ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN – POLONIA

VOL. XXXI (4) SECTIO EE 2013

[1]Departament of Animal Cytogenetics and Molecular Genetics, National Institute of Animal Production, Krakowska 1, 32-083 Balice/Kraków, e-mail: barbara.czech@izoo.krakow.pl
[2]Department of Pig Breeding and Production Technology, University of Life Sciences in Lublin, Akademicka 13, 20-950 Lublin, e-mail: marek.babicz@up.lublin.pl

BARBARA DANIELAK-CZECH[1], ANNA KOZUBSKA-SOBOCIŃSKA[1]
MAREK BABICZ[2], KATARZYNA KRUCZEK[1], BARBARA REJDUCH[1]

Cytomolecular evaluation of structural chromosome instability in sows with decreased reproductive efficiency

Cytomolekularna ocena strukturalnej niestabilności chromosomów u loch o obniżonej wydajności reprodukcyjnej

Summary. Cytomolecular evaluation of pig structural chromosome instability revealed excessive fragility of Xq21, Xq22 and Xq26 chromosome regions in sows with decreased reproductive efficiency. The highest frequency of structural defects was found in SSCXq26 genome region containing *FRM1* gene *locus* with unstable trinucleotide CGG repeats which localization was assigned by *in situ* PCR method. The results obtained suggest that heterosome X instability may be a cause of defective expression of genes related to fertility, leading to a decrease of reproductive efficiency of sows. The presented outcomes can be used in further studies on cytomolecular background of chromosome instability phenomenon and their phenotypic effects in pigs.

Key words: pigs, sows fertility, structural chromosome instability, *FRM1* gene, trinucleotide tandem repeats

INTRODUCTION

The increased spontaneous chromosome fragility (mainly chromosome X) resulting from *in vivo* exposure to environmental mutagens or clastogens is considered to have phenotypic implications and impact on reproductive capabilities [Basrur and Stranzinger 2008]. Therefore, to determine cause-effect relationships of this phenomenon, extensive *in vitro* studies aimed to identify chromosomal *fragile sites* (*FS* – nonrandom chromosomal breaks/gaps) in livestock have been performed in the past few years. The investigations concerned the different modes of *FS* induction by *in vitro* exposure to chemical agents or specific culture conditions changing genome structure, based on DNA polymerase inhibition, nucleotide substitution or folate synthesis deficit [Riggs and Rønne 2009].

The phenomenon of structural chromosome instability in farm animals was previously reported to elicit frequent clinical pathologies or reproductive disturbances (especially chromosome X defects in subfertile females) [Słota *et al.* 2000; Słota and Danielak-Czech 2002; Danielak-Czech and Słota 2002, 2004]. The latest studies in domestic animals, like in humans, link regional chromosome X fragility with instability of tandem repeated sequences, e.g. trinucleotide CGG repeats expansion of the *FRM1* gene related with fragile X syndrome (leading to neurodegeneration and ovarian dysfunction) [Hagerman 2006; Wittenberger *et al.* 2007]. Homologous CGG repeats of this gene have been recently mapped to conserved bovine, ovine and caprine heterosome X regions (BTAXp13 and OAR/CHI Xq22), which was defined as to be extremely susceptible to premutation structural changes associated with prevalent female' infertility [Danielak-Czech and Słota 2006; Kaczor *et al.* 2009; Danielak-Czech *et al.* 2010, 2011, 2012a, b]. In sows, clinical, reproductive and breeding consequences of structural chromosome instability still remain to be precisely determined.

The aim of the present paper was to perform cytomolecular evaluation of spontaneous and *in vitro* induced structural chromosome instability in sows and define influence of this phenomenon on fertility.

