



13TH INTERNATIONAL MULTICONFERENCE “BIOINFORMATICS OF GENOME REGULATION AND STRUCTURE/SYSTEMS BIOLOGY”

4–8 JULY 2022, NOVOSIBIRSK, RUSSIA

Effect of estrogen and progesterone on the frequency and spectrum of karyotypically abnormal cells in cultured uterine leiomyomas

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*Supported by Russian Science Foundation
(grant number 19-15-00108)*

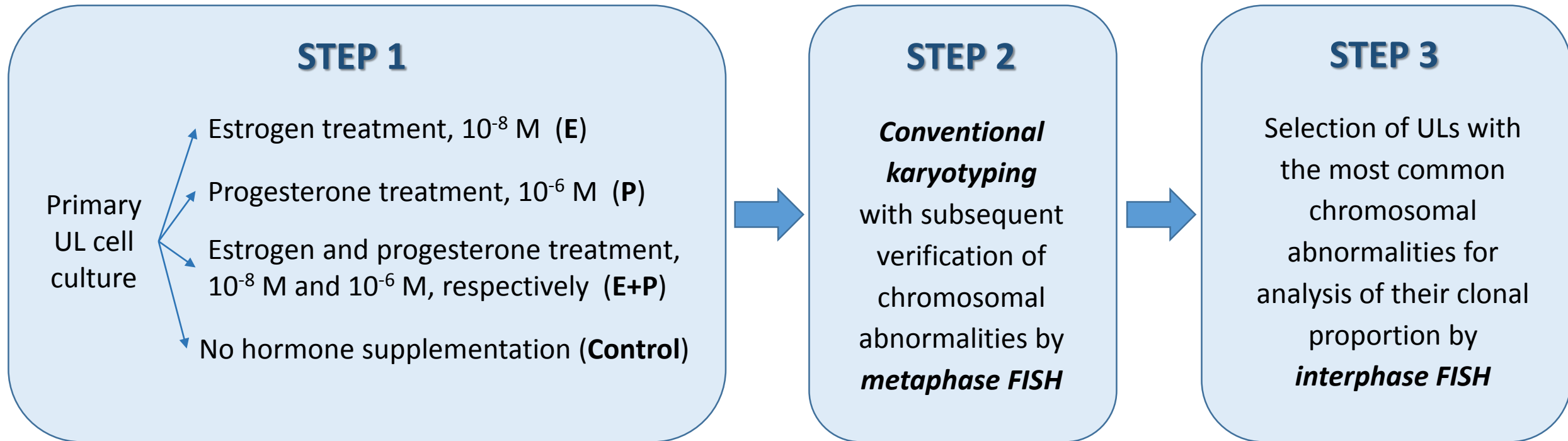
Background

Uterine leiomyomas (ULs) are the most common benign tumors of female reproductive tract. ULs are clonal sex steroid-dependent tumors with the high frequency of chromosomal abnormalities. We recently demonstrated that cytogenetically different UL cell clones have an unequal ability to grow *in vivo* and *in vitro*.

