Investigating Centromere Dynamics in Bovine Early Development

Federica Modafferi[1]; Laura Thompson[2]; Patrick Lonergan[2]; Elaine M. Dunleavy[1]

1. Centre for Chromosome Biology, University of Galway, Galway, Ireland.
2. School of Agriculture and Food Science, University College Dublin, Belfield, Dublin, Ireland.

Centromeres are chomosomal loci essential for correct chromosome segregation during cell division. Defects in their function can lead to aneuploidy and cancer. Centromeres are epigenetically defined by the presence of a histone variant called Centromere Protein A (CENP-A), which directly replaces histone H3 in the octamer core of centromeric nucleosomes.

Previous studies have highlighted the importance of the transgenerational inheritance of paternal CENP-A: in the fruit fly *(Drosophila melanogaster*), fertilisation of eggs with sperm depleted of CENP-A results in the missegregation of the paternal chromosomes and abnormal embryogenesis. In mice, studies indicate that paternal CENP-A is inherited and maintained in the male pronucleus until at least the 2-cell stage. However, the impact of centromere proteins and function on the fidelity of the first cell cycle in mammals has not yet been investigated.

Bovine *in vitro fertillisation* (IVF) studies have shown that a longer cell cycle impacts successful blastocyst formation, with early-cleaving embryos being more likely to develop to the blastocyst stage. Recently, the clustering of the genomes of parental pronuclei has been identified as a critical step in the prevention of aneuploidy during the first cell division in bovine and human embryos, occuring approximately 1.5 hours before nuclear envelope breakdown and chromatin condensation. However, the position and spatial organisation of the centromeres during the first cell cycle remains unknown. Preliminary results from our laboratory using bovine zygotes derived from IVF have shown that at the time of parental genome clustering, centromeres are positioned away from the pronuclear interphase where the centrosomes are located. This unexpected localisation poses questions about how centromeres become re-arranged during chromatin condensation in this short period of time to allow faithful chromosome segregation during the first mitotic division.

We aim to uncover the topology of centromeres in the developing bovine zygote during key phases of the first cell division cycle. Our long term goal is to study whether perturbing centromere function, or cell cycle progression (in zygotes generated using high or low fertility sperm) affects the fidelity of chromosome segregation in the first mitosis.