MATERIAL AND METHODS

Animals: Cytomolecular analyses were performed in population of 28 exterior normal, 2–5 years old sows of 990 hybrid line (divided into experimental and control groups on the basis of individual reproductive performance), kept in the Pig Hybridization Station of the National Research Institute of Animal Production. The experimental group (n = 14) involved the animals with decreased reproductive efficiency expressed by high services/conception index, long farrowing interval and considerable losses of piglets (%) resulting from abortions, stillbirths and early death after birth. The control group (n = 14) was consisted of sows having normal reproductive performance.

Cytogenetic assay: Pig metaphase chromosome slides, both exposed (24 h before harvesting) to 0.4 μM aphidicolin (APC – DNA polymerase inhibitor) or 0.1 μM 5-fluorodeoxyuridine (FudR – folate synthesis antagonist) as well as untreated by these agents, were prepared following classical cytogenetic protocols of lymphocyte culture and GTG/QFQ banding techniques. Karyotypes were arranged according to the international pig karyotype standard and locations of *fragile sites* were assigned according to the statistical model complied by Jordan *et al.* [1990].

Molecular analysis (In situ PCR technique): The pair of primers (GDB: 187391; c/f) [Fu et al., 1991] (forward) GCTCAGCTCGGTTTCGGTTTCACTTCCCGT and (reverse) AGCCCCGCACTTCCACCACCAGCTCCTCCA flanking CGG repeats of the 5'UTR region of human *FRM1* gene (0.3830 kb) were used for *in situ* PCR [Troyer *et al.* 1994] and biotin-16 dUTP labeling of the homologous porcine sequence directly on microscopic slides with metaphase chromosome spreads (in MJR PTC-100 thermocycler with metal heating block for glass slides). The reaction was carried out according to the thermal profile: 1 cycle: 94°C – 3 min, 65°C – 1 min, 72°C – 1 min; 30 cycles: 94°C – 1 min, 65°C – 1 min, 72°C – 1 min. The amplified, labeled gene fragment was detected by avidin-conjugated FITC, and hybridization signals were analyzed in Axio Imager.D2 (Zeiss) fluorescent microscope equipped with Axio Vision computer-assisted image analysis system.

Statistical analysis: The results were estimated using one-way analysis of variance – *F* test as well as χ^2 and Student's *t*-tests.

RESULTS

No visible phenotype changes and stable karyotype rearrangements were found in the animal investigated. The average values of several reproductive parameters calculated for the groups of subfertile and normally fertile sows are presented in Table 1.

Table 1. Reproductive performance parameters in groups of sows studied
Tabela 1. Parametry użytkowości rozpłodowej w grupach badanych loch

Experimental group n = 14 Grupa doświadczalna n = 14	Control group n = 14 Grupa kontrolna n = 14
services/conception – 3.6 farrowing interval (in months) – 8.4 piglets (stillborn/aborted/early dead) – 12.1%	services/conception – 1.2 farrowing interval (in months) – 6.1 piglets (stillborn/aborted/early dead) – 6.8%

The results of cytogenetic evaluation carried out in the experimental and control groups of sows are given in Table 2. The findings include the mean total frequency (%) of spontaneous and *in vitro* induced chromatid breaks/gaps identified in the whole karyotype and separately in the pair of X chromosomes, calculated for each group and compared statistically between groups. Generally, the frequencies of spontaneous and *in vitro* induced chromatid breaks/gaps were higher in the experimental group of sows than in the control one and the percentages of APC-sensitive breaks/gaps in the groups studied exceeded the proportions of folate–sensitive damages. As shown in Table 2, the frequencies of spontaneous and *in vitro* induced, both total and chromosome X-specific, structural defects (excluding the total number of folate-sensitive ones) differed statistically ($P \leq 0.05$ or $P \leq 0.01$) between the groups.