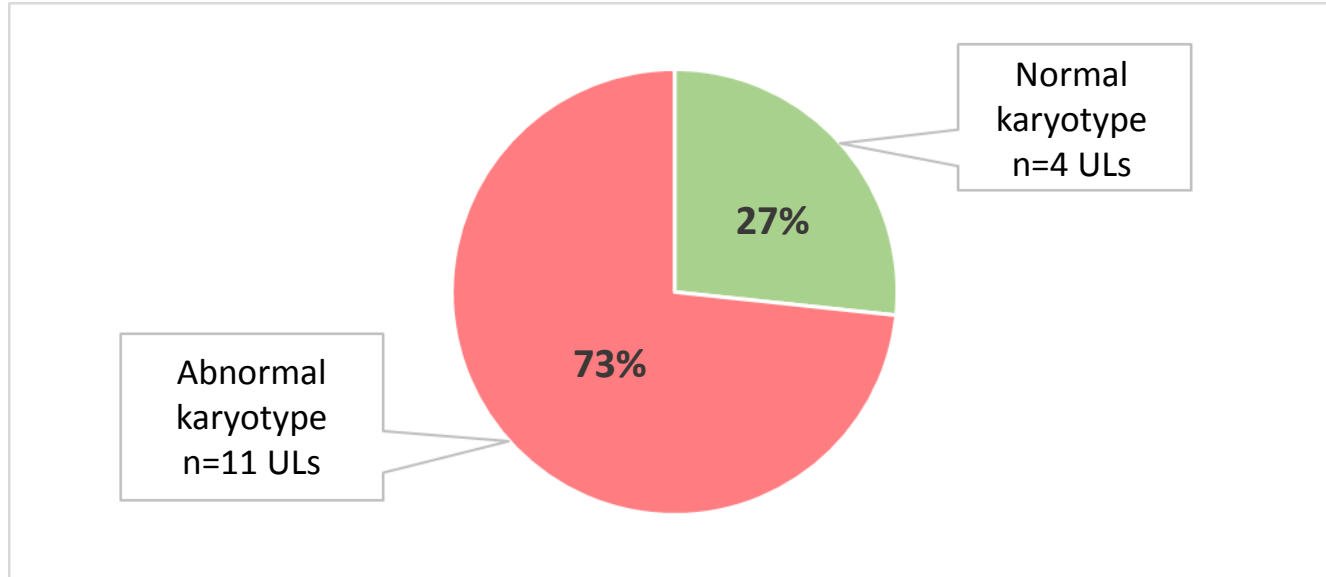
Objective

In the present study, we aimed to check whether combined and isolated estrogen (E) and progesterone (P) treatment has an effect on both clonal spectrum and clonal proportion in ULs with an abnormal karyotype *in vitro*.

