

<https://doi.org/10.7124/bc.000B47>

**A.O. Velbovets, M.V. Tomiak, R.V. Gulkovskyi,
A.M. Bezverkhiy, H.S. Demydova, N.S. Melnichuk,
T.I. Yakovenko, M.A. Tukalo, Z.Yu. Tkachuk**

Institute of Molecular Biology and Genetics, NAS of Ukraine
150, Akademika Zabolotnoho Str., Kyiv, Ukraine, 03143
anton.velbovets@gmail.com

DRUG-INDUCED POSTPARTUM EPIGENETIC REMODELING OF DNA METHYLATION IN FEMALE MICE FOLLOWING PREGNANCY AND WEANING

Background. Pregnancy, parturition, and weaning represent a period of profound physiological and psychological stress in female mammals, accompanied by epigenetic remodeling quantifiable using stress-adapted DNA methylation clocks. As nucleoside analogues directly interact with DNA methyltransferases, we hypothesized that an oligoribonucleotide-D-mannitol complex (ORN-M) drug, also known as “NucleX” could modulate DNA methylation at stress-associated loci, and aimed to evaluate this effect in postpartum female mice subjected to pregnancy, parturition, and offspring weaning. **Methods.** ORN-M was administered orally until parturition (50 days on avg.). Blood samples from 12 female mice (10 months old; control $n = 6$, ORN-M-treated $n = 6$) were collected on day 7 after parturition and weaning, and genomic DNA was analyzed using a custom Ion AmpliSeq methylation panel (Ion S5 Plus) covering 75 CpG sites of a murine stress-associated epigenetic clock. Methylation levels were compared between groups using the two-sided Mann-Whitney U test with Benjamini-Hochberg FDR correction. **Results.** Of the 75 CpG sites included in the stress panel, 34 sites were selected for the following statistical analysis, as they showed sufficiently high read depth among all samples. Among these, ORN-M administration was associated with changes in DNA methylation at 7 CpG sites within 4 amplicons ($p < 0.05$). The most prominent response was observed in the *Hsf4* gene region, where four CpG sites within a single amplicon showed consistent hypomethylation ($p = 0.0087–0.026$). Significant hypomethylation was also detected at a lncRNA locus opposite the *Unc45b* gene ($p = 0.026$) and near the *Wnt10b* promoter ($p = 0.026$), while hypermethylation was observed near the *Wif1* gene ($p = 0.0087$), a known Wnt pathway antagonist. None survived FDR correction ($\min q \approx 0.12$), consistent with limited power at $n = 6$ per group; raw p -values should be interpreted as exploratory. **Conclusions.** ORN-M induced DNA methylation changes at stress-associated CpG loci in postpartum female mice, most consistently hypomethylation across the *Hsf4* locus, which is known as a regulator of heat-shock response and cellular stress adaptation. Opposing methylation changes at *Wnt10b*- and *Wif1*-associated loci may suggest epigenetic modulation of a Wnt pathway feedback loop, though this remains hypothetical. These preliminary results support ORN-M as a candidate epigenetic modulator in the context of reproductive stress.

Keywords: DNA methylation, Wnt signaling, Reproductive stress, epigenetic modulator.

Received: 06.07.2026; Accepted: 08.09.2026; Published: 29.09.2026

Citation: Velbovets A.O., Tomiak M.V., Gulkovskyi R.V., Bezverkhiy A.M., Demydova H.S., Melnichuk N.S., Yakovenko T.I., Tukalo M.A., Tkachuk Z.Yu. (2026) Drug-induced postpartum epigenetic remodeling of DNA methylation in female mice following pregnancy and weaning. *Biopolymers & Cell*, Special issue(42), 14. <https://doi.org/10.7124/bc.000B47>

© Publisher PH "Akademperiodyka" of the NAS of Ukraine, 2026. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited