF-κB signalling pathway. The data from the present study revealed that in patients with AP, B3GALT5-AS1 is expressed in reduced amounts. Overexpression of B3GALT5-AS1 may alleviate caerulein-induced cell injury in AR42J cells through the regulation of miR-203/NFIL3 axis and by inhibiting the activation of the NF-κB signals.

\textbf{Introduction}

Acute pancreatitis (AP) is characterized by inflammation of the pancreas, and in 10\%-20\% of the cases, it may evolve into severe AP (SAP), which leads to systemic multiple organ dysfunction syndrome and ultimately death [1,2]. The mortality rate in mild AP (MAP) is considerably low (<1\%), while that in the SAP has been shown as high as 30\% [3–5]. In order to enhance the clinical outcome, it is requisite to identify the SAP at an early stage of the disease.

Contrast-enhanced ultrasound is an imaging method which is important to identify the range of necrosis in the pancreas and may be used for evaluating the severity, treatment progress, and the prognosis of diseases [6]. Moreover, several blood-based biomarkers, including levels of serum lipase and amylase, have been used for the diagnosis of AP for decades; however, so far, there has been no gold-standard parameter for the accurate prediction of the severity of this disease [7]. Despite great efforts exerted to improve imaging and diagnosing methods, most of the patients are diagnosed at the SAP stage. Therefore, exploring diagnostic biomarkers that are able to provide effective early diagnosis of AP is of great importance for curative treatment.

Genomic and transcriptomic sequencing has revealed that even though 70\% of the human genome may be transcribed into RNA molecules, the proportion of the human genome that is able to encode proteins is only about 2\%, implying that the majority of the human transcriptome is non-coding RNAs [8]. In recent years, the crucial roles of the non-coding RNAs in biological and pathological processes have received increasing attention [9–11]. Long non-coding RNAs (lncRNAs) are transcripts with longer than 200 nucleotides in length and lack protein-coding abilities [12]. Aberrant expression of lncRNAs has been reported to be involved in several inflammatory diseases [13–15]. Moreover, IncRNA Fendrr was reported to be upregulated in a caerulein-induced AP model and was also observed to promote pancreatic acinar cell apoptosis [16]. Expression of IncRNA H19 in the serum of patients with AP was discovered as augmented, and thereby, it was suggested as a potential biomarker for the diagnosis of AP [17]. However, the impact of lncRNAs associated with AP remains incomplete discovered. In a recent study, the
expression of lncRNA B3GALT5-AS1 was observed to be reduced in colon cancer tissues, implying that it regulated liver metastasis in colon cancer [18]. Nevertheless, the role of B3GALT5-AS1 in AP has not been reported to date.

The present research was planned to dig the impact of B3GALT5-AS1 in AP. Therefore, the level of B3GALT5-AS1 in the serum of patients diagnosed with AP was determined using ultrasonic imaging. Subsequently, caerulein was chosen as disposer on rat pancreatic AR42J acinar cells to produce AP-like injury. The role and molecular mechanisms of B3GALT5-AS1 in AP were explored through in vitro cell experiments. The results revealed that B3GALT5-AS1 was cut down in the patients with AP and that the overexpression of B3GALT5-AS1 alleviated caerulein-induced injury in the AR42J cells through the regulation of miR-203/nuclear factor interleukin-3 (NFIL3) axis and NF-κB signalling pathway. The present study is estimated on offering a novel strategy for the diagnosis and treatment of AP.

Materials and methods

Specimen collection

In the period from 2015 to 2018, 66 patients (46 males and 20 females; age: 30–68 years; average age: 46.6 years) who were diagnosed with AP using ultrasonic diagnosis instruments (GEpro500G, GEpro200, and SSA240 types) were selected for the present study. The range of onset time for the disease was 3 h to 5 days. The probe frequency maintained during the ultrasonic examination was 3.5 MHz. The patient lied flat, with transverse or longitudinal incision of the upper abdomen, followed by the observation of the following parameters: the transverse diameter of pancreas, the size of pancreatic head, the inner diameter of pancreatic duct, whether the echo of the pancreatic body was uniform, whether there existed a weakened echo or anechoic area around the pancreas (especially around the tail of the pancreas), whether hydrops existed in the omental sac, whether there was the occurrence of metastasis, compression, or displacement in the pancreatic peripheral organs and blood vessels, and if the peripancreatic peritoneal lymph nodes were enlarged. As described in previous studies [19,20], the selected cases were classified into two groups, the mild AP group (MAP; n = 36) and the severe AP group (SAP; n = 30), on the basis of the clinical severity scores obtained for them, including ImrieGlasgow > 2, multiple organ dysfunction score (MODS) > 2, and acute physiology and chronic health evaluation II (APACHE II) > 7. In addition, 28 healthy volunteers were recruited as healthy controls. Blood samples were obtained from the SAP patients, MAP patients, and healthy controls. The study gained the approval of the clinical research ethics committee, and the consent was written by all the selected individuals.

