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Murzina E.[1], Dosenko V.[2], Drevytska T.[2]
[1] Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine
[2] Bogomoletz Institute of Physiology of the National Academy of Sciences of Ukraine, Kyiv, Ukraine

Мурзина Э.А.[1], Досенко В.Е.[2], Древицкая Т.И.[2]
[1] Национальный университет здравоохранения Украины имени П.Л. Шупика, Киев, Украина
[2] Институт физиологии имени А.А. Богомольца Национальной академии наук Украины, Киев, Украина

Expression of Long Non-Coding RNA PRINS and G1P3 in Children with Psoriasis

Экспрессия длинной некодированной РНК PRINS и G1P3 у детей с псориазом

Abstract

Purpose. To identify and compare the expression of PRINS and G1P3 in children with psoriasis depending on the clinical-epidemiological features of the pathological process and to study the relationship between PRINS expression and G1P3 expression.
Materials and methods. 56 children with psoriasis aged from 4 to 17 years were examined. Psoriasis was diagnosed on the base of clinical data and generally accepted diagnostic criteria. PRINS and G1P3 expression levels were determined in psoriatic keratinocytes and buccal epithelium through reverse transcription and real-time PCR. Psoriasis severity indices (BSA, PASI, PGA) and body mass index (BMI) were calculated. The study materials were statistically processed using the STATISTICA 13.3 software.
Results. In children with psoriasis, statistical differences were found between the expression of PRINS in the buccal epithelium and in keratinocytes affected by psoriasis (p=0.034). Similar differences in PRINS expression were found in the group of girls (p=0.038), in the group of children with BSA >10 (p=0.019) and in the group with PGA=4 (p=0.017), in the group of children with the signs of onychodystrophy (p=0.009) and exacerbation of psoriasis for more than 5 weeks (p=0.017). The relationship between the expression of PRINS and peculiarities of the clinical manifestations of psoriasis was revealed, which is reflected in the increase of the area of skin lesions by 1% and increase of the intensity of skin manifestations by 0.29 with the increase of PRINS expression in the buccal epithelium by 0.207. G1P3 expression in psoriatic keratinocytes is 0.88±0.26. Statistical differences in G1P3 expression were revealed when comparing the groups by gender, skin lesion area (BSA), intensity of clinical signs (PGA), and BMI.
Conclusion. Dysregulation of PRINS in the pathogenesis of psoriasis was confirmed. It was found that not only the level of PRINS expression in the intact epidermis is important for the course of psoriasis, but also the level of differences with PRINS expression in psoriatic keratinocytes: high PRINS expression in the buccal epithelium and low expression in psoriatic keratinocytes lead to severe psoriasis with prolonged exacerbation and unfavorable prognosis. The role of increased G1P3 expression in psoriatic keratinocytes in the pathogenesis of psoriasis was confirmed; the more severe psoriasis is in terms of the area of skin lesions and the intensity of clinical manifestations (erythema, desquamation, infiltration of foci), the higher are the levels of G1P3 expression in psoriatic keratinocytes. The relationship between PRINS and G1P3 expression in psoriatic keratinocytes is ambiguous.
Keywords: psoriasis in children, long non-coding RNA, PRINS expression, G1P3 expression.

Резюме

Цель. Выявить и сравнить экспрессию PRINS и G1P3 у детей с псориазом в зависимости от клинико-эпидемиологических особенностей патологического процесса, изучить взаимосвязи экспрессии PRINS и экспрессии G1P3.

Материалы и методы. Обследовали 56 детей с псориазом в возрасте от 4 до 17 лет. Диагноз «псориаз» выставляли на основании клинических данных и общепринятых диагностических критериев. Уровни экспрессии PRINS и G1P3 определяли в псориатических кератиноцитах и буккальном эпителии путем обратной транскрипции и ПЦР в реальном времени. Проводили расчет индексов тяжести псориаза (BSA, PASI, PGA); индекса массы тела (ИМТ). Материалы исследования были статистически обработаны с помощью программы Statistica 13.3.