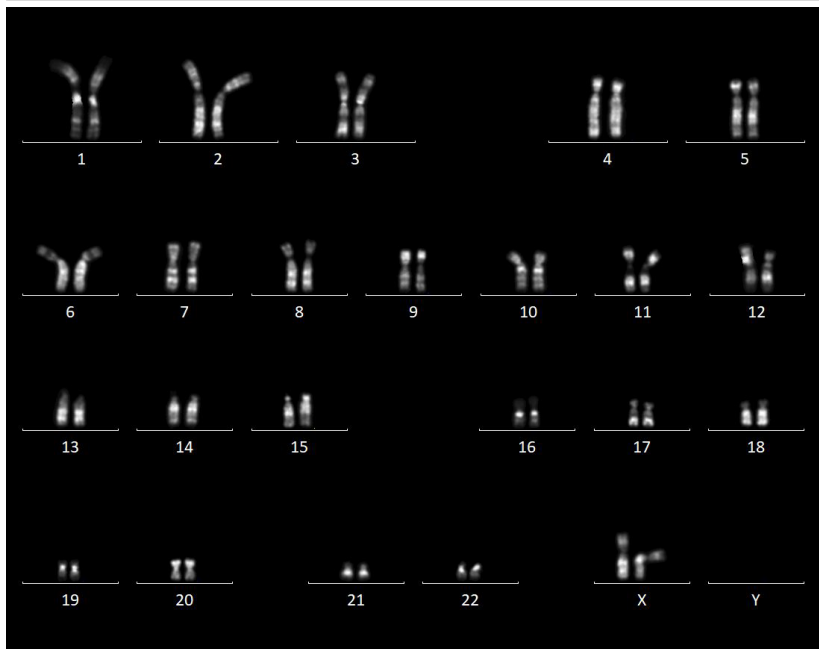
Study design



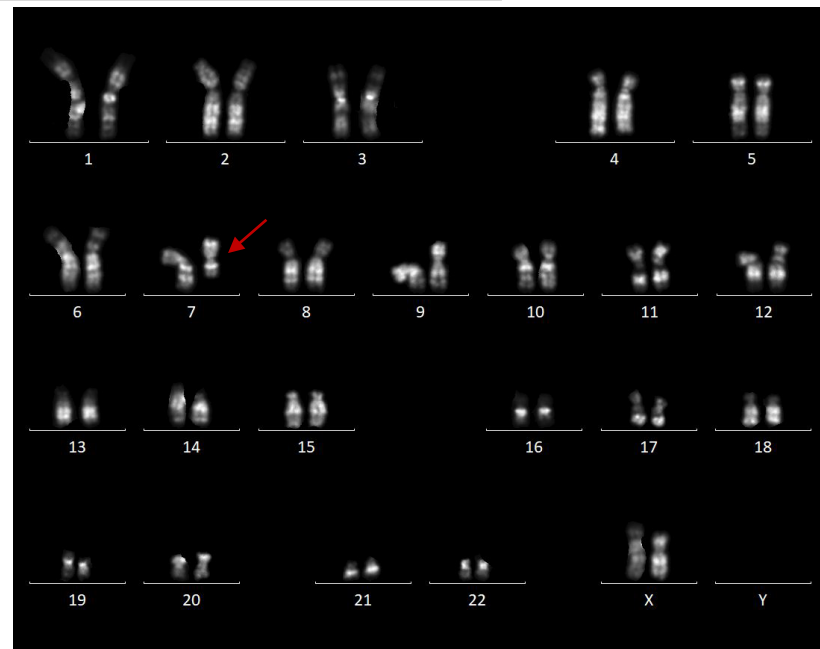
Conventional karyotyping of UL cell cultures



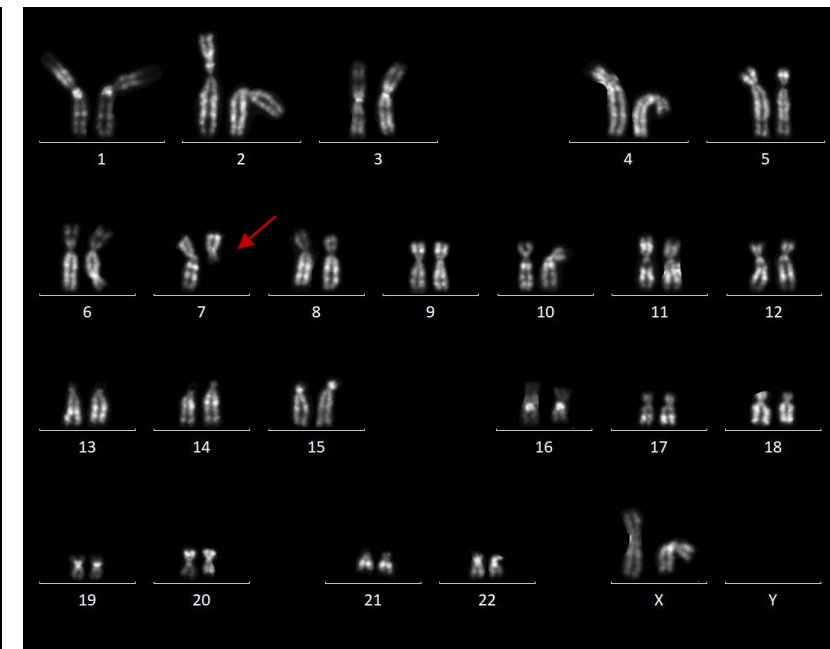
- Most ULs with an abnormal karyotype are mosaics and may have more than one abnormal clone
- Interstitial deletions in 7q (**del7q**) are the most frequent chromosomal abnormalities in our sample



46,XX



46,XX,del(7)(q11.23q31.1)

