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Attempt to generate liver organoids from rabbit iPSCs

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The liver is a major and multifunctional organ responsible for the regulating of a multitude of complex metabolic processes. Despite the huge regenerative capacity of this organ, in humans, liver diseases are a major global health problem. The rabbit is often used as a model for non-alcoholic fatty liver disease or liver cancers, thanks to the similarities of its hepatic physiology and anatomy with those of humans. Nevertheless, the liver is a delicate organ in rabbit as well, due to its sensitivity to endogenous and exogenous toxins and to parasites responsible for coccidiosis and toxoplasmosis. The structure of the liver is composed of 80% of hepatocytes organized in lobules around blood vessels and bile capillaries composed of cholangiocytes. Hepatic organoids have been mainly produced in humans from healthy and diseased liver biopsies or from induced pluripotent stem cells. Different protocols are therefore available creating organoids of various complexity and function. However, very few examples are published in agronomic species. Our project aims at producing hepatic organoids from rabbit induced pluripotent stem cells, using a protocol that mimics the embryonic development of the liver by following five phases: formation of embryoid bodies, induction of definitive endoderm, differentiation of hepatoblasts, maturation of hepatocytes and maintenance of hepatocytes. Although this type of protocol has shown efficiency in humans, each step must be adapted to rabbit cells. Here we will present preliminary data that validate the first three steps towards generating liver organoids in rabbits.