

Diagnostic histone modification  
analysis of preimplantation embryos for  
animal production

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In order to develop the diagnostic methods of embryonic epigenetic markers for animal production, we modified the genome-wide histone modification analysis of individual preimplantation embryos by taking advantage of the Well-of-the-Well (WOW) system, which was named WOW-CUT&Tag (WOW-CAT). WOW-CAT enables the processing of multiple embryos in a shorter time with less reagent and cell loss, facilitating histone modification profiling from not only a single blastocyst but also from a portion of it. Consequently, WOW-CAT allowed simultaneous analyses of two different histone modifications (H3K4me3 and H3K27ac) within the same embryo using two halves of single blastocysts. Furthermore, trophectoderm (TE) cells were biopsied and subjected to WOW-CAT in anticipation of preimplantation diagnosis of histone modifications. WOW-CAT for TE biopsies allowed the monitoring of epigenetic modifications in the main body of the embryo. For example, analysis of H3K4me3 modifications of XIST and DDX3Y in TE biopsies could be used to sex embryos in combination with quantitative PCR, but without the need for deep sequencing. By comparing the blastocysts produced by in vivo and in vitro conditions, we have identified several genes with a significant difference of H3K4me3 modifications to be candidates for quality-indicating markers in the bovine model. These markers in combination with sexing markers were diagnosed in TE parts and the remaining parts were subjected to embryo transfer. Two pregnancies are currently obtained. These results suggest the applicability of WOW-CAT for flexible epigenetic analysis of individual embryos in preimplantation epigenetic diagnosis, which can be applied for animal production.