Результаты. У детей с псориазом установлены статистические различия между экспрессией PRINS в буккальном эпителии и в пораженных псориазом кератиноцитах (p=0,034). Аналогичные различия экспрессии PRINS выявлены в группе девочек (p=0,038), в группе детей с BSA >10 (p=0,019) и в группе с PGA=4 (p=0,017), в группе детей с признаками ониходистрофии (p=0,009) и при обострении псориаза более 5 недель (p=0,017). Выявлены взаимосвязи между экспрессией PRINS и особенностями клинических проявлений псориаза, что отобразиться в увеличении площади поражения кожи на 1% и в усилении интенсивности кожных проявлений на 0,29 при увеличении экспрессии PRINS в буккальном эпителии на 0,207. Экспрессия G1P3 в кератиноцитах очагов поражения составляет 0,88±0,26. Выявлены статистические различия экспрессии G1P3 при сравнении групп по полу, площади поражения кожи (BSA), интенсивности клинических признаков (PGA), ИМТ.

Заключение. Подтверждено наличие в патогенезе псориаза нарушения регуляции PRINS. Установлено, что значение для течения псориаза имеет не только уровень экспрессии PRINS в интактном эпидермисе, но и уровень различий с экспрессией PRINS в псориатических кератиноцитах: высокая экспрессия PRINS в буккальном эпителии и низкая в псориатических кератиноцитах приводит к тяжелому псориазу с длительным обострением. Подтверждена роль повышенной экспрессии G1P3 в псориатических кератиноцитах в патогенезе псориаза. Чем тяжелее псориаз по площади поражения кожи и по интенсивности клинических проявлений (эритема, шелушение, инфильтрация очагов), тем выше уровни экспрессии G1P3 в псориатических кератиноцитах. Взаимосвязь экспрессии PRINS и G1P3 в псориатических кератиноцитах неоднозначная.

Ключевые слова: псориаз у детей, длинная некодированная РНК, экспрессия PRINS, экспрессия G1P3.

■ INTRODUCTION

Pretty much attention is paid to the research on genetic aspects of psoriasis. It was made clear that a variety of genes participate in symptom occurrence and that the disease is genetically heterogenous [1, 2]. An increase in the number of studies indicates lncRNA dysregulation to be central to psoriasis pathogenesis [3–5]. Several psoriasis-associated lncRNAs have been studied so far. Psoriasis-associated long non-coding RNA, referred to as psoriasis susceptibility-related RNA gene, induced by stress (PRINS), revealed the highest expression to take place in skin areas, unaffected by psoriasis, suggesting that it may play a critical part in psoriasis onset [6]. Széll et al. [3] reported that PRINS overexpression in the normal-appearing skin, in case of psoriasis, changes the stress response and contributes to the pathogenesis of the disease.

Contrastingly, one of the identified genes – G1P3, which plays a part in pathogenesis of human cancer with anti-apoptotic activity and is regulated by interferon alpha, is under the control of PRINS gene [7, 8]. These two features of G1P3 gene are also important in psoriasis pathogenesis [9, 10]. Szegedi and co-authors [11] have found that PRINS-regulated G1P3 RNA synthesis was increased 400-fold in the psoriatic lesional epidermis and 9-fold in the normal-appearing epidermis in patients with psoriasis as opposed to the healthy skin. The in vitro test has shown that G1P3 inhibition inhibits spontaneous keratinocyte apoptosis, which is indicative of high G1P3 expression to change apoptosis intensity in keratinocytes in case of psoriasis and triggers the disease pathogenesis.

■ PURPOSE OF THE STUDY

To detect and compare PRINS and G1P3 expression in the non-lesional psoriatic keratinocytes and psoriatic lesional keratinocytes, in children with psoriasis, depending on clinical and epidemiological features of the disease process and the effect of PRINS on G1P3 expression.

■ MATERIALS AND METHODS

We examined 56 children with psoriasis aged 4–17, who underwent treatment in Kyiv Municipal Dermatology-STI Clinic, from 2019 till the early part of 2020. The ratio between girls and boys came to 1.43: 23 boys and 33 girls (Table 1). Psoriasis was diagnosed based on clinical findings and generally accepted diagnostic criteria. Psoriasis was first-ever diagnosed in 19 (34.55%) among 56 children. Clinical findings of the disease process was predominantly represented by plaque psoriasis – 40 (71.43%), guttate psoriasis was diagnosed in 8 (14.29%) children, inverse psoriasis – in 4 (7.14%) children, scalp psoriasis – in 3 (5.36%) children and palmoplantar type – in 1 (1.79%) child. These types of psoriasis predetermined widespread psoriasis in 48 (85.71%) children and localized in 8 (14.29%) children.