Table 2. Frequency of spontaneous and induced *in vitro* chromosome structural defects in groups of sows studied
Tabela 2. Częstość spontanicznych oraz indukowanych *in vitro* strukturalnych defektów chromosomów w grupach badanych loch

Group n = 14 Grupa n = 14	Spontaneous chromatid breaks/gaps (%) Spontaniczne pęknięcia/ przewężenia chromatyd (%)		APC – induced chromatid breaks/gaps (%) Pęknięcia/przewężenia chromatyd indukowane APC (%)		Folate-sensitive chromatid breaks/gaps (%) Foliano-wrażliwe pęknięcia/ przewężenia chromatyd (%)	
	total mean ± SD ogółem średnia ± SD	heterosome X mean ± SD heterosom X średnia ± SD	total mean ± SD ogółem średnia ± SD	heterosome X mean ± SD heterosom X średnia ± SD	total mean ± SD ogółem średnia ± SD	heterosome X mean ± SD heterosom X średnia ± SD
e.	5.33** ±3.06	2.50** ±0,81	38.98* ±16.82	17.02**±8,74	13.51 ±5.72	5.32* ±2,11
c.	2.95 ±1.73	1.10 ±0,25	25.83 ±14.14	10.25 ±4,92	8.70 ±6.03	2.77 ±1,24

e. – the experimental group – grupa eksperymentalna
c. – the control group – grupa kontrolna
* significant differences ($P < 0.05$) – różnice istotne ($P < 0,05$)
** highly significant differences ($P < 0.01$) – różnice wysoko istotne ($P < 0,01$)

The most expressive *fragile sites*, shown in Figure 1, occurred with frequency above 1.5% within groups. The percentages of chromosome 1-, 13- and X-specific lesions were higher in sows with decreased reproductive efficiency. The frequencies of heterosome X-specific defects, given in Table 3, were significantly or highly significantly higher in the experimental

group comparing with the control one. The highest frequency of structural defects was found in karyotype of subfertile sows in SSC13q41 and SSC1p23autosomal bands as well as SSCXq21, SSCXq22 chromosome X bands, and especially in SSCXq26 heterosome X region comprising unstable trinucleotide CGG repeats of the *FRM1* gene, which had been mapped basing on combined *in situ* PCR method and GTG/QFQ banding techniques.

Table 3. Unstable chromosome X regions – frequency of *in vitro* induced structural defects in groups of sows studied
Tabela 3. Niestabilne regiony chromosomu X – częstość indukowanych *in vitro* defektów strukturalnych w grupach badanych loch

Chromosome X unstable regions Niestabilne regiony chromosomu X	Chromatid breaks/gaps (%) experimental group n = 14 mean ± SD Pęknięcia/przewężenia chromatyd (%) Grupa eksperymentalna n = 14 średnia ± SD	Chromatid breaks/gaps (%) control group n = 14 mean ± SD Pęknięcia/przewężenia chromatyd (%) Grupa kontrolna n = 14 średnia ± SD
Xq21 (folate-sensitive)	7.67 * ±4.20	3.24 ±1.75
Xq22 (APC-induced)	5.15** ±2.02	2.98 ±1.52
Xq26 (folate-sensitive)	8.22** ±4.01	4.17 ±2.18

* significant differences (P< 0.05) – różnice istotne (P < 0,05)
** highly significant differences (P < 0.01) – różnice wysoko istotne (P < 0,01)

