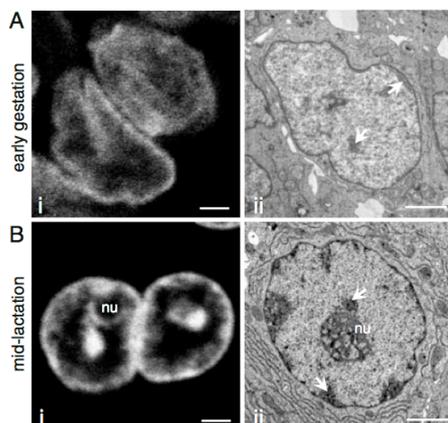


Nuclear organization of mammary epithelial cells

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In many tissues, the features of cell nuclei are specific to their differentiated state, notably in terms of the nature and distribution of nuclear compartments and the position of chromosomes and genes. This spatial organization of the nucleus reveals domains that are differentially permissive for gene expression and may constitute an epigenetic mechanism that is involved in maintaining tissue-specific expression profiles. Current knowledge on the importance of nuclear organization is mainly based on studies of immortalized cell lines or cells from erythroid or lymphoma lineages. In an attempt to unravel the structure-function crosstalk that occurs within the nucleus of eukaryotic cells in their natural environment, we work on mammary epithelial cells (MEC) which interactions with surrounding tissue are critical for correct differentiation and function [1]. During lactation, they express milk protein genes (*WAP*, *CSN*) at high levels in response to hormonal stimulations that induce activation and recruitment of transcription factors and chromatin modifications. Using the HC11 mammary cell line, we showed that milk protein genes are subject to repositioning relative to the nuclear periphery and to their respective chromosome territories when activated, in agreement with a role of nuclear architecture in gene regulation, but that they behave differently depending on their chromosomal context [2]. However, global nuclear organization and gene position proved to be different in intact mammary tissue, suggesting that cultured cell lines are not fully satisfactory models. We now focus on mammary gland development in order to describe how gene positioning evolves together with the remodelling of nuclear architecture that occurs during differentiation [3].



Changes to the nuclear morphology and heterochromatin distribution during luminal-MEC differentiation. Nuclei of rabbit luminal-MECs were observed in tissue sections at early gestation (day 3) and mid-lactation (day 15). (i) Confocal microscopy images after the staining of DNA with TO-PRO-3. (ii) Electron microscopy of ultrathin sections. Arrows indicate heterochromatin, nu: nucleolus. Scale bar: 2 μm.

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