Investigation of the mutagenic properties of the Interferon-Lambda 1, Pegylated by Electron-Beam Method

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The study of mutagenic effect of p-IFN-λ1 by method of acconting of chromosomal aberration.

The first research objective:

- To study the mutagenic effect of pegylated interferon-λ1 (p-IFN-λ1) on the manifestation of cytogenetic disorders in bone marrow cells (hereinafter BMC) during single and course intragastric administration of CBA / CaLac mice by method of accounting of chromosomal aberration

40 mature CBA / CaLac mice
Both sexes
The weight 18-22 g.
The age 2-3 months.

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STAGE 1 ACCOUNTING FOR CHROMOSOMAL ABERRATION IN THE BONE MARROW CELL OF MICE WITH A SINGLE INJECTION OF P-IFN-*λ1*.

1 group ♂ n=5
Phosphate-saline buffer 0 µg/kg Volume 0,5 ml/20 g weight intragastrically , single

2 group ♂ n=5
p-IFN-λ1 500 µg/kg Volume 0,5 ml/20 g weight intragastrically , single

3 group ♂ n=5
p-IFN-λ1 50 µg/kg Volume 0,5 ml/20 g weight intragastrically , single

4 group ♂ n=5
Cyclophosphan 20000 µg/kg Volume 0,2 ml/20 g weight intraperitoneally , single

STAGE 2 ACCOUNTING FOR CHROMOSOMAL ABERRATION IN THE BONE MARROW CELL OF MICE WITH THE COURCE ADMINISTRATION OF P-IFN-*λ1*.

5 group ♂ n=5
Phosphate-saline buffer 0 µg/kg Volume 0,5 ml/20 g weight intragastrically , for 5 days

6 group ♂ n=5
p-IFN-λ1 5 µg/kg Volume 0,5 ml/20 g weight intragastrically , for 5 days

7 group ♀ n=5
Phosphate-saline buffer 0 µg/kg Volume 0,5 ml/20 g weight intragastrically ,for 5 days

8 group ♀ n=5
p-IFN-λ1 5 µg/kg Volume 0,5 ml/20 g weight intragastrically , for 5 days

RESULTS

EFFECT OF P-IFN-Λ1 ON THE CYTOGENETIC INDICES OF CMC OF MALE CBA / CALAC MICE WITH INTRAGASTRIC ADMINISTRATION, X ± M

Experimental conditions, dose x number of administrations (number of animals)	The number of cells studied	The number of aberrations per 100 cells, (%)		Number of chromosomes with aberrations, (CA, %)	The number of cells with ultiple chromosome damages,(CD,%)	The number of cells with gaps in the chromosomes(AS,%)	Number of damaged cells, (%)
		Single and paired fragments (SF, PF)	Chromatid and chromosomal exchanges, (CE)				
1 group Control (negative), Solvent w / x 1 (5)	500	1,00±0,45	0,00±0,00	1,80±0,37	0,00±0,00	0,80±0,58	1,80±0,37
2 group p-IFN-λ1 500 mcg / kg, w / x 1 (5)	500	0,80±0,37**	0,00±0,00**	1,60±0,51**	0,00±0,00**	0,80±0,37	1,60±0,51**
3 group p-IFN-λ1 50 mcg / kg w / x 1 (5)	500	1,20±0,37**	0,00±0,00**	1,40±0,40**	0,00±0,00**	0,20±0,20**	1,20±0,37**
4 group CF (positive control) 20 mg / kg w / w x 1 (5)	500	33,00±2,07*	4,80±0,86*	44,00±2,14*	3,20±1,07*	1,40±0,51	24,20±1,50*

Note: * - significance of differences between negative and positive controls;** - significance of differences between experience and positive control; *** - significance of differences between experience and negative control

