dissociation of liver biopsies or explant tissues, for example by plating small (e.g. sub-millimetre) sections of tissue in the culture conditions described herein, with or without the addition of factors such as HGF and forskolin. Alternatively, liver tissue, gallbladder and bile duct explants may be dissociated to single primary cells or small clumps using a combination of mechanical dissociation (scrapping/ dicing) and enzymatic digestion using a matrix digesting enzyme, such as liberase, collagenase, or hyalouronidase. Single primary cells may be subsequently be labelled with antibodies for biliary markers, such as EPCAM and isolated with immune isolation methods, such as Magnetic or Fluorescent associated Cell Sorting (MACS or FACS).

Isolated single cells may be plated using the 3D culture conditions described herein or processed for single cell RNA sequencing. The data herein shows that the 3D culture conditions described herein selectively expand cholangiocyte organoids. Other liver cell types, such as hepatocytes, are not propagated in these conditions. This may be shown for example, by the downregulation of hepatic markers (Figure 2B).

The primary bile tissue may be derived from heathy individuals or from patients with known pathology to enable disease modelling.

Cholangiocytes derived from an individual with a biliary disorder may be used to generate expanded populations which display a genotype or phenotype associated with a biliary disorder. A method of producing cholangiocytes with a biliary disorder-associated genotype or phenotype may comprise;

providing a population of primary cholangiocytes from an individual with a biliary disorder,

expanding the primary cholangiocytes as described herein,

thereby producing a population of cholangiocytes with a biliary disorder-associated genotype or phenotype.

An expanded population with a biliary disorder-associated phenotype may display one or more features of the biliary disorder. In some embodiments, the one or more features of the biliary disorder may be displayed in response specific conditions or treatments. For example, the cholangiocytes may be co-cultured with one or more other cell types to elicit a biliary disorder-associated phenotype. For example, the cholangiocytes may be co-cultured with immune cells, such as T-cells, to elicit a phenotype associated with an autoimmune biliary disorder, such as Primary Biliary Cirrhosis (PBC).

Once produced, cholangiocytes with the biliary disorder-associated phenotype may be cultured,