Cell culture and treatment

Rat pancreatic acinar cell line AR42J was purchased from the American Type Culture Collection (Manassas, VA, USA). Ham’s F-12K medium (Gibco, USA) containing 10% foetal bovine serum was chosen for cell cultivation. The cultivated condition is at 37 °C with 5% CO2. In order to perform cell treatment, the AR42J cells (1 × 105 cells/mL) were seeded into each well of the 6-well plates and permitted to culture for 24 h. In order to stimulate AP, the seeded AR42J cells were treated with 10 nmol/L caerulein (Sigma-Aldrich, St Louis, MO) for different time points including 0, 4, 6, 8, and 10 h.

Cell transfection test

The cDNA encoding B3GALT5-AS1 was PCR-produced using PfU Ultra Il Fusion H DNA polymerase (Takara, Japan) and subsequently inserted into the pcDNA3.1 vector (Sangon Biotech, Shanghai, China) to construct the overexpression vector, which was named pcDNA-B3GALT5-AS1. A miR-203 mimic, miR-203 inhibitor, miR-negative controls (NC), si-NC, and si-NFIL3 were purchased from GenePharma (Shanghai, China). The cDNA encoding NFIL3 was amplified and subcloned into the pEX-2 vector (Invitrogen) to construct the overexpression vector, which was named pEX-NFIL3. Cell transfection was subsequently conducted using Lipofectamine 2000 (Invitrogen) in accordance with the manufacturer’s protocols.

Cell viability test

AR42J cells (10,000 cells) were cultured in the 96-well plates. Afterwards, AR42J cells were cultured for 12 h and then were disposed with caerulein for another 24 h of incubation before subjected to MTT assay. Briefly, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (500 µg/mL; Sigma, USA) solution was added to each well of the plate and then cultured for 3 h. Subsequently, dimethyl sulfoxide solution (200 µL; Sigma, USA) was added to dissolve the formazan that was formed in the previous step. Microplate reader (Bio-Rad Model 550; Hercules, CA, USA) was chosen for assessing the absorbance of each well at 570 nm.

Cell apoptosis test

AR42J cells (10,000 cells) were hatched into each well of the 96-well plates. Afterwards, AR42J cells were cultured for 12 h and then were disposed with caerulein for another 24 h of incubation before carrying out the apoptotic assay. According to the recommendations, FITC-Annexin V Apoptosis Detection Kit (Sangon Biotech) was used for apoptotic cells detection, and the transfected AR42J cells were double stained with FITC-Annexin V and propidium iodide (PI). Subsequently, apoptotic cells were detected in a flow cytometer (FACScan; BD Biosciences, USA) equipped with CellQuest software (BD Biosciences).

Analysis of inflammatory cytokines

Enzyme-linked immunoassay kits (ELISA, Sangon Biotech) was chosen for assessing the concentrations of TNF-α, IL-6, IL-8, and IL-1β in the cell culture following by the protocols provided by the manufacturer. The results were expressed in terms of picogram per millilitre.
Bioinformatic prediction and luciferase reporter assay

TargetScan software was chosen for predicting the binding sequence between NFIL3 and miR-203. Afterwards, luciferase reporter assay was performed to confirm NFIL3 was targeted by miR-203. Briefly, the 3'UTR sequences of NFIL3 mRNA with the miR-203 binding site were amplified through PCR and subsequently mixed together with the pGL3 vector (Promega, WI) to construct the wild-type (wt) reporter construct, which was named NFIL3-wt. The pGL3 NFIL3 mutant-type (mt) reporter produce containing point mutations in the seed sequence was generated using a site-directed mutagenesis kit (Stratagene, CA) and was named NFIL3-mt. The AR42J cells were co-transfected with the miR-203 mimic/mimic control and the NFIL3-wt/NFIL3-mt reporter construct. After 48 h of incubation post-transfection, luciferase activity for cells in each group was assessed by a Dual-Luciferase Reporter Assay System (Promega, Madison, WI, USA).

