ABSTRACT FOR THE PUBLIC

Every organism’s cell has the same genes though each cell type has a different shape, function, and role. The different architectural organization of the genes, assembled in chromatin by histone proteins, drives which genes work to ensure the organism's cell diversity. Therefore, every organism's cell type has the same genome, and each cell type has a different epigenome, intended as chromatin modifications that mirror different cell shapes, functions, and roles. How the development triggers a stable epigenetic status in each cell type remains elusive, although the histone modifications that contribute to remodeling chromatin and gene expression are widely known. Acetyl-CoA, an essential intermediate of cellular energy metabolism, is donor of acetyls to impose the histone modification in the genome. It was reported that acetyl-CoA derived from lipid metabolism is a major source of carbon for histone acetylation in hepatocytes. This makes an interesting link between the metabolite state of a cell and the chromatin architecture, guiding the change of active and inactive genes as a cellular adaptation mechanism. The cellular metabolism of the zygote, the organism's first cell, evolves dynamically during the embryo's development, producing energy and metabolites to establish chromatin modifications. The impact of lipid and fatty acid metabolisms on preimplantation development remains elusive although it is known that the mammalian oocytes and early embryos contain high amount lipid droplets. The project proposes early mouse embryo development as the ideal biological window to evaluate the impact of lipid metabolism on histone acetylation and cell fate determination. We hypothesize that the manipulation of fatty acids metabolism and Acetyl-coA pathways in preimplantation embryos will results in measurable epigenetic changes, such as histone acetylation, and profound developmental Furthermore, we propose to explore the consequence of lipid metabolism manipulation of early embryos on post-implantation development after embryo transfer. The project will leverage the more advanced biotechnologies to interrogate the link between metabolism and epigenetic programming in early-stage embryos. Mouse embryos will be the object of studies for revealing universal molecular mechanisms and propose novel molecular targets of therapeutic action in human reproduction diseases, principally for infertility linked to metabolic disease. Furthermore, a great interest in the molecular mechanisms underlying the crosstalk between metabolism and epigenetics is growing in cancer biology and immunology. Unexpected applications could result from this proposal research by revealing novel molecular targets.