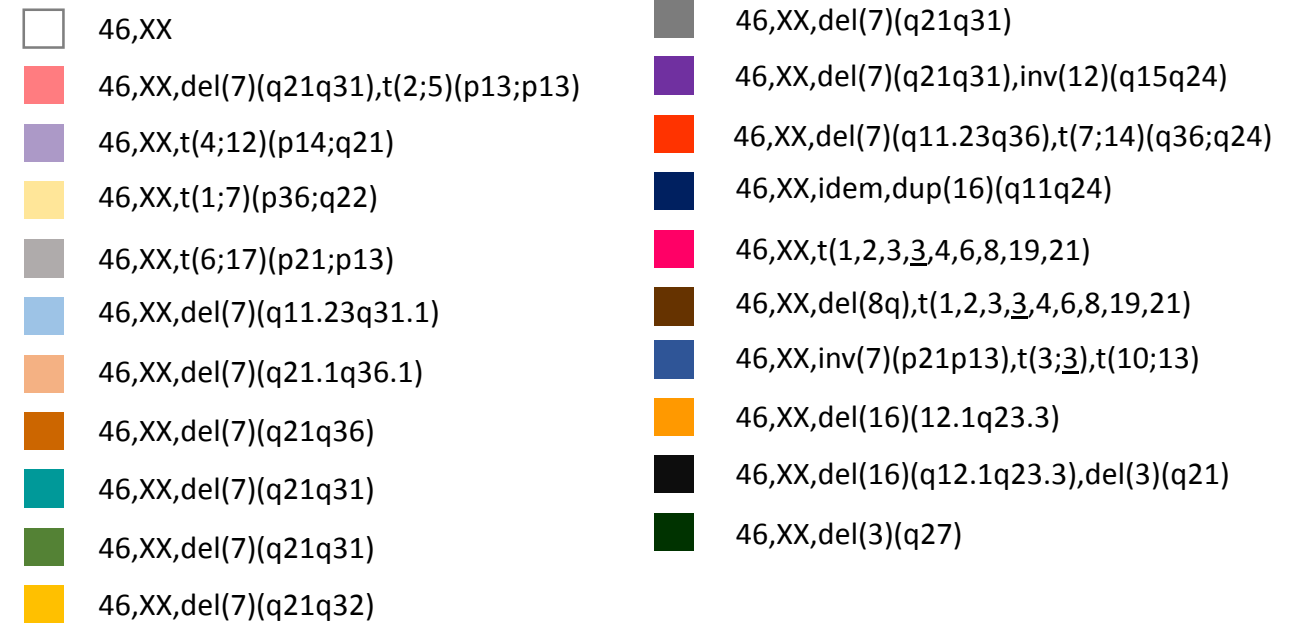


46,XX,del(7)(q21.11q36.1)

Effect of E / P / E+P treatment on clonal spectrum in cultured ULs with an abnormal karyotype