qPCR assay

We extracted the total RNA from cells and then carried out reverse transcription to produce the complementary DNA (cDNA) using High Capacity cDNA Reverse Transcription Kit (Applied Biosystems, CA, USA). Moreover, cDNA from the miRNAs was generated using the TaqMan miRNA Reverse Transcription kit (Applied Biosystems, Foster City, CA, USA). Subsequently, qPCR was carried out by TaqMan gene expression assay kits for the detection of the expressions of B3GALT5-AS1 and NFIL3, or by using TaqMan Universal Master Mix II with TaqMan microRNA assay kits for the determination of miR-203 expression. GAPDH and U6 were utilized as internal controls for RNAs and miRNAs, respectively.

Western blot test

We isolated the total protein from the cells using the radioimmunoprecipitation assay buffer (Sangon Biotech, Shanghai, China). The isolated protein samples (50 μg/lane) were separated by SDS-PAGE, followed by transfer to a polyvinylidene fluoride (PVDF) membrane previously blocked with 5% non-fat skimmed milk/TBST. The protein signals from the membrane were detected through an overnight incubation with primary antibodies for Bcl-2, Bax, pro or cleaved caspase-3, pro or cleaved caspase-9, NFIL3, c-p65 or n-p65, c-p50 or n-p50, p-1xβx or t-1xβx, Lamin B1, and β-actin (1:1,000; Abcam, Cambridge, UK) at 4°C; afterwards, the membranes were rinsed and subsequently disposed with appropriate secondary antibodies. Enhanced chemiluminescence reagents (Pierce, Rockford, IL) were chosen for assessing the levels of the target proteins.

Statistical analysis

Each experiment in this research was carried out independently with three times repeatedly. Data were expressed in terms of mean values ± standard deviation (SD). SPSS Statistics 20.0 software (IBM, Armonk, NY, USA) was chosen for data analysis. ANOVA or two-tailed Student’s t-test was chosen for calculation of differences among groups. p < .05 was chosen as the threshold of statistical significance.

Results

Ultrasonic diagnosis of AP and low expression of IncRNA B3GALT5-AS1 in patients with AP

Pancreatic size: among the 66 patients selected for the present study, 59 exhibited pancreatic enlargement, including the 56 cases of diffuse enlargement of the pancreas, five cases of pancreatic head enlargement, and 28 cases of the pancreatic body and tail enlargement, while there were 7 cases of normal pancreatic size.

Echo: in 16 cases out of the 66 cases, the capsule was smooth with fine lines and good continuity, while in rest of the 50 cases, the capsule was rough with an unclear contour.

Echo of glandular parenchyma: (1) echo reduction: among all the cases, 62 cases of glandular parenchyma exhibited reduced echo, thick spot, and an uneven distribution or uniformity. In addition, there were 48 cases of dark areas in the parenchyma; (2) echo enhancement: 55 cases of glandular parenchyma exhibited echo enhancement, thick spot, and uneven distribution; (3) no obvious abnormal echo: 9 cases of glandular parenchyma exhibited medium echo, fine spot, and even distribution, while no abnormal echo was detected.

Dilatation of pancreatic duct: 22 cases exhibited dilatation of the main pancreatic duct, while 44 cases exhibited no such dilatation.

Peripancreatic sonographic changes: 58 cases exhibited irregular fluid dark areas, 3 cases exhibited anechoic masses, and 5 cases exhibited disorderly mass echoes.

Lower peritoneal effusion: irregular liquid dark areas in the abdominal cavity, with poor sound transmission and visible light echo, were detected in 36 cases.

Gas total-reflectance echo: 18 cases exhibited obvious upper abdominal tenderness, in which the sonogram of the pancreas could not be detected, while the gas total reflect-ance echo was visible.

Besides, for investigating the impact of B3GALT5-AS1 in patients with AP, 30 patients with SAP, 36 patients with MAP, and 28 healthy volunteers were enrolled in the present research. As depicted in Figure 1(A), B3GALT5-AS1 was markedly lessened (p < .05) in serum of patients suffered with SAP and in patients with SAP relative to that in the healthy controls. Moreover, B3GALT5-AS1 expression in patients suffered with SAP was remarkably lower (p < .05) relative to that in patients with MAP. These findings implied that B3GALT5-AS1 could be playing a key role in AP and might be correlated with the severity of this disease.