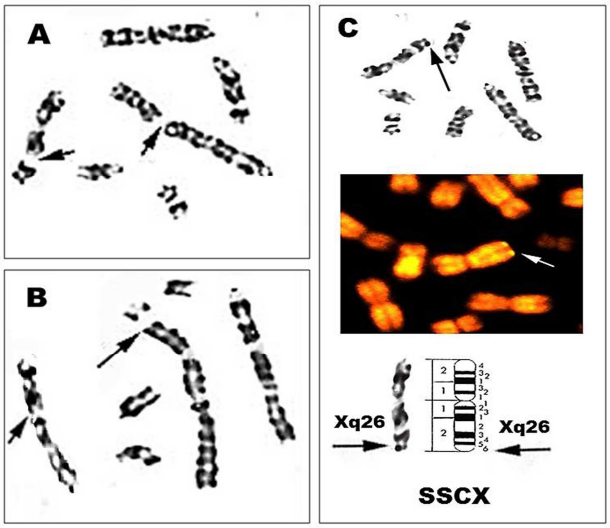

Fig. 1. *Fragile sites* (*FS*) in karyotype of sows with decreased reproductive efficiency: examples of *FS* on autosomes and heterosome X – folate-sensitive SSC13q41 i SSCXq22 (A); APC-induced SSC1p23 i SSCXq21 (B); folate-sensitive unstable SSCXq26 region comprising trinucleotide CGG repeats of *FRM1* gene regulatory sequence, mapped by *in situ* PCR method (C)
Rys. 1. Miejsca łamliwe (*FS)* w kariotypie loch o obniżonej wydajności reprodukcyjnej: przykłady *FS* na autosomach i heterosomie X – folianowrażliwe SSC13q41 i SSCXq22 (A); indukowane APC SSC1p23 i SSCXq21 (B); folianowrażliwy niestabilny region SSCXq26 zawierający trzynukleotydowe powtórzenia CGG sekwencji regulatorowej genu *FRM1*, wymapowane metodą *in situ* PCR (C)

DISCUSSION

Chromosome fragility reflects variations in structural genome stability involved in etiology of chromosome rearrangements. This tendency seems to be the case in the domestic pigs carrying many heritable karyotype defects formed *de novo*, first of all reciprocal translocations associated with producing decreased litter size (on an average about 50%) [Gustavsson 1990; Long, 1991; Danielak-Czech *et. al.* 1994, 1996, 1997]. Cytogenetic monitoring of pig populations provided some evidence of a correlation between reciprocal translocation breakpoints observed *in vivo* and location of *fragile sites* (*FS*) induced *in vitro* (by exposure to folate antagonists, APC or BudR-Hoechst 33258). From among 60 *fragile sites*, which have been described to occur up to now in the pig karyotype, above 40 autosomal sites and one X chromosome-specific site (Xp21) correspond to reciprocal translocation breakpoints [Riggs *et. al.* 1993; Yang and Long 1993; Rønne 1995]. Nine *FS* on chromosome pair 1 and seven on pair 13 were reported as the breakpoints in 31 and 15 (respectively) different translocations diagnosed in several herds. It is worth to note that the most expressive 1p23 and 13q41 autosomal regions, recognized in our experiment, were involved in 3 and 6 reciprocal translocations related to considerable decreased fertility. The present studies not only confirmed similarity of genomic distributions of these two types of breakage events but also pointed out the other X chromosome *loci* i.e. APC-sensitive Xq2.2 as well as folate-sensitive Xq2.1 and Xq26 as the most fragile genome regions observed in the group of sows with normal exterior and karyotype but lower reproductive performance. Since, in our experiment, the percent of X chromosome-specific defects have been significantly higher in the group of subfertile sows, the phenomenon of excessive expression of these *FS* was expected to be very frequent in the population studied. Furthermore, the results obtained showed the APC-dependent Xq2.2 unstable region to be coincident with the 5-AZA- and BrdU-sensitive site that in our previous experiment was ascertained to have been highly fragile in subfertile sows [Riggs *et. al*. 1993; Danielak-Czech and Słota 2002, 2004]. The hypersensitiveness of this chromosomal region is presumed to reflect structural feature changes related to specific in vivo conditions and may provide a better understanding of how environmental pressures result in genetic damage. The described chromosome fragility is suggested to increase frequency of animals with reproductive inefficiency in pig herds.