According to the latest guidelines, the severity of psoriasis in children is assessed on the BSA (Body Surface Area) index, PASI (Psoriasis Area and Severity Index) index and I/PGA (Investigator/Physician's Global Assessment Scale) or PGA [12, 13].

Body mass index (BMI) was calculated as the ratio of body weight in kilos to the squared height in meters (kg/m^2) taking into consideration a child's age according to the WHO guidelines [14]. An increased BMI was reported in 13 children and 1 child with class 1 obesity among. The excess weight in children with psoriasis ranged from 7 to 23% of an optimal value.

Current research on detecting the stress-induced long non-coding RNA, or PRINS, in individuals with psoriasis, dealt with the non-lesional psoriatic epidermis, unaffected by psoriasis as well as with the lesional psoriatic epidermis. The material was sampled using biopsy. Our study involved children with psoriasis, thus PRINS and G1P3 expression was supposed to be detected in buccal epithelial cells, which was considered as non-lesional psoriasis epidermis, and psoriatic lesional epidermis: scales from plaques and papules, considering that biopsy is another stress for children with psoriasis, capable of provoking disease exacerbation. The buccal epithelium and psoriatic lesional epidermis were taken using sterile brushes and scalpels, packaged in sterile Eppendorf tubes. The material

Table 1
Clinical and epidemiological characteristics in children with psoriasis

Indicators, units of measurement	Mean value or total number
Mean age, years	12.21 ± 0.45
Mean age of disease onset, years	8.95±0.54
Average duration of the disease, years	3.38±0.49
Average duration of psoriasis exacerbation, weeks	12.00±2.69
1–4-week duration of exacerbation, number of children	28
Duration of exacerbation ≥4 weeks, number of children	28
Average BSA, %	26.26±2.35
BSA ≤10, number of children	16
BSA >10, number of children	40
Average PASI before treatment	14.01±1.41
PASI ≤10, number of children	30
PASI >10, number of children	26
Average PASI at the end of the course of treatment	1.99±0.45
Average PGA	3.20±0.14
PGA=1–2, number of children	18
PGA=3, number of children	16
PGA=4, number of children	22
Family history is positive/negative, number of children	27/29
Normal BMI, number of children	43
Increased BMI, number of children	13

was stored at –20 °C. Specimens were transported to the lab by maintaining the cold chain environment.

In order to isolate total RNA from the normal-appearing epidermis and psoriatic lesional epidermis (scales), acid guanidinium thiocyanate-phenol-chloroform extraction was performed using TRIzol (Invitrogen) reagent. The RNA samples, isolated, were diluted in 50 µl of distilled water, whereafter the RNA concentration was measured by spectrophotometry (NanoDrop ND1000). Reverse transcription was performed in 2 phases. Initially, the mixture, consisting of 1 µl Random Hexamer primers, 6 µl of total RNA and 5 µl of nuclease-free water, was prepared. The samples, obtained, were incubated for 5 minutes at 70 °C in the thermal – cycler the Applied Biosystems Gene Amp® PCR System 2700 (USA). At the second stage, 2 µl of dNTPs, 4 µl of RT Buffer, 0.5 µl of RiboLock RNase Inhibitor and 0.9 µl of RevertAid H Minus Reverse Transcriptase were added to the mixture. The samples, obtained, were thermostated for 60 min at 42°C, then incubated for 10 min at 70 °C. A real-time polymerase chain reaction (PCR) was performed in thermal cycler – the Applied Biosystems 7500 Fast Real-Time PCR (USA). In order to perform PCR, 10 µl mixture, including 5 µl of TaqMan™ Universal PCR Master Mix, 2 µl of cDNA, 0.15 µl of a long non-coding PRINS RNA probe, 0.2 µl of Rox (1 : 9) and 2.65 µl of water, was injected into the 96-well microplate. Denaturation of cDNA was lasting for the period of 15 sec at 95°C. Probe attachment and elongation were lasting for 1 min at 60 °C. The real-time polymerase chain reaction program consisted of 50 cycles.