Caerulein-induced injury to AR42J cells

In order to stimulate AP, AR42J cells were disposed with caerulein (10 nmol/L) for various durations. The results demonstrated that, in comparison with the controls, caerulein
disposes dramatically depressed the cell viability (Figure 1B), induced cell apoptosis (Figure 1C), enhanced the secretion of inflammatory cytokines including TNF-α, IL-6, IL-1β, and IL-8 (Figure 1D), and increased the levels of amylase (Figure 1E), in a time-dependent way (*p < .05 and ** p < .01 compared to healthy control. # p < .05 compared to MAP. B: Cell viability after the treatments. C: Cell apoptosis and the expression of apoptosis-related proteins. D: The concentrations of inflammatory cytokines after the treatments. E: The levels of amylase after the treatments. F: The expression of B3GALT5-AS1 after treatments. All experiments were performed three times (n = 3), and the data were expressed as mean ± SD. *p < .05, **p < .01, and ***p < .001 compared to controls.

Alleviation of caerulein-induced injury in caerulein-stimulated AR42J cells through the overexpression of B3GALT5-AS1

For the exploration of the impact of B3GALT5-AS1 in AP, AR42J cells were treated with caerulein and subsequently transfected with pcDNA-B3GALT5-AS1, thereby inspection on the impacts of overexpression of B3GALT5-AS1 on the viability, apoptosis, cytokine secretion, and amylase levels in the caerulein-disposed AR42J cells. As depicted in Figure 2A, B3GALT5-AS1 level was markedly enhanced in the pcDNA-B3GALT5-AS1 group relative to that in the pcDNA 3.1 group (p < .001), pointing out that B3GALT5-AS1 was prosperously highly expressed in the AR42J cells through transfection with pcDNA-B3GALT5-AS1. Subsequent experiments implied that the high level of B3GALT5-AS1 remarkably alleviated the caerulein-induced injury in caerulein-stimulated AR42J cells through the promotion of cell viability (Figure 2B) and inhibition of apoptosis (Figure 2C), and by reducing the secretion of TNF-α, IL-6, IL-1β, and IL-8 (Figure 2D) and increasing the levels of amylase (Figure 2E) in the caerulein-stimulated AR42J cells (p < .05 for all).

Overexpression of B3GALT5-AS1 alleviates caerulein-disposed injury through negative regulation of miR-203 expression

As presented in Figure 3(A), miR-203 level was markedly decreased in the pcDNA-B3GALT5-AS1 group, in comparison with that in pcDNA 3.1 group (p < .01), indicating that B3GALT5-AS1 was able to negatively regulate miR-203. Moreover, a markedly taller (p < .01) level of miR-203 was discovered in the patients suffered with MAP and the patients suffered with SAP, in comparison with that in the healthy controls, and this expression was higher in patients suffered with SAP in comparison with that in the patients suffered with MAP (p < .05), indicating that miR-203 expression increased gradually with the severity of the disease (Figure 3B). In addition, caerulein treatment dramatically increased the miR-203 expression in a time-dependent way (p < .05; Figure 3C). Post-transfection, the miR-203 expression was remarkably overexpressed or distinctly inhibited by transfection of miR-203 mimic/inhibitor approaches, relative to the corresponding NC groups (p < .01; Figure 3D). In relation to caerulein + pcDNA-B3GALT5-AS1 + mimic NC group, high level of miR-203 in the caerulein + pcDNA-B3GALT5-AS1 + miR-203 mimic group markedly changeover the impacts of the overexpression of B3GALT5-AS1 on the caerulein-induced injury in the caerulein-stimulated AR42J cells to a decrease in the cell viability (p < .05; Figure 3E) and promotion of cell apoptosis (p < .01; Figure 3F), and by accelerating the secretion of inflammatory cytokines (p < .05; Figure 3G) and decreasing the levels of amylase (p < .05; Figure 3H).