Unstable porcine Xq26 region involving *FRM1 locus* (related with decreased fertility) represent evolutionary conserved *fragile site*, preserved in most mammalian species [Danielak-Czech and Słota 2006; Kaczor *et al*. 2009; Danielak-Czech *et al*. 2010, 2011]. Homologous human *fragile site* (Xq27.3) comprising *FRM1* gene, due to expansion of highly polymorphic 5'UTR CGG repeats, affects many biological processes (chromosome fragility, gene silencing, transcription, translation or splicing modulation and cell architecture) resulting in genetic disorders and reproductive disturbances [Deelen *et al.* 1994; Hagerman 2006; Wittenberger *et al.* 2007; Usdin 2008]. *FRM1* gene codes protein most commonly found in the brain and is essential for normal cognitive development and female reproductive function. In humans, the CGG segment of the *FMR1* gene promoter region is repeated approximately 5-44 times and increased expression of expanded trinucleotide repeats is associated with developmental delays and other cognitive deficits. Expansions in the range of 55 to 200 repeats result in the premutation, while the full mutation ranges from 200 to several thousand repeats and results in the fragile X syn-

drome [Auer *et al*. 2006; Hagerman 2006; Wittenberger *et al*. 2007]. Sequence analysis of the *FMR1* CGG repeats in mammals showed a high degree of length polymorphisms (in cattle and pigs 5-15 CGG alleles). In some species, including domestic pigs, CGG length exceeds the minimal length present in human gene that is prone to expand, which indicates that trinucleotide repeats may have a functional role in the harbouring genes (regulate gene expression and directly influence protein interaction properties or transcriptional level) [Pearson *et al.* 2005; Madsen *et al*. 2007; Usdin 2008]. Homologous CGG region of this gene was identified in genomes of several farm animals but its chromosomal location and overall genomic context need to be precisely assigned in further experiments. The excessive instability of this orthologous porcine chromosome X region is supposed to implicate parallel effects on reproduction and *FRM1 locus* may be a candidate gene for fertility impairment associated with chromosomal fragility in pigs. Therefore, similar molecular background of sow reproductive dysfunction in the form of repeating breeding and recurrent prenatal or perinatal mortality can be assumed. The findings can be applied in cytomolecular comparative studies to evidence relationships between chromosome instability and reproductive performance in the other breeding animals.

It is worth to note that the pig karyotype display really great variation, with a prevalence of 1/200 of structural chromosomal rearrangements, mainly reciprocal translocations with reiterating chromatid breakpoints involving analogical unstable regions (specific tandemly repeated DNA sequences or *fragile sites*), associated with several clinical defects such as congenital malformations, intersexuality or reproductive dysfunction observed by reduction of the fertility/prolificacy of the carriers and/or their mates [Danielak-Czech and Słota 2008; Słota and Danielak-Czech 2010; Danielak-Czech *et al.* 2013]. Therefore, future cytomolecular studies of relevant repetitive sequences promoting chromosome aberrations can be essential to identify crucial agents predisposing for recurrent reciprocal translocations and predict their clinical consequences before use of young carriers in reproduction, prevent genetic defects from spreading in breeding populations and limit economic effects.

CONCLUSIONS

1. On the basis of reported studies the phenomenon of structural genome instability was proved to be involved in the etiology of chromosome fragility and pig genome rearrangements.

2. The presented outcomes suggest that chromosome X structural instability may lead to defective expression of genes related with pig fertility and decrease of reproductive efficiency.

2. The results obtained can be used in further studies on cytogenetic and molecular background of chromosome instability phenomenon and their phenotypic effects in pigs.

REFERENCES

Auer R.L., Dighiero G., Goldin L.R., Syndercombe-Court D., Jones C., McElwaine S., Newland A.C., Fegan C.D., Caporaso N., Cotter F.E., 2006. Trinucleotide repeat dynamic mutation