EFFECT OF P-IFN-Λ1 ON CYTOGENETIC INDICES OF CMC OF CBA / CALAC MICE WITH COURSE INTRAGASTRIC ADMINISTRATION, X±M

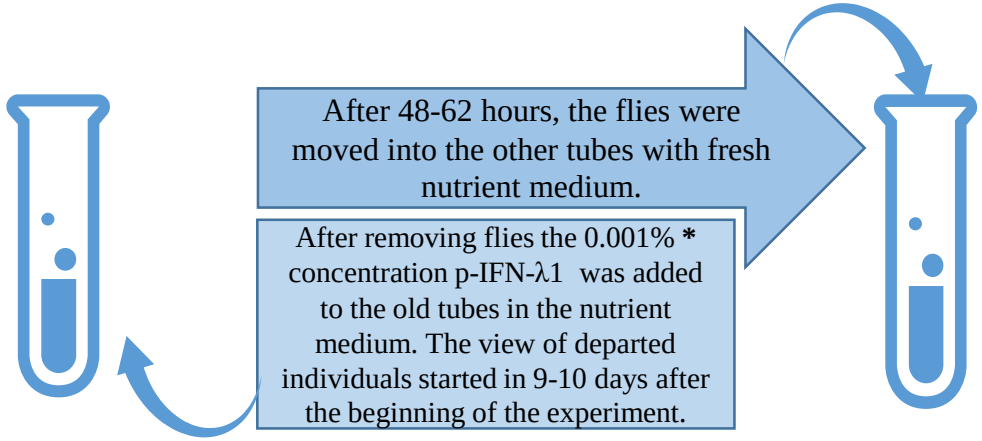
Experimental conditions, dose x number of administrations (number of animals)	The number of cells studied	The number single fragments (SF,%)	The number chromosomes with aberrations, (CA,%)	The number of cells with gaps in the chromosomes, (AS,%)	The number of damaged cells, (%)
5 group Controlsolvent x 5 (5 males)	500	0,80±0,37	1,40±0,24	0,60±0,40	1,20±0,20
6 group p-IFN-λ1, 5 mcg / kg x 5 (5 males)	500	0,80±0,20	0,80±0,20	0,00±0,00	0,80±0,20
7 group Control, solvent x 5 (females-5)	500	1,00±0,32	1,40±0,37	0,40±0,24	1,40±0,24
8 group p-IFN-λ1, 5 mcg / kg x 5 (females 5)	500	0,40±0,24	1,60±0,51	1,20±0,58	1,60±0,51

The study of mutagenic properties of p-IFN-λ1 the somatic mosaicism system

- **The second research objective:**

To study the mutagenic properties of p-IFN- λ1 in the somatic mosaicism test system.

Two drosophila test lines were used:
line 1 - yellow - g / g genotype (y-recessive gene, which causes the development of yellow color of the body and bristles)
line 2 - w, sn^3 - genotype w sn^3 / Y (w– white - white eye color, sn^3 – singed^3 - crimped twisted form of setae; both genes are recessive).



The mutant bristles (phenotype of yellow or singed color) were registered in the heterozygous females of the first generation. The total number of inspected females and separately with single (y, sn^3) and double spots (y sn^3) were counted.
In total, more than 1000 females were viewed in the experiment and control.

ACCOUNTING FOR SOMATIC RECOMBINATION IN DROSOPHILA MELANOGASTER USING YELLOW AND SINGED MARKERS UNDER THE INFLUENCE OF P-IFN-Λ1

Indicators	Control solvent	**0.001% SEG p-IFN- λ1**
The total number of females viewed	1005	**1001**
The number of mutant spots "sn^3"	3	**1**
The number of mutant spots'y'	0	**0**
The number of mutant spots "y sn^3"	0	**0**
Total mutant spots	3	**1**
χ^2	**1,006**	-

* The female survival rate was more than 50% with a 0.001% concentration compared the control group. It was suggested that p-IFN-λ1 was not toxic, so the 0.001% concentration was proposed to the experiment.

CONCLUSION

- According to the results of the studies, it was found that a single intragastric administration of p-IFN-λ1 at a dose of 500 μg / kg and 50 μg / kg, as well as its course administration (at a dose of 5 μg / kg x 5) does not increase the level of cytogenetic disorders in bone marrow cells of CBA / CaLac mice.

- An increasing of the number of mutant tests and spots on the body and head of *Drosophila melanogaster* was not detected in the somatic recombination test system used yellow and singed markers.