

## **In vitro embryo production and genomic selection harnessing Danish elite cattle breeding (EliteOva)**

Emma Lorenzen<sup>1</sup>, Søren E Madsen<sup>2</sup>, Elisabeth Ravnevand<sup>2</sup>, Lotte Strøbech<sup>4,3</sup>, Nadia Hashem<sup>3</sup>, Jan Secher<sup>4</sup>, Jan Lassen<sup>5,6</sup>, Søren Borchersen<sup>5</sup>, Mogens S Lund<sup>6</sup>, Haja N. Kadarmideen<sup>7</sup>, Jørgen S Agerholm<sup>4</sup>, Peter Sandøe<sup>8</sup> and Poul Hyttel<sup>1</sup>

*<sup>1</sup>Department of Veterinary and Animal Sciences, University of Copenhagen, <sup>2</sup>TransEmbryo Genetics, Tirsvad, <sup>3</sup>EmbryoTrans Biotech, Lynæs, <sup>4</sup>Department of Veterinary Clinical Sciences, University of Copenhagen, <sup>5</sup>Viking Genetics, Randers, <sup>6</sup>Aarhus University, <sup>7</sup>DTU Compute, Danish Technical University and <sup>8</sup>Department of Food and Resource Economics, University of Copenhagen*

**Background and scope of EliteOva:** Breeding can significantly improve feed-conversion efficiency and resilience and lower methane-emission in cattle. Since the beginning of 2000, genomics has made it possible to accelerate the rates of genetic gain in domestic cattle by genomic selection of calves. The association between phenotypic traits and genomic markers are getting more and more reliable and includes increasing focus on resilience and feed-efficiency. Denmark is one of the leading countries with regards to correlation of phenotypes for production and health to genomic markers in the form of single nucleotide polymorphisms (SNPs) using the Illumina BeadChip. Likewise, Denmark is the leading country in registration of methane-emissions in dairy cows with the prospect of identifying genomic markers for low emission. EliteOva will develop and implement technologies for in vitro production (IVP) and genomic selection of elite embryos in Danish Holstein cattle to secure a competitive Danish milk production. Top quality eggs (oocytes) are collected by ultrasound-guided ovum pick-up (OPU) and embryos generated by IVP using refined media derived from EmbryoTrans Biotech (distributed by IVF Bioscience). Biopsies from the embryos will be genotyped for estimation of breeding values including disease-resistance and resilience as well as novel traits as feed-efficiency and methane-emission. The embryos will be transferred to recipients for production of at least 100 calves. IVP has historically been associated with abnormal epigenetic fetal programming resulting the large offspring syndrome (LOS). Hence, the quality of embryos and calves will be studied meticulously for epigenetic (DNA-methylation and histone-modifications) and transcriptomic aberrations and phenotypic characteristics in order to verify their normality. Bioinformatics and systems biology analyses will be imposed to analyze the potential impact of IVP. EliteOva will run for four years (2018-2021) and aims to deliver successful implementation of methods for IVP and genetic selection of embryos in Danish dairy breeding. As part of the project attitudes to the technology will be measured among Danish dairy-farmers and members of the general public as a basis for assessing the society readiness level.

**Present results:** Over the first three quarter of a year, 20 OPU sessions have been performed yielding a total of 173 oocytes. The OPU-sessions were performed at TransEmbryo Genetics, Tirsvad, and the oocytes were submitted to in vitro maturation in portable incubators while transported to University of Copenhagen, where in vitro fertilization was performed. The resulting embryos were cultured to the blastocyst stage, and the 173 oocytes resulted in 63 blastocysts (36%; 30, 20 and 13 of quality A, B and C, respectively). The blastocysts were transported back to Tirsvad for transfer into recipients or cryopreservation. A total of 43 blastocysts (17, 17 and 5 of quality A, B and C, respectively, and 4 cryopreserved) have been transferred to recipients resulting in 20 pregnancies (47%; 19 from fresh transfers and one from a cryopreserved blastocyst). On September 9, 2018, the first calf was born and appeared healthy. At present, EliteOva is in the process of implementing the process of taking biopsies from the blastocysts for SNP-Chip analyses of the breeding value of the embryos according to total Nordic merit, but also including SNP selection for feed-efficiency and methane-emission.

EliteOva is supported by Innovation Fund Denmark.