identifying susceptibility in familial and sporadic chronic lymphocytic leukaemia. Br. J. Haematol. 136, 73-79.
Basrur P.K., Stranzinger G., 2008. Veterinary cytogenetics: past and perspective. Cytogenet. Genome Res. 120, 11-25.
Danielak-Czech B., Słota E., 2002. Unstable chromosomal regions in subfertile animals. Ann. Anim. Sci. 2, 4-14.
Danielak-Czech B., Słota E., 2004. Mutagen-induced chromosome instability in farm animals. J. Anim. Feed Sci. 13, 257-267.
Danielak-Czech B., Słota E., 2006. Cytogenetic localization of *FRM1* gene in farm animals. Proc. 17th Europ. Colloq. Anim. Cytogenet. Gene Mapping, 28.
Danielak-Czech B., Słota E., 2008. Karyotype control system of AI boars in Poland: the current survey. Ann. Anim. Sci. 3, 255-262.
Danielak-Czech B., Babicz M., Kozubska-Sobocińska A., Rejduch B., Kruczek K., 2012a. Cytogenetic identification of locus-specific unstable trinucleotide repeats in selected *Bovidae* species and *Sus scrofa domestica.* Annales UMCS, Sec. EE, Zootechnica 30 (3), 24–29.
Danielak-Czech B., Babicz M., Rejduch B., Kozubska-Sobocińska A., 2012b. Cytogenetic and molecular analysis of chromosome instability in cattle with reproductive problems. Annales UMCS, Sec. EE, Zootechnica 30 (4), 18–25.
Danielak-Czech B., Kaczor U., Sharan M., 2010. Cytomolecular analysis of chromosome X fragility in subfertile sheep. Anim. Biol. 12, 234-239.
Danielak-Czech B., Kozubska-Sobocińska A., Babicz M., Rejduch B., 2011. Heterosome X premutation structural changes associated with fertility of Romanov sheep. Annales UMCS, Sec. EE, Zootechnica 29 (3), 28–34.
Danielak-Czech B., Kozubska-Sobocińska A., Słota E., Rejduch B., Okularczyk S., 1996. Decrease in pig fertility as a result of reciprocal translocations and associated economic effects on the basis of rcp(7;13)(q13;q46). J. Appl. Genet. 36, 373–384.
Danielak-Czech B., Rejduch B., Kozubska-Sobocińska A., 2013. Identification of telomeric sequences in pigs with rearranged karyotype using PRINS technique. Ann. Anim. Sci. 3, 495–502.
Danielak-Czech B., Słota E., Świtoński M., 1994. Identification of the first reciprocal translocations in the pig population bred in Poland. Proc.11th Eur. Colloq. Cytogenet. Domest. Anim., 20–24.
Danielak-Czech B., Świtoński M., Słota E., 1997. First identification of reciprocal translocations in Polish pigs. J. Anim. Breed. Genet. 114, 69–78.
Deelen W., Bakker., Halley D.J.J., Oostra B.A., 1994. Conservation of CGG region in FRM1 gene in mammals. Am. J. Med. Genet. 51, 513–516.
Fu Y-H, Kuhl D.P.A., Pizzutti A., Pieretti M., Richards S., Verkerk A.J.M.H., Warren S.T., Oostra B.A., Nelson D.L., Caskey C.T., 1991. Fragile X site: A polymorphic and highly mutable CGG repeat in the FMR-1 gene. Cell 67, 1047–1058.
Gustavsson I., 1990. Chromosomes of the pigs. Adv. Vet. Sci. Comp. Med. 34, 73-107.
Hagerman R.J., 2006. Lessons from fragile X regarding neurobiology, autism, and neurodegeneration. J. Dev. Behav. Pediatr. 27, 63–74.
Jordan D.K., Burns T.C., Divelbiss J.E., Woolson R.F., Patil S.R., 1990. Variability in expression of common fragile sites: in search of a new criterion. Hum. Genet. 85, 462–466.
Kaczor U., Danielak-Czech B., Sharan M., 2009. Comparative mapping of the CGG tandem repeats of the human *FRM1* gene in farm animals. Anim. Biol. 11, 242–246.
Long S., 1991. Reciprocal translocations in the pig (*Sus scrofa*): a review. Vet. Rec. 128, 275–278.
Madsen L.B., Thomsen B., Solvsten C.A.E., Bendixen C., Fredholm M., Jorgensen A.L., Nielsen A.L., 2007. Identification of the porcine homologous of human disease causing trinucleotide repeat sequences. Neurogenetics 8, 207–218.
Pearson C.E., Edamura K.N., Cleary J.D., 2005. Repeat instability: mechanisms of dynamic mutations. Nat. Rev. Genet. 6, 729–742.