PRINS expression in non-lesional epidermis, taken from 20 children without chronic skin conditions – the control group, served for controlling and comparing the results.

Study records were statistically processed using in Statistica 13.3 software (developed by StatSoft.Inc). The Student's t-test was used when comparing the mean values of data sets, with the level of statistical significance p≤0.05. A correlation analysis was conducted by applying the Pearson's correlation coefficient. The values of the correlation coefficient (r) were interpreted according to the Chaddock scale. The prognostic model of a dependency between a quantitative variable and factors, represented by quantitative indicators, was designed using simple and multiple linear regressions.

■ RESULTS

Overall PRINS and G1P3 expression

In children with psoriasis, PRINS expression in buccal epithelial cells was of statistically significant difference to the measurements of PRINS expression in psoriatic lesional keratinocytes in plaques and papules, and more than 5-8 times higher as compared to PRINS expression in buccal epithelial cells of children from the control group (Table 2).

Table 2
PRINS expression in the psoriatic lesion epidermis and non-lesion skin depending on clinical and epidemiological features of psoriasis

Grouping based on various features		PRINS expression		Statistical significance
		Psoriatic lesion epidermis	Psoriatic non-lesion epidermis	
Children with psoriasis (n=56)		0.60±0.09	1.38±0.34	**P=0.034***
Healthy children (n=20)		–	0.26±0.06	
Statistical significance			**P=0.002***	
Sex	Boys (n=23)	0,66±0,14	0.86±0.23	P=0.435
	Girls (n=33)	0.56±0.12	1.67±0.50	**P=0.038***
Statistical significance		P=0.554	P=0.137	
Clinical types of psoriasis	Plaque psoriasis (n=40)	0.62±0.11	1.42±0.38	P=0.053
	Others (n=16)	0.57±0.10	128±0.51	P=0.187
Statistical significance		P=0.771	P=0.825	
BSA	≤10 (n=14)	0.77±0.18	0.76±0.38	P=0.991
	>10 (n=42)	0.55±0.09	1.60±0.42	**P=0.019***
Statistical significance		P=0.309	P=0.147	
PGA	1–2 (n=18)	0.72±0.17 *	1.19±0.41 *	P=0.289
	3 (n=16)	0.81±0.13*/ **	1.85±0.55	P=0.077
	4 (n=22)	0.38±0.04 **	1.19±0.32*	**P=0.017***
Statistical significance		* P=0.696 ** **P=0.005***	* P=0.059	
PASI	≤10 (n=30)	0.74±0.17	1.72±0.52	P=0.085
	>10 (n=26)	0.47±0.07	0.97±0.41	P=0.245
Statistical significance		P=0.169	P=0.266	

Table 2 end

Body mass index	Increased (n=13)	0.48±0.11	1.00±0.34	P=0.161
	Normal (n=43)	0.64 ±0.11	1.49±0.42	P=0.057
Statistical significance		P=0.340	P=0.375	
Psoriatic onychodystrophy	Occurs (n=15)	0.57±0.11	1.83±0.44	**P=0.009***
	Not found (n=41)	0.62±0.11	1.22±0.40	P=0.165
Statistical significance		P=0.754	P=0.276	
Duration of exacerbation	1–4 weeks (n=28)	0.48±0.11	1.28±0.45	P=0.099
	≥4 weeks (n=28)	0.72±0.14	1.47±0.52	**P=0.017***
Statistical significance		P=0.200	P=0.776	

Note: * discrepancies in scores are statistically significant (p<0.05).

G1P3 expression in children with psoriasis was identified only in psoriatic lesional keratinocytes. G1P3 expression in buccal epithelium was detected only in 2 children with psoriasis and 2 children from the control group. G1P3 expression in the normal-appearing skin in children with psoriasis averaged out at 39.08±1.59, being 100 times higher than G1P3 expression rates in children from the control group – 0.39±0.02. It means that research on G1P3 expression in the non-lesional psoriatic epidermis in children with psoriasis using non-invasive sampling techniques demands improvement (Table 3).