NFIL3 is targeted by miR-203

Cheng and his colleagues pointed out that miRNAs play pivotal impacts in diseases through the adjustment of their
The targets of miR-203 were therefore explored for digging the possible regulatory pattern of miR-203 in AP. Using TargetScan, NFIL3 was predicted as the potential target of miR-203 (http://www.targetscan.org/cgi-bin/targetscan/vert_71/). The targeted sequence between NFIL3 and miR-203 is presented in Figure 4(A). Also, by luciferase reporter test, the luciferase activity of NFIL3-wt was markedly depressed by the miR-203 mimic ($p < .05$; Figure 4(B)), while the luciferase activity of NFIL3-mut remained unchanged, confirming that NFIL3 was a target of miR-203.

**Figure 2.** Overexpression of B3GALT5-AS1 alleviated caerulein-induced injury in caerulein-stimulated AR42J cells. AR42J cells were treated with caerulein and then transfected with pcDNA-B3GALT5-AS1 or pcDNA 3.1. A: The expression of B3GALT5-AS1 after transfection. B: Cell viability after treatments. C: Cell apoptosis and the expression of apoptosis-related proteins. D: The concentrations of inflammatory cytokines after treatments. E: The levels of amylase after treatments. All experiments were performed three times ($n = 3$), and the data are expressed as mean ± SD. $^*p < .05$, $^{**}p < .01$, and $^{***} p < .001$ compared to the corresponding controls.
miR-203. In addition, NFIL3 expression levels were dramatically depressed in the miR-203 mimic group, while it was changeover by miR-203 inhibitor application (p < .01; Figure 4(C–4D)), pointing out that the NFIL3 expression was negatively regulated by miR-203.

High level of miR-203 aggravates caerulein-disposed cell injury through suppression of NFIL3

For verify the impact of miR-203 in the process of AP via NFIL3 targeting, NFIL3 was overexpressed/depressed by approaches of pEX-NFIL3 and si-NFIL3 transfection, respectively (p < .001; Figure 5(A)). The co-transfection effects of miR–203 mimic and pc-NFIL3 on the caerulein-produced injury in caerulein-stimulated AR42J cells were investigated.

Relative to the caerulein + mimic NC group, miR-203 high level in the caerulein + miR-203 mimic group was observed to markedly decrease the cell viability (p < .05; Figure 5(B)), induce apoptosis (p < .01; Figure 5(C)), increase the secretion of inflammatory cytokines (p < .05; Figure 5(D)), and suppress the amylase levels (p < .05; Figure 5(E)). Furthermore, in relation to the caerulein + miR-203 mimic + pEX-2 group, overexpression of NFIL3 in the caerulein + miR-203 mimic + pEX-NFIL3 group remarkably changeover the impacts of miR-203 mimic on the caerulein-produced injury in caerulein-stimulated AR42J cells, through an increase in cell viability (p < .05; Figure 5(B)), inhibition of apoptosis (p < .01; Figure 5(C)), suppression of inflammatory cytokine production (p < .05; Figure 5(D)), and the promotion of amylase levels (p < .05; Figure 5(E)).
Effects of B3GALT5-AS1 on caerulein-induced cell injury through regulation of the NF-κB signalling signals

Rakonczay and his team pointed out that NF-κB activation was participating in the pathogenesis of AP [23]. Therefore, the association between B3GALT5-AS1 dysregulation and NF-κB signals was investigated in the caerulein-stimulated AR42J cells. In this study, IkBα, p65, and p50 were investigated as allusive symbols for NF-κB excitation. As depicted in Figure 5(F–5G), the NF-κB signals were excited by caerulein. Both p50 and p65 were majorly existed in the cytoplasm. When the NF-κB signal was excited, the position of p50 and p65 was changed to the nucleus. With the overexpression of B3GALT5-AS1, the levels of intranuclear p50 and p65 were observed to decrease in the caerulein+pcDNA-B3GALT5-AS1 group, in comparison with their levels in the caerulein+pcDNA 3.1 group. However, the combined effect of B3GALT5-AS1 overexpression and miR-203 overexpression was observed to increase the intranuclear levels of p50 and p65 again.

Discussion

Clinical management of AP is dependent on the severity of the disease. It has been reported that MAP is self-limited
without being accompanied by organ failure or complications, while SAP is often associated with multiple organ failure and complications. Therefore, an accurate evaluation of disease severity in AP patients in an early stage would facilitate obtaining optimal outcomes [5]. In recent years, lncRNAs have been implicated in numerous physiological and pathological processes, and aberrant expression of these lncRNAs has emerged as a promising biomarker for the diagnosis of various diseases [24–26]. Therefore, the identification of key lncRNAs involved in AP is important for the clinical diagnosis and treatment of this disease.