Riggs P.K., Rønne M., 2009. Fragile sites in domestic animals: molecular insights and challenges. Cytogenet. Genome Res. 126, 97–109.

Riggs P.K., Kuczek T., Chrisman C.L., Bidwell C.A., 1993. Analysis of aphidicolin-induced fragility in the domestic pig (*Sus scrofa*). Cytogenet. Cell Genet. 62, 110–116.

Rønne M., 1995. Localization of fragile sites in the karyotype of *Sus scrofa domestica*: present status. Hereditas. 122, 153–162.

Słota E., Danielak-Czech B., 2002. Unstable chromosome regions in subfertile farm animals. Chromosome Res. 10, 1.

Słota E., Danielak-Czech B., 2010. Zastosowanie metod cytogenetyki molekularnej w diagnostyce i profilaktyce wad genetycznych u świń. In: Zastosowanie osiągnięć naukowych z zakresu genetyki i biotechnologii rozrodu w nowoczesnej produkcji trzody chlewnej. Różycki M., Rocz. Nauk. Zoot., (Monografie i Rozprawy) 44, 9–20.

Słota E., Danielak-Czech B., Pietraszewska J., Kozubska-Sobocińska A., 2000. Preliminary identification of the fragile X in two crossbred cows. Vet. Med.-Czech 45, 308–310.

Troyer D.L., Goad D.W., Xie H., Rohrer G.A., Alexander L.J., Beattie C.W., 1994. Use of direct in situ single-copy (DISC) PCR to physically map five porcine microsatellites. Cytogenet. Cell Genet. 67, 199–204.

Wittenberger M.D., Hagerman R.J., Sherman S.L., McConckie-Rosell A., Welt C.K., Rebar R.W., Corrigan E.C., Simpson J.L., Nelson L.M., 2007. The *FRM1* premutation and reproduction. Fertil. Steril. 87, 456–465.

Usdin K., 2008. The biological effects of simple tandem repeats: Lessons from the repeat expansion diseases. Genome Res. 18, 1011–1019.

Yang M.Y., Long S.E., 1993. Folate sensitive common fragile sites in chromosomes of the domestic pig (*Sus scrofa*). Res. Vet. Sci. 55, 231–235.

This work was conducted as part of research project no N N311 082540, financed by the Polish Ministry of Science and Higher Education

Streszczenie. Cytomolekularna ocena strukturalnej niestabilności chromosomów świń ujawniła szczególną łamliwość Xq21, Xq22 i Xq26 regionów chromosomowych u loch o obniżonej wydajności reprodukcyjnej. Największą częstość defektów strukturalnych indukowanych *in vitro* stwierdzono w regionie genomu SSCXq26 zawierającym *locus* genu *FRM1* z niestabilnymi trzynukleotydowymi powtórzeniami CGG, których lokalizację określono metodą *in situ* PCR. Uzyskane wyniki sugerują, że strukturalna niestabilność heterosomu X może być powodem nieprawidłowej ekspresji genów związanych z płodnością, prowadząc do obniżenia wydajności reprodukcyjnej loch. Prezentowane wyniki mogą być wykorzystane w dalszych badaniach dotyczących cytomolekularnego podłoża zjawiska niestabilności chromosomów oraz jego fenotypowych efektów u świń.

Słowa kluczowe: świnie, płodność loch, strukturalna niestabilność chromosomów, gen *FRM1*, trzynukleotydowe powtórzenia tandemowe