Table 3
G1P3 expression in the psoriatic lesion epidermis depending on clinical and epidemiological features of psoriasis

Grouping based on various features		**G1P3 expression in the psoriatic lesion epidermis**	**Statistical significance**
Children with psoriasis (n=56)		0.88±0.26	
Sex	Boys (n=23)	1.41±0.52	**P=0.031***
	Girls (n=33)	0.46±0.22	
Clinical types of psoriasis	Plaque psoriasis (n=40)	0.75±0.24	**P=0.025***
	Others (n=16)	0.15±0.02	
BSA	≤10 (n=16)	0.26±0.11	**P=0.030***
	>10 (n=40)	1.03±0.32	
PGA	1–2 (n=18)	0.35±0.09 **	** **P=0.014*** *** **P=0.023***
	3 (n=16)	1.50±0.42 **/***	
	4 (n=22)	0.42±0.14 ***	
PASI	≤10 (n=30)	1.11±0.44	P=0.398
	>10 (n=26)	0.65±0.30	
Body mass index	Increased (n=13)	0.10±0.04	**P=0.012***
	Normal (n=43)	0.95±0.31	
Psoriatic onychodystrophy	Occurs (n= 13)	0.85±0.28	P=0,956
	Not found (n=43)	0.89±0.34	
Duration of exacerbation	1–4 weeks (n=28)	0.60±0.29	P=0.324
	≥4 weeks (n=28)	1.12±0.42	

Note: * discrepancies in scores are statistically significant (p<0.05).

PRINS and G1P3 expression depending on sex

At almost identic PRINS expression in the psoriatic lesional epidermis, PRINS expression in the non-lesional psoriatic epidermis in the girl's group was higher than expression in the group of boys; however, there is no significant difference. In contrast to boys, in girls, statistically significant differences were detected between PRINS expression in the psoriatic lesional epidermis and non-lesional skin. G1P3 expression was probably higher in the group of boys than in the girl's group, so in boys it correlated with PRINS expression in the non-lesional psoriatic epidermis (r=0.41; p=0.049).

PRINS and G1P3 expression depending on clinical types of psoriasis

When comparing PRINS expression in groups of children with plaque psoriasis and the group, referred to as "Others", including all other types of psoriasis, namely: guttate, palmoplantar, scalp and inverse psoriasis, statistically significant differences were not found to exist between PRINS expression both in the non-lesional and psoriatic lesional epidermis. In case of plaque psoriasis, G1P3 expression was probably higher than G1P3 expression in the group of "Other" clinical types, so PRINS and G1P3 expression in psoriatic lesional keratinocytes correlated with each other (r=0.32; p=0.041).

PRINS and G1P3 expression depending on the severity of psoriasis

PRINS expressions in psoriatic lesional epidermis and buccal epithelium in groups of children depending on BSA severity were comparable. However, in the group of children with BSA >10, there was a statistically significant difference (p=0.019) between the levels of PRINS expression in psoriatic lesional keratinocytes and in the unaffected epithelium, which was not detected with BSA <10 (p=0.991). Relationships between PRINS expression in buccal epithelium in the group of children with BSA ≤10 and duration of the pathological process exacerbation (r=0.50; p=0.063) were also established. The level of G1P3 expression at BSA>10 was probably higher than the expression level at BSA ≤10 (p=0.03).

PRINS expression in psoriatic lesional epidermis was the lowest at PGA=4 (p=0.005), and, although PRINS expression in buccal epithelium was comparable between groups by the PGA index (p=0.059), but, with increasing severity of psoriasis in terms of intensity of skin manifestations, the statistically significant difference between PRINS expression levels in psoriatic lesional keratinocytes and intact epithelium increased (from p=0.289 to p=0.017). The level of G1P3 expression at PGA=3 was significantly higher than at PGA=1–2 (p=0.014) and PGA=4 (p=0.023). The correlation between G1P3 and PRINS expression in psoriatic lesional keratinocytes was the highest in case of PGA=1–2 (r=0.51; p=0.027), it lost the significance level in case of PGA=3 (r=0.48; p=0.059) and when PGA=4 it was totally non-existent. PRINS and G1P3 expression did not differ between groups depending on the PASI index both in the psoriatic lesional epidermis and normal-appearing skin.