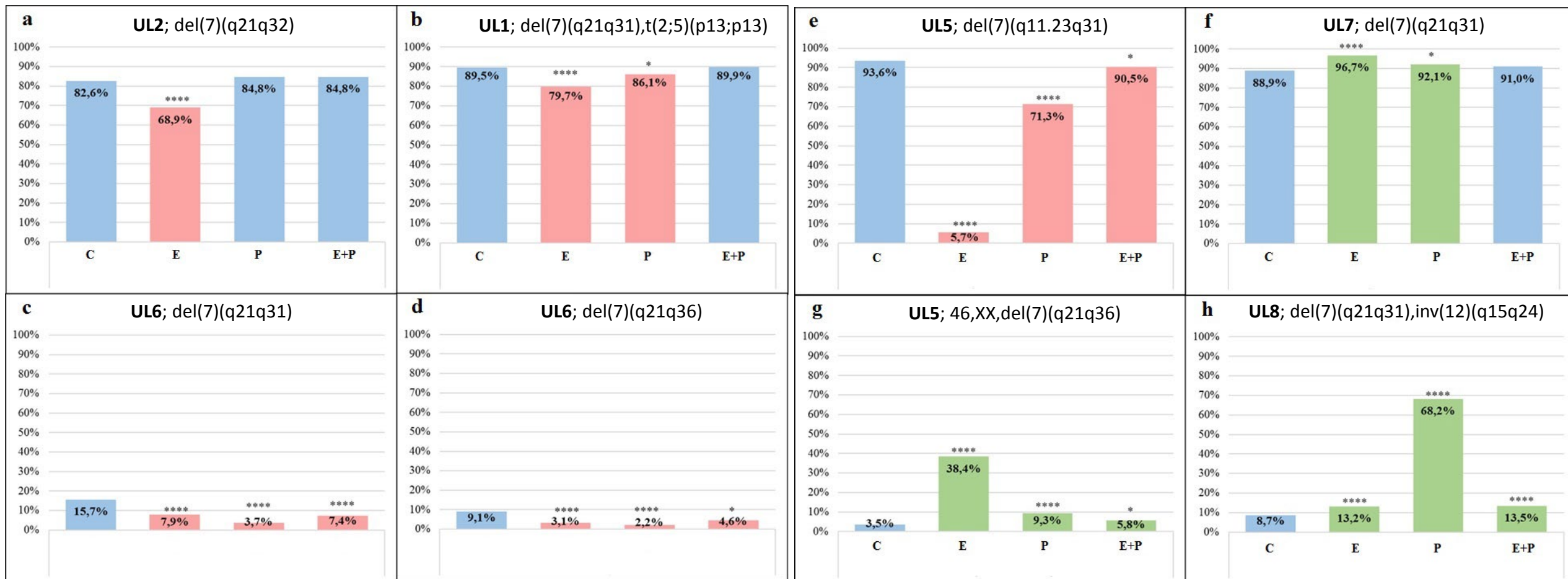
Spectrum of detected clones in ULs with an abnormal karyotype

UL	Control	E	P	E+P
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				



- A total of twenty different chromosomal abnormalities were detected in 11 ULs
- The number of chromosomally different clones in ULs varied from two to five
- In nine of 11 ULs (82%) with abnormal karyotype, the spectrum of clones detected in hormone-treated samples differed from than in the controls
- The widest variety of chromosomal abnormalities was detected in control and as in E+P samples

Effect of E / P / E+P treatment on clonal proportion in cultured ULs with del7q



Among ULs with one del7q clone, two (UL1, UL2) demonstrated significantly decreased frequency of del7q cells (**a**, **b**) after hormone supplementation, while in the rest two ULs (UL7, UL8), del7q clones (**f**, **h**) significantly increased in number. In UL5 with two unrelated del7q, one clone decreased in number while other clone became significantly more numerous after hormone supplementation (**e**, **g**). In contrast, UL6 with two unrelated del7q showed significantly decreased frequency of both clones after hormone supplementation (**c**, **d**). *Statistical analysis: Chi-square with Yates' correction, $p < 0.05$.*

Conclusions

- Estrogen and progesterone treatment causes changes in the spectrum of chromosomal rearrangements detected by conventional karyotyping in 82% of ULs.
- Interstitial deletions in the long arm of chromosome 7 (del7q) are the most frequent chromosomal abnormalities (n=6; 55%).
- Both isolated and combined estrogen and progesterone supplementation have the same effect on the frequencies of each del7q clone in cultured ULs. However, the frequencies of different del7q clones may shift up or down in cultured ULs.
- In most ULs, isolated hormone treatment has more pronounced effect on the frequency of del7q cells than combined one.

! *An important finding in our study is that ULs consist of a variety of cell populations, which differ not only karyotypically, but also by their response to sex steroids*

Related publications:

- Koltsova AS et al. Cytogenomic Profile of Uterine Leiomyoma: In Vivo vs. In Vitro Comparison. *Biomedicines*. 2021;9(12):1777. doi: 10.3390/biomedicines9121777.
- Koltsova AS et al. Uterine Leiomyomas with an Apparently Normal Karyotype Comprise Minor Heteroploid Subpopulations Differently Represented in vivo and in vitro. *Cytogenet Genome Res*. 2021;161(1-2):43-51. doi: 10.1159/000513173.

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