In the present study, it was revealed that B3GALT5-AS1 expression was decreased in the patients with AP, in comparison with that in the healthy controls. In addition, overexpression of B3GALT5-AS1 was observed to alleviate the caerulein-induced injury in AR42J cells by promoting cell viability, inhibiting cell apoptosis, decreasing cytokine production, and increasing the amylase levels. Apoptosis is defined as cellular suicide or programmed cell death, which may be a favourable response to acinar cells and reflects disease severity [27]. In the pancreatic acinar cells, induction of apoptosis may decrease the severity of AP [28]. Moreover, cytokines have been identified to serve as the mediators of local and systemic manifestations of pancreatitis, and proinflammatory cytokines such as TNF-α, IL-6, IL-1β, and IL-8 have been reported to be able to aggravate pancreatitis [29,30]. In addition, the serum levels of amylase serve as a common indicator for predicting the course of AP [31]. Although the role of B3GALT5-AS1 in AP has not been deciphered so far, the results of the present study indicate that B3GALT5-AS1 might be having a protective role in AP.

An increasing number of studies have revealed the association patterns among lncRNA and miRNAs in the identity of ceRNA [32,33]. In a previous study, lncRNA B3GALT5-AS1 was reported to inhibit liver metastasis in colon cancer through the suppression of miR-203 [18]. Currently, miR-203 was observed to be negatively regulated by B3GALT5-AS1. Although the role of miR-203 in the biological process of AP has not been deciphered so far, the functional involvement of this miRNA has been reported in several inflammatory diseases [34,35] or cancers including pancreatic cancer [36,37]. We deduced that the overexpression of B3GALT5-AS1 alleviated caerulein-induced injury through the suppression of miR-203. Therefore, it was speculated that miR-203 might be able to mediate the development of AP and that B3GALT5-AS1 may be involved in AP through the inverse regulation of miR-203. Despite this finding, the existence of interactions between B3GALT5-AS1 and miR-203 requires further investigation and confirmation.

Furthermore, it was discovered that there was a downside regulatory pattern between miR-203 and NFIL3. This finding was consistent with the findings of a previous study in which miR-203 was observed to accelerate lipopolysaccharide (LPS)-induced apoptosis and inflammation in cardiomyocytes through NFIL3 targeting. NFIL3 is a member of the mammalian basic leucine zipper (bZIP) family, and has been implicated in the promotion of cell survival and inhibition of apoptosis in cardiomyocytes [38,39]. Currently, overexpression of NFIL3 was discovered to dramatically changeover the impacts of the miR-203 mimic on the caerulein-produced injury in caerulein-disposed AR42J cells. These results deduced that miR-203 might be able to modulate AP via NFIL3 targeting.

Lastly, it was confirmed that the impacts of B3GALT5-AS1 on the caerulein-produced cell injury were produced through the involvement of NF-κB signals. NF-κB signal was discovered to be crucial in several inflammatory diseases [40]. NF-κB excitation has been confirmed as an early and central event in the progression of inflammation during AP [41]. Li et al. [42] demonstrated that the TLR4-mediated NF-κB signal was a pivotal mediator in the regulation of HMGB1-induced pancreatic injury in the mice with SAP. In the present study, it was discovered that the overexpression of B3GALT5-AS1 depressed the excitation of the NF-κB signal in the caerulein-stimulated AR42J cells, and this effect was remarkably reversed in the cells with a combination of B3GALT5-AS1 overexpression and miR-203 overexpression. Therefore, it was speculated that B3GALT5-AS1 might be regulating caerulein-induced cell injury in AR42J cells by modulating the excitation of the NF-κB signals.

To sum up, the data from the current research implied that B3GALT5-AS1 expression was reduced in patients with AP. Overexpression of B3GALT5-AS1 might be able to alleviate the caerulein-induced cell injury in AR42J cells through the regulation of the miR-203/NFIL3 axis and the inhibition of exciting the NF-κB signals. B3GALT5-AS1 may, thereby, be suggested as a promising diagnostic marker or therapeutic target for AP. However, the present study was limited in certain terms as only one cell line was used in the present study and no in vivo (animal) experiments were performed. Therefore, further investigations are needful to confirm the findings of the present study.

Acknowledgements

This study received no financial support to disclose.

Disclosure statement

There is no conflict of interest to declare.

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