PRINS and G1P3 expression depending on BMI

Significant differences between PRINS expression in children with psoriasis, depending on BMI, did not exist. G1P3 expression in case of a

normal BMI in children with psoriasis was significantly higher than in children with an increased BMI. Correlation between G1P3 and PRINS expression in the psoriatic lesional epidermis (r=0.97; p<0.001) was identified in children with an increased BMI, which in turn correlated with PRINS expression in the non-lesional psoriatic epidermis (r=0.83; p<0.001).

PRINS and G1P3 expression depending on the occurrence of onychodystrophy

PRINS and G1P3 expression in children in the occurrence of psoriasis-associated nail plate lesions was compared with expression in children with psoriasis without onychodystrophy both in the lesional epidermis and non-lesional psoriatic epidermis. However, in the occurrence of onychodystrophy, PRINS expression in the non-lesional psoriatic epidermis was apparently higher than PRINS expression in the psoriatic lesional epidermis (p=0,009). There was also a correlation between PRINS and G1P3 expression in psoriasis plaques (r=0.66; p=0.007) in children with onychodystrophy.

PRINS and G1P3 expression depending on the duration of disease exacerbation

The duration of psoriasis exacerbation did not affect PRINS and G1P3 expression. Although when the disease process lasted more than 4 weeks, the significance level of a statistically significant difference between PRINS expression in the normal-appearing skin and PRINS expression in the psoriatic lesional epidermis increased from 90% to 95%.

■ DISCUSSION

The detected increased rates of PRINS expression in the non-lesional psoriatic epidermis in children with psoriasis are fully consonant with the research by Széll et al. [3] and Szegedi et al [11], who reported that PRINS overexpression in intact skin in case of psoriasis changes the stress response, inhibits keratinocyte apoptosis and triggers the disease pathogenesis.

In our study PRINS expression levels in children with psoriasis depending on the gender were comparable, although some studies indicate a more severe course of the disease in men and a predominance of psoriatic arthritis in psoriasis in men [15], and an earlier onset and severe course of the disease in girls in childhood [42, 47]. Therefore, PRINS overexpression in the buccal epithelium in the group of girls and significant expression of G1P3, which affected the processes of apoptosis in boys, determined the course of psoriasis in children, which, based on clinical features, did not differ between girls and boys in our study (Table 4).

When studying G1P3 mRNA regulation in various tumors and in case of autoimmune diseases, a noticeable increase is observed [16, 17], including malignancies of viral etiology, such as hepatocellular carcinoma, malignancies-associated with chronic inflammation such as stomach cancer [18], and malignant tumors with endocrine dysregulation such as breast and ovarian cancer. Additionally, immune dysregulation serves as a distinctive feature of an autoimmune system in case of diseases such as lupus, psoriasis and multiple sclerosis. G1P3 expression correlated with the severity in patients with lupus [19]. In the same way, G1P3 was noticeably increased in biopsy samples of the skin affected as compared to the adjacent healthy

Table 4
Clinical features of psoriasis depending on sex

	Boys	Girls
Mean age, years	12.78±0.71	11.82±0.56
Mean age of disease onset, years	9.43±0.84	8.06±0.72
Average duration of psoriasis exacerbation, weeks	11.78±4.36	12.15±3.45
BSA	26.03±3.55	26.41±3.16
PGA	3.09±0.17	3.03±0.15
PASI	11.07±4.38	11.91±1.83

skin and correlated both with the extent of body surface involvement and symptoms of dermatosis (erythema, exfoliation and infiltration) [20]. Increased G1P3 expression was found not only in biopsy samples taken from psoriatic lesions, but also from psoriatic lesional keratinocytes, which was demonstrated in our study. Moreover, G1P3 expression was probably higher in more severe psoriasis both in terms of the body surface area affected and the intensity of skin manifestations (erythema, exfoliation and infiltration). And a more severe and common clinical type – plaque psoriasis was likely to have higher G1P3 expression than other clinical types of psoriasis. Expectable PRINS overexpression in non-lesional psoriatic epidermis in contrast to PRINS expression in psoriatic lesional epidermis was detected, similarly, in case of severe and widespread types of psoriasis. Additionally, it was determined that an increase in PRINS expression in buccal epithelial cells in children with psoriasis by 0.207, which almost corresponds to PRINS expression in the group of healthy children, will lead to 1% increase in the extent of body surface involvement, while an increase in PRINS expression in buccal epithelial cells by 1.406 – to an increase in psoriasis severity on the PGA index by 1.

Obesity is considered to be an independent predictor of psoriasis [21]. Adipose tissue is metabolically active, secretes pro-inflammatory cytokines that further alter the metabolism of interleukins (IL) 1, IL-6, TNF-α and anti-inflammatory cytokine, adiponectin. The number of these pro-inflammatory cytokines rises in obesity, while adiponectin gene expression decelerates [22, 23]. However, in our study, no additional effect of adipose tissue on the level of PRINS expression was found. It is possible that the lack of differences in PRINS expression levels is due to the fact that there is only 1 obese child in the group of overweight children, and other children have only an excess of optimal weight. And, the level of G1P3 expression in children with elevated BMI was statistically lower than in normal BMI, and the presence of very high correlations between PRINS and G1P3 expression levels in psoriatic keratinocytes indicated an additional regulation of these processes by metabolically active adipose tissue.

Associations have been established between the development of psoriatic onychodystrophy and prolonged, more severe course of the disease, psoriatic arthritis, early onset of psoriasis, the presence of a strong family history [24, 25]. Consideration of psoriatic onychodystrophy as a factor complicating the course of psoriasis was justified in determining the PRINS expression levels in groups of children with and without onychodystrophy. Excessive expression of PRINS in the buccal epithelium, which was statistically higher than the expression of PRINS in the psoriatic

lesional epidermis in a group of children with onychodystrophy, may be a negative prognostic sign of psoriasis.

Psoriasis is a chronic skin condition without a well-defined etiology and effective treatment. The negative impact of psoriasis on the quality of human life may be rather substantial. The Global Burden of Disease Study 2010 by the WHO, conducted in 2010, revealed that the average global DALY (Disability-adjusted life year) for psoriasis was estimated at 1050660 years, which is twice as high as compared to hepatitis C [26]. It results from the durable course of the disease and durable psoriasis exacerbations. Previous studies have confirmed the dependence of the duration of exacerbation of psoriasis on the PRINS expression in the intact epidermis [20]. In our study, PRINS and G1P3 expression levels did not differ between groups depending on the disease duration. However, exacerbations of psoriasis lasting more than 4 weeks were characterized by significant differences between the PRINS expression levels in lesional keratinocytes and buccal epithelium. Therefore, the difference between the expression in the buccal epithelium and psoriatic lesional kertinocytes is important for the duration of psoriasis exacerbation. It was also calculated that increasing the expression of PRINS in the buccal epithelium by 0.044 will increase the duration of psoriasis exacerbation by 1 week.

Growing data from various studies reveal that lncRNAs are key regulatory molecules present at virtually every level of cellular physiology. Many human diseases are associated with changes in lncRNAs. This is not only a new level of complexity in the molecular component of human disease; it also opens up the potential of using lncRNAs as diagnostic markers and therapeutic targets. LncRNAs have advantages as biomarkers because they can be easily detected in body fluids. In addition, as compared to mRNA, lncRNA is a functional molecule and its level of expression may be a better indicator of disease. Although these suggestions are still under development, the use of lncRNA in clinical medicine has already begun [27].

The largest number of reports on the importance of lncRNA in the disease diagnosis concerns malignant tumours. Thus, the role of lncRNA HOTAIR in determining the tumour invasion and dissemination is shown. Its expression levels in primary breast tumours positively correlate with metastasis and poor outcome [28]. Another example of lncRNA involved in cancer malignancy is metastasis-associated lung adenocarcinoma transcript 1 (MALAT1), widely expressed in normal human tissues but upregulated in different types of cancer [29, 30]. LncRNAs were identified in various neural pathologies. A recent study has detected over 200 differentially expressed lncRNAs in autism disorders, enriched for genomic regions containing genes related to neurodevelopment and psychiatric disease, while another recent work has identified lncRNAs deregulated in Huntington's disease [31, 32].

LncRNAs are essential components of cellular regulatory networks and, therefore, may influence all aspects of physiology. This leads to a constant increase in the number of studies to determine lncRNA not only in malignant tumours, but also in somatopathies: systemic lupus erythaematosus, psoriasis, uraemia, facioscapulohumeral muscular dystrophy, a-Talasaemia, cardiovascular diseases and hypertension [27].

In patients with psoriasis, a high PRINS expression was detected in unaffected keratinocytes and low expression in psoriatic keratinocytes, but

also higher than in the skin of healthy volunteers [3, 6, 11]. The results of PRINS overexpression in the buccal epithelium of children with psoriasis compared with the expression in psoriatic scales from psoriatic lesions and compared with the PRINS expression levels in the healthy children's buccal epithelium were obtained in our study. These data suggest that PRINS is a transcript ubiquitously expressed in the human body. It may be determined not only in the skin using biopsy or in the blood, but also in cells collected by non-invasive methods. Therefore, the PRINS expression determination in the buccal epithelium of children with psoriasis at the present-day stage can be used for the differential diagnosis of psoriasis and the establishment of the diagnosis.

We also showed in our study that not only is the PRINS expression level in non-lesional psoriatic epidermis important, but the comparison with the PRINS expression levels in psoriatic keratinocytes as well. The severe and prolonged course of psoriasis in children is characterized by the PRINS overexpression levels in the buccal epithelium compared to the PRINS expression in psoriatic keratinocytes. It was also established that PRINS changes the stress response of unaffected keratinocytes, and they become more sensitive to stress and proliferative signals [6, 33-35]. Therefore, a comparison of the PRINS expression levels in psoriasis-affected and intact keratinocytes at the beginning of treatment may represent the state of stress readiness of keratinocytes for the psoriasis development and be additional instrument for a decision to be made on therapeutic approach.

■ CONCLUSION

The results of a study of PRINS expression in children with psoriasis confirmed the presence of dysregulation of Psoriasis-susceptibility-Related RNA Gene Induced by Stress – PRINS, in the disease pathogenesis, as evidenced by overexpression of PRINS in children with psoriasis in intact epidermis - buccal epithelium - as compared with PRINS expression levels in psoriatic lesional keratinocytes and compared with a group of healthy children. Essential for the course of psoriasis is not only the PRINS expression level in the intact epidermis, but also the differences between the PRINS expression levels in the buccal epithelium and psoriatic epidermis: the more likely the difference between the PRINS expression levels in the buccal epithelium and in the psoriatic lesional epidermis is, the longer and more severe the course of psoriasis is in terms of the area of skin lesions and the intensity of clinical signs with an unfavourable prognosis for the future.

The PRINS expression determination in the buccal epithelium in children can be used to improve the efficiency of the diagnosis of psoriasis. Determination and comparison of PRINS expression in buccal epithelium along with PRINS expression in psoriatic keratinocytes can be employed to predict the development of severe dermatosis in children and to administer appropriate treatment for children using systemic drugs.

Expression of G1P3 was determined only in psoriatic keratinocytes, which was significantly higher in severe psoriasis both in terms of the area of skin lesions and the intensity of skin manifestations of the pathological process (erythema, desquamation, infiltration). The lack of G1P3 expression in the buccal epithelium of children with psoriasis and healthy children did not allow comparing it by analogy with the PRINS expression and

comparing it with the parameters of healthy skin in children with psoriasis and those of healthy children. Therefore, the question arises concerning the identification of other environments in children with psoriasis to determine the G1P3 expression as a control, but with no additional skin traumatization. Based on the results obtained, it will be possible to determine the role of G1P3 in the pathogenesis of psoriasis and the possibility of using it for the diagnosis, prognosis and treatment of children with psoriasis.

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Contacts/Контакты: elvina2003@ukr.net